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Die Nutzung von GKV-Daten und ihre Verknüpfung mit Befragungsdaten zur Beantwortung epidemiologischer, versorgungsbezogener und methodischer Fragestellungen

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Zusammenfassung

Die Nutzung von Sekundärdaten ist neben der Erhebung von Primärdaten ein bedeutender Bestandteil der gesundheitswissenschaftlichen Forschung. Zudem hat die Planung und Durchführung von Studien, die Daten aus verschiedenen Datenquellen miteinander verknüpfen (Datenlinkage), in den vergangenen Jahren zugenommen. Dabei ist hervorzuheben, dass die Arbeit mit Sekundärdaten eine besondere Herausforderung darstellt und spezifisches Wissen beispielsweise zur zugrundeliegenden Datenstruktur und zu den enthaltenen Dateninhalten erfordert, da die Daten für die Analyse und Beantwortung der zu untersuchenden Fragestellungen zugänglich gemacht und aufbereitet werden müssen. Auch die Handhabung von Studien mit Datenlinkage setzt gezieltes Wissen voraus. Aus diesem Grund wurden von führenden ExpertInnen – unter aktiver Mitwirkung der Autorin der vorliegenden Habilitationsschrift – im Jahr 2019 Standards für die Durchführung von Forschungsvorhaben in der Gesundheits- und Sozialforschung publiziert, die auf einem Datenlinkage personenbezogener Daten nach wissenschaftlichen Grundsätzen basieren.

Die Auseinandersetzung mit den Möglichkeiten sowohl zur Nutzung von Daten der gesetzlichen Krankenversicherung (GKV-Daten), die originär für Abrechnungszwecke erhoben werden, als auch ihrer Verknüpfung mit Befragungsdaten zur Beantwortung von epidemiologischen, versorgungsbezogenen oder methodischen Fragestellungen ist das übergeordnete Ziel der vorliegenden Habilitationsschrift. Die Habilitationsschrift soll einen Einblick in die am Institut für Versorgungsforschung und Gesundheitsökonomie durch mich und weitere wissenschaftliche MitarbeiterInnen durchgeführten Projekte mit Sekundärdaten oder Datenlinkage geben und die im Rahmen dieser Projekte untersuchten Forschungslücken darstellen und schließen. Dabei wird deutlich, welche Limitationen und Stärken GKV-Daten und das Datenlinkage aufweisen.

Die für die Habilitationsschrift ausgewählten Arbeiten kommen aus verschiedenen Themenbereichen. Drei primär inhaltlich ausgerichtete Arbeiten befassen sich im Rahmen der *Alterstraumatologischen Versorgungsforschung* mit der Epidemiologie und Versorgung von Beckenfrakturen. Zwei weitere Arbeiten, die aus einer Studie zur Rolle der Depression als *psychische Komorbidität des Diabetes* stammen, setzen durch die Durchführung einer Non-Responderanalyse auf Basis von GKV-Daten und einer durch Datenlinkage realisierten Erfassung und Gegenüberstellung von Prävalenzen der depressiven Störung, die mittels GKV-Daten und anhand zwei weiterer Instrumente bestimmt wurden, sowie einer Charakterisierung der identifizierten Gruppen einen methodischen Schwerpunkt.

Die erste dieser Habilitationsschrift zugrundeliegende Arbeit beschäftigt sich mit der Schätzung der Inzidenz von Beckenfrakturen in der deutschen Bevölkerung im Alter von 60 Jahren oder älter. Dazu wurde eine retrospektive bevölkerungsbezogene Beobachtungsstudie auf Basis von ambulanten und stationären GKV-Daten durchgeführt, auf deren Basis stratifiziert alters- und geschlechtsspezifische Inzidenzraten von Erstfrakturen im Studienzeitraum von 2008 bis 2011 berechnet wurden. Die beobachteten Inzidenzen waren deutlich höher als in der internationalen Literatur beschrieben, auch wenn nur stationär behandelte Beckenfrakturen betrachtet wurden. Die Studie zeigte, dass bei Nichteinbeziehung ambulanter Daten ein relevanter Anteil der Beckenfrakturen nicht berücksichtigt und die Inzidenz von Beckenfrakturen unterschätzt wird (Andrich et al. 2015).

Ziel der zweiten Arbeit war es, die Übersterblichkeit bei Personen im Alter von 60 Jahren oder älter bis zu einem Jahr nach einer Beckenfraktur im Vergleich zu einer Population ohne Beckenfraktur zu analysieren. Beschrieben wurden auf Basis von GKV-Daten sowohl Überlebenswahrscheinlichkeiten als auch in Regressionsmodellen berechnete Effektmaße für Übersterblichkeit im Studienzeitraum von 2008 bis 2011. Die Darstellungen erfolgten stratifiziert für stationär/ambulant behandelte Personen mit Beckenfraktur und Personen mit sogenannten minor/major – d.h. leichte und schwere – Beckenfrakturen (jeweils im Vergleich zu Kontrollen ohne Beckenfraktur). Es ließ sich eine deutliche Übersterblichkeit bei älteren Menschen in den ersten acht Monaten nach einer Beckenfraktur beobachten, selbst nach vollständiger Adjustierung für relevante Drittvariablen wie Pflegestufe oder Komorbidität. Die Übersterblichkeit war bei Männern zu Beginn höher, ebenso bei stationär behandelten Personen. Bei ambulant behandelten Personen wurde innerhalb der ersten drei Monate keine Übersterblichkeit festgestellt. Aufgeschlüsselt nach Schweregrad war die Übersterblichkeit für die meisten als leicht eingestuften Beckenfrakturen – mit Ausnahme der Schambeinfraktur – nicht mehr signifikant. Bislang sind nur wenige Studien verfügbar, die die Übersterblichkeit nach Beckenfraktur mittels stationärer und ambulanter Daten beschreiben. Die Arbeit hat den Kenntnisstand zur Übersterblichkeit nach Beckenfrakturen aufgrund ihrer detaillierten Analysen erheblich erweitert und wurde in einem TOP10-Journal publiziert (Andrich et al. 2017).

Im Rahmen der dritten Arbeit, die auf der gleichen Versichertenpopulation basiert wie die zuvor beschriebenen Analysen zur Mortalität, wurden GKV-Daten zur Beschreibung der medizinischen Leistungsinanspruchnahme und der Kosten für die ambulante und stationäre Behandlung, Arzneimittel und Sonstiges (u.a. Rehabilitation) im Jahr nach Beckenfraktur im Vergleich zu einer Population ohne Beckenfraktur herangezogen. Unsere Studie zeigte einen starken Anstieg der Inanspruchnahme der stationären Versorgung und deutliche Mehrkosten bei älteren Menschen im ersten Jahr nach einer Beckenfraktur im Vergleich zu einer Population ohne Beckenfraktur – letzteres sogar nach Adjustierung von relevanten Drittvariablen. Die Mehrkosten waren in den ersten Monaten besonders hoch und hauptsächlich auf die stationäre Behandlung zurückzuführen. Subgruppenanalysen, in denen nach Schweregrad stratifiziert wurde, ergaben, dass Mehrkosten auch für Personen mit leichten Beckenfrakturen anfielen (Andrich et al. 2021).

Die vierte Arbeit kann als Beispiel für die Durchführung einer Non-Responderanalyse auf Basis von Sekundärdaten dienen. Dabei wurden GKV-Daten zur Auswertung von Nicht-Teilnahme (Non-Response) in einer Querschnitts-Befragungsstudie zu Depression bei Menschen mit Diabetes verwendet. Im Gegensatz zu Non-Responderanalysen im Rahmen von populationsbasierten Primärdatenstudien, in denen zur Erfassung der wichtigsten Charakteristika der Nicht-Teilnehmenden nach Möglichkeit ein Kurzfragebogen zum Einsatz kommt, lagen aus GKV-Daten umfangreiche soziodemografische und gesundheitsbezogene Angaben sowohl für die Teilnehmenden als auch für die Nicht-Teilnehmenden vor, um die Repräsentativität der Teilnehmenden zu analysieren. Die Analysen verdeutlichten Unterschiede in Bezug auf Alter, Geschlecht, Diabetesbehandlung und Medikamenteneinnahme zwischen Teilnehmenden und Nicht-Teilnehmenden, die die Ergebnisse der Studie verfälschen könnten. Allerdings unterschieden sich Teilnehmende und

Nicht-Teilnehmende nicht in ihrem Depressionsstatus, dem Hauptoutcome der Studie (Linnenkamp et al. 2020).

Die fünfte für die Habilitationsschrift berücksichtigte Arbeit thematisiert die Erfassung einer depressiven Störung mithilfe von verschiedenen Methoden bei Menschen mit Diabetes sowie die Charakterisierung der identifizierten Populationen. Bei der zugrundeliegenden Studienpopulation handelt es sich wie bei der vierten Arbeit um GKV-Versicherte mit Diabetes, für die im Jahr 2013 im Querschnitt Befragungsdaten erhoben und mit longitudinalen GKV-Daten verknüpft wurden, die für den Zeitraum von vier Quartalen vor und nach dem Quartal der Primärdatenerhebung vorlagen. Drei Methoden wurden zur Identifizierung einer depressiven Störung eingesetzt: die Allgemeine Depressionsskala des Centre for Epidemiological Studies (CES-D), der Patient Health Questionnaire-9 (PHQ-9) und das Heranziehen spezifischer Depressionsdiagnosen aus GKV-Daten. Dabei sollten insbesondere Überschneidungen und Unterschiede in den identifizierten Personengruppen (insgesamt 8 Gruppen, von Gruppe 1 - mit allen Methoden identifiziert bis Gruppe 8 - mit keiner der Methoden identifiziert) sowie mögliche Zusammenhänge zwischen individuellen und klinischen Merkmalen und der eingesetzten Methode beschrieben werden. Es ließ sich konstatieren, dass die verschiedenen Methoden nicht dieselben Personen mit depressiver Störung identifizierten. Obwohl die Überschneidungen gering und Zusammenhänge mit individuellen und klinischen Merkmalen sichtbar waren, konnte letztlich kein klares Muster zwischen den Charakteristika der identifizierten Personen und den verwendeten Instrumenten festgestellt werden. Es gab jedoch Hinweise darauf, dass die Wahl der Methode mit spezifischen zugrundeliegenden Merkmalen in der untersuchten Population einhergeht (Linnenkamp et al. 2023).

Die vorliegende Habilitationsschrift unterstreicht die Bedeutung von Sekundärdaten für die Epidemiologie und für die Versorgungsforschung. Durch die Bandbreite der in den vorgestellten Arbeiten adressierten Forschungsfragen und die eingängige Schilderung ihrer methodischen Umsetzung erweitert sie den bisherigen Wissens- wie auch methodischen Kenntnisstand. Die Habilitationsschrift trägt zu einem tiefergehenden Verständnis bei, wie insbesondere GKV-Daten und ihre Verknüpfung genutzt werden können, um epidemiologische, versorgungsbezogene und methodische Fragestellungen zu beantworten.

Übersicht der beitragenden Originalarbeiten

Andrich, S.; Haastert, B.; Neuhaus, E.; Neidert, K.; Arend, W.; Ohmann, C.; Grebe, J.; Vogt, A.; Jungbluth, P.; Rösler, G.; Windolf, J.; Icks, A. (2015). Epidemiology of Pelvic Fractures in Germany: Considerably High Incidence Rates among Older People. *PLoS One* 10 (9):e0139078. https://doi.org/10.1371/journal.pone.0139078

IF: 3.057 (TOP 25 in der Kategorie *Multidisciplinary Sciences* der *Science Citation Index Expanded*-Datenbank (SCIE))

Andrich, S.; Haastert, B.; Neuhaus, E.; Neidert, K.; Arend, W.; Ohmann, C.; Grebe, J.; Vogt, A.; Jungbluth, P.; Thelen, S.; Windolf, J.; Icks, A. (2017). Excess Mortality After Pelvic Fractures Among Older People. *J Bone Miner Res* 32 (9):1789–1801. https://doi.org/10.1002/jbmr.3116

IF: 6.314 (TOP 10 in der Kategorie *Endocrinology & Metabolism* der *Science Citation Index Expanded*-Datenbank (SCIE))

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IF: 5.071

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IF: 7.196 (TOP 10 in der Kategorie *Public, Environmental & Occupational Health* der *Science Citation Index Expanded*-Datenbank (SCIE))

Linnenkamp, U.; Gontscharuk, V.; Ogurtsova, K.; Brüne, M.; Chernyak, N.; Kvitkina, T.; Arend, W.; Schmitz-Losem, I.; Kruse, J.; Hermanns, N.; Kulzer, B.; Evers, S. M. A. A.; Hiligsmann, M.; Hoffmann, B.; Icks, A.; **Andrich, S.** (2023). PHQ-9, CES-D, health insurance data-who is identified with depression? A Population-based study in persons with diabetes. *Diabetol Metab Syndr* 15 (1):54. https://doi.org/10.1186/s13098-023-01028-7 geteilte Letztautorenschaft

IF: 4.8

1. Einleitung

1.1. Einführung in das Thema der Habilitationsschrift

Die Nutzung von Sekundärdaten ist neben der Erhebung von Primärdaten ein bedeutender Bestandteil der gesundheitswissenschaftlichen Forschung. Zudem hat die Planung und Durchführung von Studien, die Daten aus verschiedenen Datenquellen miteinander verknüpfen (Datenlinkage), in den vergangenen Jahren zugenommen. Dabei ist hervorzuheben, dass die Arbeit mit Sekundärdaten eine besondere Herausforderung darstellt und spezifisches Wissen beispielsweise zur zugrundeliegenden Datenstruktur und zu den enthaltenen Dateninhalten erfordert, da die Daten für die Analyse und Beantwortung der zu untersuchenden Fragestellungen zugänglich gemacht und aufbereitet werden müssen. Auch die Handhabung von Studien mit Datenlinkage setzt gezieltes Wissen voraus. Die Auseinandersetzung mit den Möglichkeiten sowohl zur Nutzung von Daten der gesetzlichen Krankenversicherung (GKV-Daten), die originär für Abrechnungszwecke erhoben werden, als auch ihre Verknüpfung mit Befragungsdaten zur Beantwortung von epidemiologischen, versorgungsbezogenen oder methodischen Fragestellungen ist das übergeordnete Ziel der vorliegenden Habilitationsschrift. Es handelt sich bei den im Rahmen der Habilitationsschrift vorgestellten Publikationen um konkrete Anwendungsbeispiele, die als Grundlage dienen können ähnliche Fragestellungen zu untersuchen.

Die Habilitationsschrift gliedert sich wie folgt: Zunächst wird in Kapitel 2 zum Hintergrund und Forschungsstand der konzeptionelle Rahmen erörtert, indem die Forschungsgebiete der Epidemiologie und der Versorgungsforschung in ihren Grundlagen skizziert werden. Es wird grundlegend dargelegt, was unter Sekundärdaten und einer Sekundärdatenanalyse zu verstehen ist. Im Fokus stehen die Nutzung von GKV-Daten und das Datenlinkage. In diesem Zusammenhang wird auch auf die obligatorischen datenschutzrechtlichen Aspekte eingegangen. Hinsichtlich der im Rahmen der Habilitationsschrift vorgestellten Originalarbeiten werden der wissenschaftliche Hintergrund, die Relevanz und der bestehende Forschungsbedarf dargestellt, bevor auf die den Originalarbeiten zugrundeliegenden Forschungsfragen und Ziele eingegangen wird. Im Anschluss erfolgen in Kapitel 3 die Vorstellung der Originalarbeiten sowie in Kapitel 4 eine Gesamtdiskussion hinsichtlich der Nutzung von GKV-Daten und ihrer Verknüpfung mit Befragungsdaten zur Beantwortung epidemiologischer, versorgungsbezogener und methodischer Fragestellungen. Dabei wird deutlich, welche Limitationen und Stärken GKV-Daten und das Datenlinkage aufweisen. Die Habilitationsschrift schließt in Kapitel 5 mit einem Fazit und Ausblick.

2. Hintergrund und Forschungsstand

2.1 Epidemiologische Forschung und Versorgungsforschung

Bei den nachfolgenden Ausführungen zu den Forschungsbereichen der Epidemiologie und der Versorgungsforschung handelt es sich um kurze grundlegende Definitionen und allgemeine Darstellungen zum Gegenstand des jeweiligen Forschungsinteresses. Ausführliche Abhandlungen zur tiefergehenden Beschäftigung sind beispielsweise in Lehrbüchern, aber auch Leitlinien/Memoranden von ihren Fachgesellschaften zu finden (Kreienbrock et al. 2012; Fletcher et al. 2019; Pfaff et al. 2017; Pfaff et al. 2009; Glaeske et al. 2009).

Die Epidemiologie wird als eine Wissenschaft verstanden, die sich „mit der Verteilung von Krankheiten, deren Vorstufen und Folgen sowie mit den Faktoren, die diese Verteilung beeinflussen“ (Kreienbrock et al. 2012, S. 1) befasst. Im ersten Vorwort der Leitlinien zur *Guten Epidemiologischen Praxis (GEP)* von 1999, die mittlerweile mehrfach modifiziert und durch Einbezug weiterer Leitlinien (wie die Gute Praxis Sekundärdatenanalyse von Swart et al. 2015) ergänzt wurden, wird ihr Anwendungsbereich folgendermaßen beschrieben: „Gegenstand epidemiologischer Studien ist die Untersuchung der Bedingungen von Gesundheit sowie von Ursachen, Auftreten, Verlauf und Folgen von Erkrankungen in menschlichen Populationen bzw. in definierten Bevölkerungsgruppen.“ (DGEpi 2018, S. 8). Als deskriptive Maßzahlen zur Beschreibung des Auftretens von Krankheiten sind die Prävalenz, die den als Anteil Erkrankter an der Gesamtpopulation wiedergibt, und die kumulative Inzidenz bzw. die Inzidenzrate als Neuerkrankungswahrscheinlichkeit bzw. Neuerkrankungen pro Zeit (Geschwindigkeitsmaß) zu nennen. Maßzahlen wie die (krankheitsbezogene) Mortalität, die den Anteil der Todesfälle in einer Population ausdrückt, und die Letalität, ein Maß, das die Sterblichkeit einer Erkrankung beschreibt, stehen für die tödlichen Folgen des Auftretens einer Erkrankung. Darüber hinaus werden Erklärungen für die Verteilung von Krankheiten/Outcomes in verschiedenen Populationen gesucht. Dazu werden Vergleiche der Erkrankungsrisiken angestellt und in Zusammenhangsanalysen Ursachen oder Risikofaktoren für Erkrankungen/Outcomes untersucht (Kreienbrock et al. 2012).

Die Versorgungforschung gewinnt in Deutschland zunehmend an Bedeutung und wurde in den vergangenen zehn bis 15 Jahren sowohl durch Gesetzgebung, z.B. durch das GKV-Versorgungsstärkungsgesetz als auch durch eigens vorgesehene Fördergelder – insbesondere durch den Innovationsfonds des G-BA – gestärkt (Schrappe und Pfaff 2017; G-BA Innovationsfonds 2023). Dabei haben sich das zugrundeliegende Verständnis und die entsprechend geltenden Definitionen analog zur Entwicklung des Forschungsfelds gewandelt. Zu Beginn lag der Fokus auf dem Umsetzungsdefizit zwischen in klinischen, kontrollierten Studien erzieltem Wissen und nachgewiesener Wirksamkeit (efficacy) und Anwendung dieses Wissens und seiner Wirksamkeit (effectiveness) unter Alltagsbedingungen. Sukzessive wurde er auf die Umsetzung und Evaluation komplexer Interventionen unter komplexen Kontextbedingungen (doppelte Komplexität) gelegt. Dabei ist zu beachten, dass sich der Kontext auf verschiedene Ebenen beziehen kann: die Patientenebene, die professionelle Ebene, die Ebene der Organisation und die Gesundheitssystemebene. Die Versorgungsforschung gilt heute als „ein fachübergreifendes Forschungsgebiet, das ausgehend von der Patienten- sowie Populationsperspektive und vor dem Hintergrund komplexer Kontextbedingungen die Versorgungsstrukturen und -prozesse der Gesundheitsversorgung untersucht, den Outcome auf Ebene der Alltagsversorgung beschreibt

und komplexe Interventionen zur Verbesserung der Versorgung evaluiert.“ (Schrappe und Pfaff 2017, S. 11). Anhand des erweiterten Throughput-Modells, welches das Umsetzungsdefizit systematisieren soll, können die verschiedenen Schwerpunkte und Fragestellungen dargestellt werden. Das Systemmodell unterscheidet in Input-Throughput-Output-Outcome-Dimensionen. Es stellt die Transformation der eingehenden Faktoren (Input-Faktoren 1. Ordnung) – dazu zählen z.B. Versorgungsbedarf, Inanspruchnahme und Ressourcen auf den verschiedenen Ebenen – ergänzt um komplexe Interventionen und aktiven Kontext (Input-Faktoren 2. Ordnung) im Rahmen der Versorgungsprozesse (Throughput) dar, resultierend in Versorgungsleistungen (Output) und folglich in Ergebnissen (Outcomes), die sowohl auf Patienten- als auch Populationsebene zu beobachten sind. In das aktualisierte Modell wurden auch Rückkopplungsmechanismen von den Dimensionen Output und Outcome auf die Dimensionen Input und Throughput integriert, wodurch verdeutlicht werden soll, dass es sich grundlegend um ein lernendes System handelt. Anhand des Modells lassen sich die konkreten Aufgaben der Versorgungsforschung wie folgt zusammenfassen: Versorgung beschreiben, Ursachen/Bedingungen erklären, Konzepte und Interventionen entwickeln, Wirksamkeit und Nutzen unter Alltagsbedingungen evaluieren und Implementation und Umsetzung evaluativ begleiten sowie Probleme benennen. Letztlich kann die Verbesserung der Gesundheitsversorgung durch komplexe Interventionen als eines der zentralen Ziele erachtet werden (Schrappe und Pfaff 2017).

Zur Beantwortung von epidemiologischen und versorgungsbezogenen Fragestellungen können sowohl Primär- als auch Sekundärdaten herangezogen werden. Dabei gilt die möglichst spezifische und operationalisierbare Fragestellung als Ausgangspunkt für das gewählte Studiendesign und die eingesetzten Methoden (DGEpi 2018; Swart et al. 2015; March et al. 2019). Im Hinblick auf die reine Sekundärdatenanalyse und das Datenlinkage ergeben sich aus der Fragestellung notwendige Beurteilungen zur Eignung der Daten bzw. zum Nutzen der Sekundärdatenanalyse und des Datenlinkages allgemein.

2.2 Sekundärdatenanalyse und Datenlinkage

2.2.1 Sekundärdaten

In Abgrenzung zu Primärdaten, die entsprechend ihrer zugrundeliegenden Fragestellung und somit für ihren ursprünglich vorhergesehenen Verwendungszweck erhoben und ausgewertet werden, sind Sekundärdaten Daten, „die einer Auswertung über ihren originären, vorrangigen Verwendungszweck hinaus zugeführt werden. Maßgeblich für die Einstufung als Sekundärdaten sind Unterschiede zwischen dem primären Erhebungsanlass und der nachfolgenden Nutzung“ (Swart et al. 2015, S. 125–126). Gothe et al. heben ebenfalls als zentrales Element hervor, dass es sich um bereits vorliegende Daten handelt, die jedoch Tücken mit sich bringen, da sie aus anderen Kontexten (z.B. aus Abrechnungsprozessen im Rahmen der medizinischen Versorgung) kommen und nicht per se für die Wissenschaft generiert wurden (Gothe et al. 2021). In ihren Leitlinien und Empfehlungen Gute Praxis Sekundärdatenanalyse (GPS) setzen Swart et al. die Sekundärdatenanalyse mit der Begrifflichkeit der „Nutzung von Sekundärdaten“ (Swart et al. 2015, S. 126) gleich und führen erklärend aus: „Die Sekundärdatenanalyse schließt die für die Analyse notwendigen Erhebungs- und Aufbereitungsschritte des Sekundärdatenkörpers ein. Erst durch diese Aufbereitungsschritte sind die Daten für wissenschaftliche Fragestellungen zugänglich“ (Swart et al. 2015, S. 126). Dabei kann die GPS als Ratgeber und zugleich als wissenschaftlicher Standard für die Durchführung der Sekundärdatenanalyse hinzugezogen werden, da sie im Rahmen von elf Leitlinien die verschiedenen zu bedenkenden Schritte der Planung, Durchführung und Analyse adressiert und weiterführende Empfehlungen aufführt. Im Hinblick auf die zugrundeliegenden Eigenschaften der Sekundärdaten kommen im Rahmen der Nutzung insbesondere der Qualitätssicherung mit Durchführung von Plausibilitätsprüfungen (Leitlinie 5), der Datenaufbereitung anhand eines zuvor formulierten Konzepts resultierend in der Anfertigung eines Auswertedatensatzes (Leitlinie 6), der Datenanalyse gemäß eines zuvor erstellten Analyseplans (Leitlinie 7) und der Einhaltung der geltenden Datenschutzvorschriften (Leitlinie 8) eine wesentliche Bedeutung zu. Die GEP trägt den genannten Punkten ebenfalls Rechnung und stellt in der Empfehlung 2.3 darauf ab, dass der Erhebungsanlass der Sekundärdaten ebenso wie die Erfassungsregeln und Auswertungsprozeduren transparent darzustellen und die sich aus den Daten ergebenden Besonderheiten im Hinblick auf die daraus folgenden Limitationen bei der Interpretation der Ergebnisse zu beachten sind (DGEpi 2018). Die Entscheidung für die Durchführung einer Sekundärdatenanalyse scheint häufig durch das Wissen um das Vorliegen von Daten geleitet zu sein, die zur Beantwortung der entsprechenden Forschungsfrage aufbereitet und genutzt werden können. Eine sehr umfassende Übersicht zu grundsätzlich verfügbaren Sekundärdaten (u.a. Darstellung der Datenquellen, gesetzlichen Grundlage der Datenerfassung und -übermittlung, Datenzugänge und Dateninhalte) findet sich im Gutachten von Panteli et al. mit dem Titel *Internationale Datengrundlagen für die Versorgungsforschung – Impulse für Deutschland* (Panteli et al. 2020, s. Tabelle 1.2). Aus der Übersicht ist zu entnehmen, dass neben Daten der GKV auch die Daten anderer Sozialversicherungen, z.B. die Daten der Rentenversicherung (Forschungsdatenzentrum der Rentenversicherung 2023), Daten aus der amtlichen Statistik (Forschungsdatenzentrum Statistische Ämter 2023) oder Daten aus Scientific Use Files des Robert-Koch-Instituts (RKI - Datenangebot 2023) zu in der wissenschaftlichen Forschung nutzbaren Sekundärdaten zählen. Zusammenfassend ist festzuhalten, dass die Arbeit mit Sekundärdaten eine besondere Herausforderung darstellt und spezifisches Wissen

beispielsweise zur zugrundeliegenden Datenstruktur und zu den enthaltenen Dateninhalten erfordert, um die Daten durch die weitere Aufbereitung für entsprechenden Analysen zu nutzen.

2.2.2 Nutzung von GKV-Daten

In Deutschland gibt es derzeit (Stand 01.01.2023) knapp 100 GKVen, bei denen etwa 90 % der Bevölkerung (~73 Millionen Personen) versichert sind (GKV-Spitzenverband 2023). Da GKV-Daten aufgrund ihres Abrechnungscharakters die individuell stattgefundene Versorgung unter Zugrundelegung des spezifischen Behandlungsanlasses personenbezogen dokumentieren, sind sie für die Versorgungsforschung als Datengrundlage zur Beschreibung der Versorgungsrealität von sehr hohem Wert (Swart et al. 2014a; Schubert et al. 2008). Die wissenschaftliche Nutzung von GKV-Daten hat in den 1970er Jahren begonnen (Schäfer 2015) und sich seit der Jahrtausendwende als Bestandteil der Versorgungsforschung weiterentwickelt (Paquet 2015; Hoffmann 2015). Durch den Zusammenschluss der Arbeitsgruppe Erhebung und Nutzung von Sekundärdaten (AGENS) der Deutschen Gesellschaft für Sozialmedizin und Prävention (DGSMP) und der Deutschen Gesellschaft für Epidemiologie (DGEpi) nahmen die strukturierten Forschungsbestrebungen weiter zu (AGENS 2023).

GKV-Daten finden für verschiedene Zwecke Verwendung: So können sie unter Hinzuziehung von Stammdaten der Versicherten sowohl zur Schätzung der Inzidenz von und Mortalität nach Ereignissen bzw. Erkrankungen als auch zur sektorübergreifenden Beschreibung der medizinischen Leistungsinanspruchnahme der Versichertenpopulation und damit einhergehender Kosten herangezogen werden (Schubert et al. 2008; Scholz et al. 2014; Hoffmann und Glaeske 2017). In Stammdaten enthaltene individuelle Angaben sind beispielsweise die eindeutige Versicherungsnummer, das Geschlecht, das Geburtsdatum, der (aktuelle) Wohnort mit Postleitzahl, die Versicherungszeiten, die Versicherungsgruppe und mögliche Austrittsgründe (hier auch Austrittsgrund Tod) der Versicherten (Grobe und Ihle 2014). Stammdaten werden insbesondere für die Definition der Studienpopulation (z. B. Berücksichtigung nur durchgängig Versicherter, Altersgrenzen) genutzt (Swart et al. 2018). GKV-Daten umfassen darüber hinaus verschiedene Fachbereiche bzw. Sektoren. Sie bilden die ambulante und stationäre Versorgung sowie die Heilmittel- (Rehabilitation, Physiotherapie) und Hilfsmittelversorgung mit den zugehörigen Diagnosen, die gemäß der Internationalen statistischen Klassifikation der Krankheiten und verwandter Gesundheitsprobleme, 10. Revision (ICD-10) geschlüsselt werden (Bundesinstitut für Arzneimittel und Medizinprodukte 2023a), und die erbrachten Leistungen/Prozeduren anhand des Einheitlichen Bewertungsmaßstab (EBM) (Kassenärztliche Bundesvereinigung 2023) oder von Operationen- und Prozedurenschlüsseln (OPS) (Bundesinstitut für Arzneimittel und Medizinprodukte 2023b) aus Sicht der Leistungserbringenden ab. Zudem sind Daten zu Arzneimittel-Verordnungen, zu Arbeitsunfähigkeit oder Disease-Management-Programmen (DMP) sowie zum Pflegestatus enthalten, da die GKVen meist auch als Pflegekasse fungieren (Schubert et al. 2008; Hoffmann und Glaeske 2017; Horenkamp-Sonntag et al. 2014a; Müller et al. 2014). Exemplarische Besonderheiten der Daten sind, dass ambulante Diagnosen im Rahmen eines Behandlungsfalls bei einem Arzt/in einer Arztpraxis i. d. R. nur auf das Quartal bezogen vorliegen (Grobe und Drähter 2014) oder zu den Arzneimittel-Verordnungsdaten über die

enthaltene Pharmazentralnummer (PZN) umfassende Angaben aus der Arzneimittel-StammdateiPlus des GKV-Arzneimittelindex z.B. zu Wirkstoffen bzw. Wirkstoffgruppen (entsprechend der Anatomisch-Therapeutisch-Chemischen (ATC)-Klassifikation) oder die Menge der verordneten Tagesdosen (DDD) hinzugespielt werden können (Schröder 2014).

Bei der Nutzung von GKV-Daten ist der Datenschutz von zentraler Bedeutung, wobei die Ausgestaltung variieren kann. Im Folgenden werden einige datenschutzrechtliche Aspekte komprimiert dargestellt. Zusätzlich zur EU-Datenschutz-Grundverordnung (DSGVO) bilden die Bundes- und Landesdatenschutzgesetze und die Auflagen der Sozialgesetzbücher, insbesondere das *Zehnte Buch Sozialgesetzbuch* (SGB X), die rechtliche Grundlage für die Verarbeitung von personenbezogenen Daten (Ihle 2008; March et al. 2014a). Konkret bedeutet dies, dass in jedem Forschungsvorhaben, das auf pseudonymisierten Daten basiert, zunächst die datenschutzrechtlichen Rahmenbedingungen erfüllt sein müssen, bevor die Daten überhaupt an die auswertende Stelle übermittelt werden können. Pseudonymisiert bedeutet nach Art. 4 Abs. 5 DSGVO „die Verarbeitung personenbezogener Daten in einer Weise, dass die personenbezogenen Daten ohne Hinzuziehung zusätzlicher Informationen nicht mehr einer spezifischen betroffenen Person zugeordnet werden können, sofern diese zusätzlichen Informationen gesondert aufbewahrt werden und technischen und organisatorischen Maßnahmen unterliegen, die gewährleisten, dass die personenbezogenen Daten nicht einer identifizierten oder identifizierbaren natürlichen Person zugewiesen werden“ (Datenschutz-Grundverordnung). Im Rahmen der Pseudonymisierung der Daten bei der GKV wird die Krankenversichertennummer durch ein spezielles kryptographisches Verfahren zu einer Pseudo-ID umgewandelt und der Zuordnungsschlüssel verbleibt dort. Weiterhin sind folgende Überlegungen abzuwägen: Laut §67b SGB X bzw. Art. 9 DSGVO sind Gesundheitsdaten, wie sie bei der GKV vorgehalten werden, besonders schützenswert. Weiter schreibt der Paragraph vor, dass die schriftliche, freiwillige Einwilligung der betroffenen Person eingeholt und sie über den Zweck der Datennutzung informiert werden muss. Wenn die Einholung der Einwilligung der betroffenen Person unzumutbar ist und das Forschungsvorhaben gefährdet, kann unter Angabe von entsprechenden Gründen von diesem Vorgehen abgerückt und eine Genehmigung der jeweiligen obersten Aufsichtsbehörde zur *Übermittlung von Sozialdaten für die Forschung und Planung* nach Antrag gemäß *§75 SGB X* eingeholt werden. Grundsätzlich ist bei der Verarbeitung von personenbezogenen Daten dem Grundsatz der Datensparsamkeit (EU DSGVO Art. 5c) Folge zu leisten und zu überprüfen, ob die angeforderten Angaben zwingend erforderlich sind. Zudem ist die auswertende Stelle verpflichtet, die zur Verfügung gestellten Daten und sonstige überlassenen Unterlagen und Informationen durch technische und organisatorische Maßnahmen gemäß Art. 32 EU-DSGVO vor dem Zugriff und Einsichtnahme durch Unbefugte zu schützen. Für die Abstimmungen zum Datenschutz ist es unerlässlich, möglichst frühzeitig / zu Beginn des Forschungsvorhabens mit den eigentlichen Dateneignern und den involvierten Datenschutzbeauftragten der beteiligten Stellen und den zuständigen Aufsichtsbehörden in den Austausch zu treten und ein entsprechendes Datenschutzkonzept zu entwickeln (Ihle 2008; Swart et al. 2015). Wenn alle datenschutzrechtlichen Rahmenbedingungen bzw. gesetzlichen Bedingungen erfüllt sind, ist es – sollte es keine weiteren Vorgaben z.B. seitens der Forschungseinrichtung geben – nicht zwingend erforderlich, für die reine Sekundärdatenanalyse ein Ethikvotum einzuholen. Zur Nachvollziehbarkeit bzw. Überprüfbarkeit der Ergebnisse der Sekundärdatenanalyse wird in

der GPS empfohlen, die Daten für 10 Jahre aufzubewahren (Swart et al. 2015). Die Nutzungsdauer bzw. Löschfrist wird in der mit dem Dateneigner zur schließenden Vereinbarung über Datenverwendung und Datenschutz fixiert (das Datenschutzkonzept wird dabei als Anlage geführt).

Neben dem grundlegenden Vorteil, dass GKV-Daten unter Alltagsbedingungen entstehen, ist ein wesentlicher Aspekt bei der Nutzung von GKV-Daten, dass Analysen für alle per Definition zur Studienpopulation gehörenden Versicherten durchgeführt und somit auch vulnerable Subgruppen oder Personen einbezogen werden, die an Primärdatenerhebungen häufig nicht teilnehmen (Schubert et al. 2008; Hoffmann und Glaeske 2017). Ebenso enthalten sie keinen Recall Bias, d.h. keine Verzerrung der selbstberichteten Angaben aufgrund von Erinnerungsfehlern oder sozialer Erwünschtheit, wie es in Primärdatenstudien vorkommen kann (Schubert et al. 2008; Hoffmann et al. 2008b). Wenn Daten einer einzelnen (oder auch von mehreren) GKV analysiert werden, darf jedoch nicht außer Acht gelassen werden, dass Fragen zur Übertragbarkeit und Generalisierbarkeit adressiert werden müssen. Im Rahmen dieser Habilitationsschrift werden sie im Hinblick auf die vorgestellten Arbeiten im Kapitel Diskussion aufgegriffen. In diesem Zusammenhang werden auch weitere Vor- und Nachteile von GKV-Daten erörtert.

Derzeit sind für einzelne Sektoren, wie den ambulanten oder den stationären Bereich, kassenübergreifende Daten vorhanden, die über die Kassenärztlichen Vereinigungen beim Zentralinstitut für die kassenärztliche Versorgung in der Bundesrepublik Deutschland (Zi) oder beim Institut für das Entgeltsystem im Krankenhaus (InEK) beantragt werden können. Der mit dem GKV-Modernisierungsgesetz (§303a-e SGB V) seit 2004 angestrebte kassenübergreifende Datenpool wurde im Rahmen der im Jahr 2012 in Kraft getretenen Datentransparenz-verordnung beim Deutschen Institut für Medizinische Dokumentation und Information (DIMDI) aufgebaut. Allerdings ergaben sich hinsichtlich der Nutzbarkeit Limitationen, da sie relevante Angaben nicht enthielten (es fehlten beispielsweise Codes zu Prozeduren oder Kennzeichen für die ambulanten und stationären Leistungserbringer) und die Daten mit einem großen Zeitverzug verfügbar waren (Hoffmann und Glaeske 2017; Swart et al. 2018). Durch das Digitale-Versorgung-Gesetz (DVG) und die Verordnung zur Neufassung der Datentransparenzverordnung und zur Änderung der Datentransparenz-Gebührenverordnung soll die Nutzbarkeit der Daten für Forschungszwecke nun zukünftig ausgebaut werden, indem zunächst die Daten der GKV und perspektivisch weitere Datenkörper in einem Forschungsdatenzentrum gehalten und für die Forschung zugänglich gemacht werden (Gothe et al. 2020). Die Autorin der Habilitationsschrift hat mit anderen Fachvertretern gemeinsam zehn Statements formuliert, die auf das Potential eines Forschungsdatenzentrums eingehen und Vorschläge für die zukünftige Ausgestaltung und Entwicklung mit dem Ziel aufführen, eine Weiterentwicklung bestmöglich zu gestalten (March et al. 2023).

2.2.3 Verknüpfung verschiedener Datenquellen

Als Datenlinkage wird die Verknüpfung von Primär- und Sekundärdaten oder auch die Verknüpfung von verschiedenen Sekundärdatenquellen mittels geeigneter Schlüsselvariablen bezeichnet, die in beiden Datenquellen enthalten und eineindeutig sind (March et al. 2014b). Dabei umfasst der Begriff ähnlich wie der der Sekundärdatenanalyse den gesamten Prozess,

d.h. die Planung des Vorhabens, die Zusammenführung der Datenquellen, die Auswertung und auch die perspektivische Nutzung durch weitere Forschende sowie die Löschung der Daten (March et al. 2019). Ein Datenlinkage kommt beispielsweise dann zum Einsatz, wenn eine Datenquelle nicht ausreichend Informationen zur Beantwortung der zu untersuchenden Fragestellung liefert und ein Erkenntnisgewinn durch das Datenlinkage erzielt werden kann (March et al. 2018; March et al. 2019). Neben dem Vorteil von Primärdaten, dass ihnen gezielte Forschungsfragen zugrundeliegen und im Rahmen der Erhebung seitens der Durchführenden der größtmögliche Einfluss auf die Erfassung der Daten genommen werden kann, weisen sie auch Nachteile auf (Hoffmann et al. 2008b; Slagman et al. 2023). So können Angaben aufgrund eingeschränkter Umsetzbarkeit in der Datenerhebung, punktueller Follow-Up-Untersuchungen oder sich im Verlauf neu ergebender Fragestellungen fehlen, die aus GKV-Daten entnommen werden können. Dabei greift das Prinzip der Datensparsamkeit: Eine Verknüpfung stellt zumindest teilweise auf bereits vorliegende Daten ab, ohne dafür neue Daten erheben zu müssen. Die verschiedenen Datenquellen können auch eine Gegenüberstellung bzw. Validierung von Inhalten, die sich in beiden/allen Datenquellen finden, und eine Einschätzung der Datenqualität ermöglichen (Stallmann et al. 2015; March et al. 2019). Darüber hinaus führt das Datenlinkage zu methodischen Erkenntnissen bzgl. der Durchführung selbst und zu Möglichkeiten und ggf. Grenzen der Nutzung. Die Einhaltung des Datenschutzes ist auch im Kontext des Datenlinkages zu beachten. Dabei ist von einem erhöhten Schutzbedarf der verknüpften Daten auszugehen. Für die Durchführung eines Datenlinkage ist grundsätzlich ein Ethikvotum einzuholen. Zudem ist für die Verknüpfung von Primär- und Sekundärdaten in den meisten Studien entsprechend §67b SGB X eine Einwilligung zur Verknüpfung personenbezogener Daten erforderlich und dabei über den Zweck bzw. die geplante Nutzung des Datenlinkages aufzuklären (March et al. 2019; Stallmann et al. 2015; Swart et al. 2014b). Darüber hinaus greifen die bereits für die Sekundärdatenanalyse ausgeführten Aspekte (z.B. die Erstellung eines Datenschutzkonzeptes). Das Linkage von GKV-Daten mit Befragungsdaten kann auf unterschiedliche Weise durchgeführt werden. Eine Möglichkeit wäre, dass die GKV ihre Versicherten anschreibt, Fragebögen zusendet und mittels Einverständniserklärung, die dann von den Versicherten zurückgesendet wird, um Zustimmung zur Verknüpfung der Daten mit den GKV-Daten bittet. In diesem Fall werden nur pseudonymisierte Daten an die Forschungseinrichtung übermittelt (Kvitkina et al. 2016). Da die Handhabung von Studien mit Datenlinkage gezieltes Wissen voraussetzt und bislang wenige Erfahrungsberichte veröffentlicht wurden, haben führende ExpertInnen – unter aktiver Mitwirkung der Autorin der vorliegenden Habilitationsschrift – im Jahr 2019 Standards für die Durchführung von Forschungsvorhaben in der Gesundheits- und Sozialforschung publiziert, die ein Datenlinkage personenbezogener Daten nach wissenschaftlichen Grundsätzen adressieren (March et al. 2019). Studien mit Datenlinkage werden seit einigen Jahren gezielt gefördert. So wurde im Rahmen der ersten Ausschreibung des Innovationsfonds im April 2016 im Bereich Versorgungsforschung das Themenfeld „Einsatz und Verknüpfung von Routinedaten zur Verbesserung der Versorgung“ ausgeschrieben. Im Rahmen dieser Förderlinie wurde ein Antragsvorhaben zur *Versorgung, Funktionsfähigkeit und Lebensqualität nach proximaler Femurfraktur: ProFem* bewilligt, in dem GKV-Daten mit individuell erhobenen Primärdaten verknüpft wurden und für das die Autorin der vorliegenden Habilitationsschrift als eine der Studienkoordinatorinnen tätig war (Andrich et al. 2019).

2.3 Hintergrund der Originalarbeiten – Forschungsbedarf

Die für die Habilitationsschrift ausgewählten Arbeiten kommen aus verschiedenen Themenbereichen. Drei primär inhaltlich ausgerichteten Arbeiten befassen sich im Rahmen der *Alterstraumatologischen Versorgungsforschung* mit der Epidemiologie und Versorgung von Beckenfrakturen auf Basis von GKV-Daten. Zwei weitere Arbeiten, die aus einer Studie zur Rolle der *Depression als psychische Komorbidität des Diabetes* stammen, setzen durch die Durchführung einer Non-Responderanalyse auf Basis von GKV-Daten und einer durch ein Datenlinkage realisierten Erfassung zum Vorliegen einer depressiven Störung bei Menschen mit Diabetes, insbesondere durch Gegenüberstellung der mittels GKV-Daten und anhand von zwei weiteren Instrumenten ermittelten Prävalenzen sowie der Charakterisierung der identifizierten Populationen, einen methodischen Schwerpunkt.

2.3.1 Alterstraumatologische Versorgungsforschung

Geriatrische Frakturen spielen in der gesundheitlichen Versorgung in der älteren Bevölkerung bereits heutzutage eine große Rolle. Neben proximalen Femurfrakturen zählen distale Radiusfrakturen, proximale Humerusfrakturen und Beckenfrakturen zu den häufigsten Frakturen in der älteren Bevölkerung (Court-Brown et al. 2014). Verglichen mit den Kenntnissen zur Epidemiologie und zur Versorgung von Hüftfrakturen auf Basis internationaler Daten war die Datenlage zur Epidemiologie und Versorgung von Beckenfrakturen zum Zeitpunkt der Veröffentlichungen der Originalarbeiten, diese sind im Jahr 2015, im Jahr 2017 und im Jahr 2021 erschienen, begrenzt. Kenntnisse über Inzidenzen und Trends von Beckenfrakturen sowie damit verbundene Kosten und Inanspruchnahmen von gesundheitlichen Leistungen sind bei einer immer älter werdenden Bevölkerung und den aktuell geringen Ressourcen des Gesundheitssystems jedoch hoch relevant. Ebenso ist es wichtig zu beschreiben, wie sich die Folgen nach dem Auftreten einer Beckenfraktur darstellen und welche Subgruppen möglicherweise eine höhere Sterblichkeit aufweisen.

Die zum Zeitpunkt der Veröffentlichung der Originalarbeit vorliegenden Studien zur Inzidenz von Beckenfrakturen basierten überwiegend auf Krankenhaus- oder Registerdaten (Nanninga et al. 2014; Kannus et al. 2005; King et al. 2009). Es ist jedoch zu beachten, dass ein erheblicher Anteil der Personen mit Beckenfrakturen ambulant behandelt wurde bzw. wird (Prieto-Alhambra et al. 2012; Boufous et al. 2007). Daraus lässt sich folgern, dass Studien, die nur auf Krankenhaus- oder Registerdaten beruhen, die tatsächliche Inzidenz von Beckenfrakturen vermutlich unterschätzen. Neben einer Unterschätzung der Inzidenz wäre auf Grundlage dieser Studien auch die Analyse zur Mortalität nach Beckenfrakturen verzerrt, da sich Personen mit stationär behandelten Frakturen wahrscheinlich von denen unterscheiden, die ambulant behandelt werden. Für die Betrachtung der Mortalität nach Beckenfrakturen ist darüber hinaus zu berücksichtigen, dass die Sterblichkeit in der älteren Bevölkerung im Allgemeinen hoch ist. Um Unterschiede in der Sterblichkeit in dieser vulnerablen Bevölkerungsgruppe zu bewerten, sind Daten zur Übersterblichkeit (Excess-Mortalität) erforderlich. Nach unserem Kenntnisstand haben bislang nur drei Studien die Übersterblichkeit bei älteren Menschen nach einer Beckenfraktur untersucht (Rapp et al. 2010; Prieto-Alhambra et al. 2012; Hill et al. 2001). Die Studien weisen jedoch Limitationen auf, da sie nur hospitalisierte Beckenfrakturen in einer Population von Pflegheimbewohnern betrachten (Rapp et al. 2010), keine Komorbidität berücksichtigen (Pike et al. 2011; Hill et al.

2001) oder aus einer kleinen Studienpopulation bestehen (Hill et al. 2001). Nur die Studie von Prieto-Alhambra et al. differenziert bei der Beschreibung der Mortalität zwischen stationärer und ambulanter Behandlung. Die Studien zur Kosten- und Inanspruchnahme berücksichtigen in der Regel sowohl den stationären als auch den ambulanten Versorgungsbereich. Im Hinblick auf die Leistungsinanspruchnahme und die direkten medizinischen Kosten liegen jedoch nur wenige Belege auf Basis von administrativen Daten für die durch Beckenfrakturen verursachte finanzielle Belastung vor (Kilgore et al. 2009; Ohsfeldt et al. 2006; Pike et al. 2010). Diese Studien zeigen, dass Beckenfrakturen (ebenso wie Hüftfrakturen) zu hohen Kosten führen. Dabei haben nur Kilgore et al. einen inkrementellen Kostenansatz und Pike et al. einen Exzess-Kostenansatz verwendet, um die Mehrkosten durch die Beckenfraktur zu beschreiben. Bislang wurde keine Studie publiziert, die die Mehrkosten in Zeitintervallen von vier Wochen im Jahr nach dem Ereignis analysiert und die den Schweregrad der Frakturen für die Kostenbewertung berücksichtigt.

Der hier skizzierte Forschungsbedarf wurde im Rahmen einer vom Bundesministerium für Bildung und Forschung (BMBF) geförderten Studie (FKZ 01GY1136, Förderzeitraum 01.02.2012 bis zum 30.09.2015) zu „Beckenfrakturen in der älteren und betagten Bevölkerung - Inzidenzen und Trends, Versorgung und Mortalität“ auf Basis von GKV-Daten adressiert. Die Studie wurde von der Ethikkommission der Medizinischen Fakultät der Heinrich-Heine-Universität Düsseldorf genehmigt (Ethikvotum 3839). Die Nutzung der Sekundärdaten erfolgte retrospektiv und unter Beachtung der geltenden Normen und gesetzlichen Regelungen zum Datenschutz. Das Vorgehen entsprach der Deklaration von Helsinki und vergleichbaren ethischen Standards (z.B. GEP und GPS).

2.3.2 Depression als psychische Komorbidität des Diabetes

In der Literatur besteht Konsens, dass Menschen mit Diabetes im Vergleich zur Allgemeinbevölkerung eine höhere Prävalenz einer Depression aufweisen (Harding et al. 2019; Ali et al. 2006). Dabei ist unklar, wie genau die Richtung des Zusammenhangs von Diabetes und Depression ist, d.h. ob Diabetes zu Depressionen führt oder vice versa oder ob ein wechselseitiger Zusammenhang besteht (Nouwen et al. 2019; Nouwen et al. 2010; Mezuk et al. 2008). Es ist zudem beschrieben worden, dass Depressionen einen negativen Einfluss auf das Wohlbefinden eines Menschen und seine Fähigkeit, seinen Diabetes selbst zu managen, haben können (Katon et al. 2004; Egede et al. 2009; Semenkovich et al. 2015; Gonzalez et al. 2007). Sowohl im Hinblick auf die Diabetes-Erkrankung selbst als auch auf damit einhergehende Folgeerkrankungen sind für Menschen mit Diabetes und einer komorbiden Depression negative Auswirkungen, z. B. eine geringere Therapietreue, höhere HbA1c-Werte, verstärkte Diabetes-Symptome oder ungünstige mikro- und makrovaskuläre Ereignisse (Katon et al. 2004; Egede et al. 2009; Semenkovich et al. 2015; Gonzalez et al. 2007; Genis-Mendoza et al. 2022), festgestellt worden. Brüne et al. berichteten für Menschen mit Diabetes und Depressionen im Vergleich zu Menschen mit Diabetes ohne Depressionen von fast doppelt so hohen medizinischen Kosten aus GKV-Perspektive (Brüne et al. 2021). Trotz der dargestellten Relevanz komorbider Depressionen bei Menschen mit Diabetes werden laut Katon et al. nur 50 % der Menschen mit Diabetes und komorbider Depression erkannt und ein noch geringerer Anteil angemessen behandelt (Katon et al. 2004). Nationale und internationale Leitlinien sehen vor, Menschen mit Diabetes regelmäßig auf das Vorhandensein einer Depression zu

untersuchen (Kulzer et al. 2022; Kulzer et al. 2013; International Diabetes Federation Guideline Development Group 2014). Dafür kommen verschiedene Methoden in Frage: Häufig werden strukturierte diagnostische Interviews, z.B. das aktuelle SCID-5-CV nach den Kriterien des Diagnostischen und Statistischen Manuals Psychischer Störungen (DSM-5), als Goldstandard angesehen (Wittchen et al. 2010; Joode et al. 2019); sie sind jedoch nur von Ärzten oder geschulten Interviewern durchführbar. Eine weitere Möglichkeit ist die Erfassung einer depressiven Symptomatik mithilfe eines Screening-Instruments. De Joode et al. haben im Rahmen einer Meta-Analyse zur diagnostischen Genauigkeit von Depressionsfragebögen dargelegt, dass die Center of Epidemiological Studies-Depression Scale (CES-D) und der Patient Health Questionnaire-9 (PHQ-9) im Rahmen von populationsbasierten Studien die am häufigsten eingesetzten Depressionsfragebögen bei mit Menschen mit Diabetes sind (Joode et al. 2019; Radloff 1977; Hautzinger et al. 2012; Kroenke et al. 2001; Gräfe et al. 2004). Die Autoren berichten, dass sie sich hinsichtlich ihrer Sensitivität (beim CES-D am höchsten) und ihrer Spezifität (beim PHQ-9 am höchsten) nicht signifikant unterscheiden und konstatieren, dass weitere Studien erfoderlich sind, um die diagnostische Genauigkeit dieser (und weiterer) Depressionsfragebögen bei Personen mit Diabetes zu bestätigen. Grundsätzlich gibt es in den verschiedenen Leitlinien bis heute keine Festlegung dazu, welches Instrument verwendet werden sollte. Durch alle beschriebenen Methoden und Instrumente wird das Vorhandensein und somit die Prävalenz der Depression/depressiven Symptomatik bestimmt. Dabei ist denkbar, dass die Prävalenzen variieren, je nachdem welche Methode bzw. welches Instrument zum Einsatz kommt. So gibt es bereits Belege, dass die Prävalenz in Studien, in denen ein Fragebogen zum Einsatz kam, zwei- bis dreimal so hoch war wie in Studien, in denen ein diagnostisches Interview durchgeführt wurde (Khaledi et al. 2019; Anderson et al. 2001; Ali et al. 2006). Außerdem könnte es sein, dass es in den durch die verschiedenen Instrumente und Methoden identifizierten Populationen Unterschiede und Überschneidungen hinsichtlich individueller und klinischer Merkmale gibt. Neben dem Einsatz der Instrumente zur Erfassung der Depression in populationsbasierten Studien stellen GKV-Daten eine weitere Datenquelle dar, aus der Angaben zur Depression entnommen werden können, da – beispielsweise aufgrund der durchgeführten strukturierten Interviews – ICD-10 Diagnosen gestellt werden, die in GKV-Daten enthalten sind. Bis dato wurde keine Studie publiziert, die untersucht hat, ob verschiedene Instrumente unterschiedliche Personen identifizieren, und die zur Gegenüberstellung der Methoden und Beschreibung der identifizierten Gruppen hinsichtlich ihrer möglichen Unterschiede und Überschneidungen auch GKV-Daten herangezogen hat.

Eine zusätzliche Herausforderung bei Primärdatenerhebungen (Querschnitts- oder Kohortenstudien) ist, dass nicht alle für die Studie vorgesehenen Teilnehmende der Einladung zur Studienteilnahme folgen. Daher ist es bei Primärdatenstudien (hier zur Rolle der Depression) grundsätzlich ratsam, eine Analyse zum Rücklauf bzw. zur Studienteilnahme durchzuführen, um einen potentiellen Selektionsbias hinsichtlich der Nichtteilnahme oder Nichtverfügbarkeit von Daten (Non-Response) abschätzen zu können (DGEpi 2018). Im Rahmen einer solchen Analyse wird geprüft, ob sich Responder und Non-Responder in relevanten Charakteristika unterscheiden, was zu einer Verzerrung der Studienergebnisse durch Non-Response führen könnte. Häufig werden Non-Responderanalysen auf Basis einen Kurzfragebogens durchgeführt, wie beispielsweise in der Heinz Nixdorf Recall Studie (Stang et al. 2005). Allerdings beteiligen sich nicht alle Personen, die die Teilnahme an einer Studie

ablehnen, noch an einer solchen Kurzbefragung. Im Rahmen einer Non-Reponderanalyse sollte angestrebt werden, möglichst umfassende soziodemografische und gesundheitsbezogene Angaben – sowohl für die Teilnehmenden als auch für Nicht-Teilnehmende – zu berücksichtigen, um die Repräsentativität der Teilnehmenden zu analysieren. Wie bereits in Kapitel 2.2.1 dargestellt, ist die Nutzung von GKV-Daten für Non-Responderanalysen von Vorteil, da die Daten keinen Selektionsbias aufweisen (Schubert et al. 2008; Hoffmann und Glaeske 2017). Bis heute wurden nur wenige Studien publiziert, die ein Datenlinkage (GKV- bzw. administrative Daten mit Survey-Daten) bei der Durchführung einer Non-Responderanalyse nutzen und Unterschiede zwischen Respondern und Non-Respondern in Bezug auf die interessierenden gesundheitsbezogenen Outcomes darstellen (Callhoff et al. 2020; Stewart et al. 2021; Dad et al. 2018; Momen et al. 2022).

Die vom BMBF geförderte DiaDec-Studie zu „Lebensqualität, Einschränkungen, Inanspruchnahme und Kosten von Patienten mit Diabetes: Die Rolle der Depression“(FKZ 01GY1133, Förderzeitraum 01.02.2012 bis zum 31.07.2016) erlaubte es, durch ihre methodische Konzeption und ihre Datengrundlage den dargelegten Forschungslücken zu begegnen. Für die Durchführung der Studie wurde ein Ethikvotum der Ethikkommission der Medizinischen Fakultät der Heinrich-Heine-Universität Düsseldorf eingeholt (Ethikvotum 3762). Sie erfolgte unter Beachtung der gesetzlichen Vorgaben zum Schutz von Sozialdaten nach wissenschaftlichen Standards gemäß der Deklaration von Helsinki sowie den Leitlinien zur GEP und GPS.

2.4 Forschungsfragen und Ziele

Die untersuchten Forschungsfragen lassen sich im erweiterten Throughput-Modell den Dimensionen Output und Outcome zuordnen und lauten wie folgt:

<u>Arbeiten aus dem Bereich der Alterstraumatologischen Versorgungsforschung:</u>

Nutzung von GKV-Daten zur Schätzung der Inzidenz

- Wie ist die Inzidenz von Beckenfrakturen in der deutschen Bevölkerung im Alter von 60 Jahren oder älter auf Basis von ambulanten und stationären GKV-Daten?
- Gibt es Variablen, die die Inzidenz erklären können, beispielsweise Geschlecht, Alter, Kalenderjahr oder Region?

Nutzung von GKV-Daten zur Schätzung der Mortalität

- Wie ist die Übersterblichkeit von Personen im Alter von 60 Jahren oder älter nach einer Beckenfraktur im Vergleich zu Personen ohne Beckenfraktur in Deutschland auf der Grundlage von ambulanten und stationären GKV-Daten?
- Wie stellt sich die Übersterblichkeit dar, wenn das Behandlungssetting (ambulant/stationär) und der Schweregrad der Frakturen berücksichtigt werden?

Nutzung von GKV-Daten zur Beschreibung der Leistungsinanspruchnahme und von damit einhergehenden Kosten

- Wie gestaltet sich die Inanspruchnahme medizinischer Leistungen von Personen im Alter von 60 Jahren oder älter nach einer Beckenfraktur im Vergleich zu Personen ohne Beckenfraktur in Deutschland auf der Grundlage von GKV-Daten?
- Wie gestalten sich die mit der Inanspruchnahme medizinischer Leistungen einhergehenden Kosten von Personen im Alter von 60 Jahren oder älter nach einer Beckenfraktur im Vergleich zu Personen ohne Beckenfraktur in Deutschland auf der Grundlage von GKV-Daten?
- Wie stellen sich die Kosten stratifiziert für das Behandlungssetting (ambulant/stationär) und den Schweregrad der Frakturen dar?

<u>Arbeiten aus dem Bereich der Rolle der Depression als psychische Komorbidität des Diabetes:</u>

Nutzung von GKV-Daten zur Auswertung von Non-Response in einer Querschnittsstudie zur Rolle der Depression bei Menschen mit Diabetes

- Unterscheidet sich der Depressionsstatus (Vorhandensein einer Depression) zwischen Respondern und Non-Respondern?
- Stehen soziodemografische Merkmale im Zusammenhang mit dem Teilnahmeverhalten (Response)?
- Stehen Diabetesbehandlung, Komorbiditäten und Inanspruchnahme des Gesundheitswesens in Zusammenhang mit dem Teilnahmeverhalten (Response)?

Datenlinkage – Gegenüberstellung von verschiedenen Methoden zur Erfassung einer depressiven Störung bei Menschen mit Diabetes mittels Verknüpfung von Befragungs- und longitudinalen GKV-Daten

- Wie ist die Prävalenz von Depression/depressiven Störungen bei Menschen mit Diabetes, wenn verschiedene Methoden zur Erfassung verwendet werden?
- Gibt es Überschneidungen und Unterschiede zwischen den Gruppen, die mittels verschiedener Methoden identifiziert wurden?
- Lassen sich Zusammenhänge zwischen individuellen und klinischen Merkmalen und der zur Identifizierung einer Person verwendeten Methode oder mögliche Interaktion beobachten?

Die nachfolgend vorgestellten fünf Publikationen sollen die Möglichkeiten sowohl zur Nutzung von GKV-Daten als auch ihrer Verknüpfung mit Befragungsdaten zur Beantwortung der aufgeführten Fragestellungen darlegen.

3. Eigene Originalarbeiten

3.1 Nutzung von GKV-Daten zur Schätzung der Inzidenz von Beckenfrakturen

Andrich, S.; Haastert, B.; Neuhaus, E.; Neidert, K.; Arend, W.; Ohmann, C.; Grebe, J.; Vogt, A.; Jungbluth, P.; Rösler, G.; Windolf, J.; Icks, A. (2015). Epidemiology of Pelvic Fractures in Germany: Considerably High Incidence Rates among Older People. *PLoS One* 10 (9):e0139078.

Die erste dieser Habilitationsschrift zugrundeliegende Arbeit beschäftigt sich mit der Schätzung der Inzidenz von Beckenfrakturen in der deutschen Bevölkerung im Alter von 60 Jahren oder älter. Dazu wurde eine retrospektive bevölkerungsbezogene Beobachtungsstudie auf Basis von ambulanten und stationären Daten der AOK NordWest durchgeführt, auf deren Basis stratifiziert alters- und geschlechtsspezifische Inzidenzraten von Erstfrakturen im Studienzeitraum von 2008 bis 2011 berechnet wurden. Um Beckenfrakturen zu identifizieren, wurde in den stationären und ambulanten Daten nach spezifischen Diagnosecodes der 10. Revision der Internationalen Klassifikation der Krankheiten (ICD-10) für Beckenfrakturen gesucht, die mit Datumsangabe enthalten waren. Für die Inzidenzbestimmung wurden nur Erstfrakturen berücksichtigt, die durch einen ereignisfreien Zeitraum von mindestens einem Jahr vor dem Ereignis definiert waren. Bei der Erfassung von Erstfrakturen wurde zwischen ausschließlich ambulant und irgendwann im Studienverlauf stationär behandelten Frakturen unterschieden.

Die Inzidenzraten (IR) der ersten Beckenfraktur wurden unter Annahme einer Poisson-Verteilung für alle (ambulanten und stationären) Ereignisse sowie nur für stationär behandelte Beckenfrakturen gesamt und stratifiziert nach Geschlecht und Alter (in 5 Jahresaltersklassen) pro 10.000 Personenjahre (PJ) mit approximativen 95 %-Konfidenzintervallen [95 %-KI] berechnet. Zudem erfolgte eine Alters-Geschlechts-Standardisierung auf die deutsche Bevölkerung 2009. Mittels multipler Poisson-Regressionen wurden relative Risiken (RR) zur Beschreibung der Assoziation zwischen dem Risiko einer ersten Beckenfraktur und dem Geschlecht, dem Alter, dem Kalenderjahr und der Region geschätzt.

Die Gesamtzahl der Personen mit einer ersten Beckenfraktur belief sich auf 8.041. Während des Studienzeitraums mussten 5.978 Versicherte (74 %) stationär behandelt werden. Insgesamt betrug die alters- und geschlechtsstandardisierte Inzidenzrate aller ersten Beckenfrakturen 22,4 [22,0-22,9] pro 10.000 PJ und die alters- und geschlechtsstandardisierte Inzidenzrate der stationär behandelten Frakturen 16,5 [16,1-16,9]. Wie erwartet waren die Inzidenzraten bei Frauen höher als bei Männern. Diese Unterschiede zeigten sich in allen Altersgruppen, waren für Frauen in den höheren Altersgruppen jedoch noch stärker ausgeprägt (s. Abbildung 1).

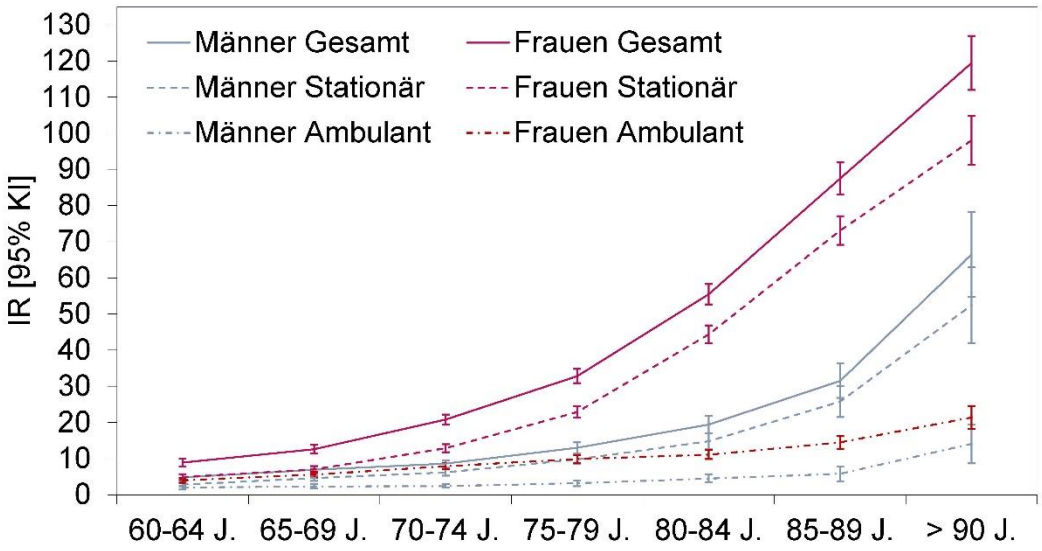

Abbildung 1: Geschlechtsspezifische Inzidenzen für alle ersten Frakturen insgesamt sowie stationär und ambulante Erstfrakturen nach Altersklassen. Entnommen aus dem Abschlussbericht zum Projekt *Beckenfrakturen in der älteren und betagten Bevölkerung* und modifiziert nach (Andrich et al. 2015). Abdruck mit freundlicher Genehmigung des Public Library of Science Verlages.

Im Rahmen der durchgeführten Regressionsanalyse zeigte sich ein signifikanter Geschlechts- (RR 2,38 [2,23-2,55], p < 0,001, Männer als Referenz) und Alterseffekt (höheres Risiko mit zunehmendem Alter, p < 0,001) auf das Erstfrakturrisiko. Zudem war ein leichter Zusammenhang zwischen Kalenderjahr (höheres Risiko in späteren Jahren im Vergleich zu 2008, p = 0,0162) und Erstfrakturrisiko und ein weiterer signifikanter Zusammenhang mit der Region (RR 0,92 [0,87-0,98], p = 0,006, Westfalen-Lippe als Referenz) und dem Erstfrakturrisiko zu beobachten.

Zusammenfassend lässt sich festhalten, dass die beobachteten Inzidenzen deutlich höher waren als in der internationalen Literatur beschrieben, auch wenn nur stationär behandelte Beckenfrakturen betrachtet wurden. Die Studie zeigte, dass bei Nichteinbeziehung ambulanter Daten ein relevanter Anteil der Beckenfrakturen nicht berücksichtigt und die Inzidenz von Beckenfrakturen unterschätzt wird. Die dargelegten Ergebnisse können beispielsweise von politischen Entscheidungsträgern für die Planung der Gesundheitsversorgung, von medizinischen Dienstleistungen oder von Präventionsangeboten, wie z. B. Sturzpräventionsprogramme, genutzt werden.

3.2 Nutzung von GKV-Daten zur Schätzung der Mortalität nach Beckenfraktur

Andrich, S.; Haastert, B.; Neuhaus, E.; Neidert, K.; Arend, W.; Ohmann, C.; Grebe, J.; Vogt, A.; Jungbluth, P.; Thelen, S.; Windolf, J.; Icks, A. (2017). Excess Mortality After Pelvic Fractures Among Older People. *J Bone Miner Res* 32 (9):1789–1801.

Ziel der zweiten Arbeit war es, die Übersterblichkeit bei Personen im Alter von 60 Jahren oder älter bis zu einem Jahr nach einer Beckenfraktur im Vergleich zu einer Population ohne Beckenfraktur auf Basis von Daten der AOK NordWest im Zeitraum von 2008-2011 zu schätzen. Die Darstellungen zur Übersterblichkeit erfolgten stratifiziert für stationär/ambulant

behandelte Personen mit Beckenfraktur und Personen mit sogenannten minor/major Beckenfrakturen jeweils im Vergleich zu Personen ohne Beckenfraktur (Kontrollen). Wie in der ersten Arbeit bereits dargelegt, wurden Personen mit erster Beckenfraktur (Fälle) anhand von ICD-10-Codes identifiziert, die aufgrund klinischer Expertise zudem als Approximation für den Schweregrad in minor (leichte) und major (schwere) Frakturen eingeteilt wurden. Für die Mortalitätsanalysen wurde zwischen erstmals ambulant und akut stationär behandelten Beckenfrakturen unterschieden. Die Stratifizierung von leichten und schweren Beckenfrakturen wurde auf Grundlage des Vorliegens einer entsprechenden Diagnose in der Indexwoche (entspricht der Woche des Auftretens der Beckenfraktur und einer zufällig gewählten Indexwoche bei den Kontrollen) getroffen: Wenn mindestens ein als major klassifizierter ICD-10-Code während der Indexwoche auftrat, wurde eine schwere Beckenfraktur dokumentiert.

Die Analysen umfassten zum einen die Darstellung von Überlebenswahrscheinlichkeiten im ersten Jahr nach dem Indexdatum getrennt für Fälle (weiter stratifiziert nach stationär/ambulant behandelten oder leichten/schweren Beckenfrakturen) und Kontrollen anhand von Kaplan-Meier-Kurven. Zum anderen wurden zeitabhängige Hazard Ratios (HRs) mit 95 %-Konfidenzintervallen [95 %-KI] zur Messung der Übersterblichkeit in 4-Wochen-Intervallen bis zu 52 Wochen (1 Jahr nach Ereignis) mittels Cox-Regressionsmodellen berechnet. In die Regressionsmodelle gingen außerdem folgende Variablen als potentielle Confounder mit ein: Alter, Geschlecht, Versicherungsregion, Versorgungsgrad, Komorbidität, Vorjahreskosten und Art der Beckenfraktur.

Insgesamt kamen auf 5.685 Fälle mit Beckenfraktur 193.159 Kontrollen ohne Beckenfraktur. Es verstarben 21 % der Fälle und 11 % der Kontrollen innerhalb eines Jahres. Im adjustierten Modell sanken die HRs erheblich (3,0 [2,6-3,4] und 1,0 [0,8-1,4]), waren aber bis Woche 32 signifikant erhöht. Die adjustierten HRs waren bei Frauen niedriger als bei Männern: 2,8 [2,4-3,2] und 1,0 [0,7-1,48] gegenüber 3,8 [2,9-5,0] und 1,2 [0,6-2,3].

In den nach Versorgungssetting stratifizierten Analysen – 59 % der Personen wurden akut stätionär behandelt – zeigte sich, dass Personen mit akut stationär behandelten Beckenfrakturen innerhalb eines Jahres eine höhere Mortalität aufwiesen als Personen mit erstmalig ambulant behandelten Beckenfrakturen. Insbesondere in den ersten Wochen nach der Aufnahme ins Krankenhaus deuten die adjustierten HRs (Woche 1-4 Frauen: 4,1 (3,5-4,8); Männer: 6,0 (4,5-8,0)) auf eine erhöhte Sterblichkeit für akut stationär behandelte Männer und Frauen im Vergleich zu ihren Kontrollen hin. Die adjustierten HRs waren bei stationär behandelten Frauen und Männern im Vergleich zu denen ohne Beckenfraktur in den ersten 4 Monaten signifikant erhöht. Bei ambulant behandelten Personen (Männern und Frauen) wurde innerhalb der ersten drei Monate keine und auch nur zu einzelnen Zeitintervallen im Verlauf des Jahres eine Übersterblichkeit festgestellt.

Stratifiziert nach Schweregrad der Beckenfraktur – für 64 % der Personen wurde eine schwere Beckenfraktur dokumentiert – war eine etwas höhere Mortalität bei Personen mit schwerer Beckenfraktur zu erkennen. Das Sterberisiko bei Personen mit leichten Beckenfrakturen war jedoch immer noch höher als bei den Kontrollen. Auch die HRs ergaben vor allem zu Beginn eine Übersterblichkeit sowohl für Personen mit leichten als auch mit schweren Beckenfrakturen im Vergleich zu Personen ohne Beckenfrakturen. In einer weiteren Analyse

war anhand der zeitabhängigen HRs bezogen auf die einzelnen ICD-10-Codes für schwere Beckenfrakturen eine signifikante Übersterblichkeit zu Beginn abzulesen, während die Übersterblichkeit für die meisten als leicht eingestuften Beckenfrakturen nicht mehr signifikant war.

Insgesamt ließ sich eine deutliche Übersterblichkeit bei älteren Menschen in den ersten acht Monaten nach einer Beckenfraktur beobachten, selbst nach vollständiger Adjustierung für relevante Drittvariablen, wie Pflegestufe oder Komorbidität. Die Übersterblichkeit war bei Männern zu Beginn höher, ebenso bei stationär behandelten Personen. Bei ambulant behandelten Personen wurde innerhalb der ersten drei Monate keine Übersterblichkeit festgestellt. Aufgeschlüsselt nach Schweregrad war die Übersterblichkeit für die meisten als leicht eingestuften Beckenfrakturen – mit Ausnahme der Schambeinfraktur – nicht mehr signifikant.

Wie bereits in der ersten Orginalarbeit dargelegt, ist die Inzidenzrate von Beckenfrakturen in Deutschland hoch. Ein Anstieg der Inzidenzraten hat nicht nur erhebliche Auswirkungen auf das Individuum und die Gesellschaft, sondern wird auch mit einem hohen Sterberisiko einhergehen. Erschwerend kommt hinzu, dass auch die Übersterblichkeit höher als erwartet war. Unsere Ergebnisse unterstreichen die Bedeutung präventiver Maßnahmen, wobei insbesondere Personen mit stationärer Behandlung nach Beckenfrakturen als Zielgruppe berücksichtigt werden sollten. Die vorliegende Arbeit hat den Kenntnisstand zur Übersterblichkeit nach Beckenfrakturen aufgrund ihrer detaillierten Darstellung erheblich erweitert und wurde in einem TOP10-Journal publiziert.

3.3 Nutzung von GKV-Daten zur Beschreibung der Leistungsinanspruchnahme und von damit einhergehenden Kosten nach Beckenfraktur

Andrich, S.; Haastert, B.; Neuhaus, E.; Frommholz, K.; Arend, W.; Ohmann, C.; Grebe, J.; Vogt, A.; Brunoni, C.; Jungbluth, P.; Thelen, S.; Dintsios, C.-M.; Windolf, J.; Icks, A. (2021). Health care utilization and excess costs after pelvic fractures among older people in Germany. *Osteoporos Int* 32 (10):2061–2072.

Im Rahmen der dritten Arbeit, die auf der gleichen Versichertenpopulation basiert wie die zuvor beschriebenen Analysen zur Mortalität (zur Selektion s. bitte Ausführungen bei Originalarbeit 2, Fälle mit Beckenfraktur = 5.685 und Kontrollen ohne Beckenfraktur = 193.159), wurden GKV-Daten zur Beschreibung der medizinischen Leistungsinanspruchnahme und von damit einhergehenden Kosten im Jahr nach Beckenfraktur herangezogen. Ziel war es, zusätzliche Leistungsinanspruchnahme und Mehrkosten, also zusätzliche Kosten aufgrund der Beckenfraktur, aus GKV-Perspektive im ersten Jahr nach Beckenfraktur im Vergleich zu einer Population ohne Beckenfraktur zu schätzen und dabei (wie auch bei den Analysen zur Mortalität) wichtige Drittvariablen und den Schweregrad der Beckenfraktur zu berücksichtigen.

Prävalenzen und Mittelwerte zur Inanspruchnahme und mittlere Gesamtkosten mit 95 %-Konfidenzintervallen [95 %-KI] wurden mittels BCA-Bootstrap-Verfahren für verschiedene Zeitintervalle vor und nach dem Indexdatum berechnet: Die Kennzahlen zur Inanspruchnahme bezogen sich auf 52 Wochen vor und nach dem Indexdatum, die Vorjahreskosten wurden

kumuliert und in Quintile eingeteilt. Die Kosten nach dem Indexdatum wurden einerseits für 52 Wochen kumuliert und andererseits proportional in 13 Zeitintervalle von vier Wochen aufgeteilt. Mittels gemischter Two-Part-Modelle und Adjustierung für potentielle Confounder, wie Alter, Geschlecht, Indexjahr, Versicherungsregion, Pflegestufe, Komorbidität, Vorjahreskosten, Tod, Beobachtungszeit und die Interaktion der Vorjahreskosten mit Fall/Kontrolle sowie Messwiederholungen wurden Relative Risiken (RR) und Cost Ratios (CR) mit 95 %-Konfidenzintervallen [95 %-KI] geschätzt.

Es war auffällig, dass bereits im Vorjahr die Leistungsinanspruchnahme bei den Fällen höher war als bei den Kontrollen – dies galt insbesondere bei Krankenhausaufenthalten. So stieg der Anteil der stationären Behandlungen bei den Fällen im Jahr nach dem Indexdatum auf fast 90 %, während er bei den Kontrollen nahezu gleich blieb (um die 30-35 %).

Ähnlich fielen die Beobachtungen auch für die mittleren Gesamtkosten aus (s. Abbildung 2). Während sich die mittleren Gesamtkosten bei den Fällen im Vergleich zum Vorjahr fast verdoppelten, blieben die mittleren Gesamtkosten bei den Kontrollen fast gleich. Die Kosten der Fälle stiegen somit im Vergleich zu den Kosten der Kontrollen überproportional an (für Vorjahreskosten adjustiertes CR = 1,6 [1,5-1,7]). Mehrkosten entfielen primär auf stationäre Kosten.

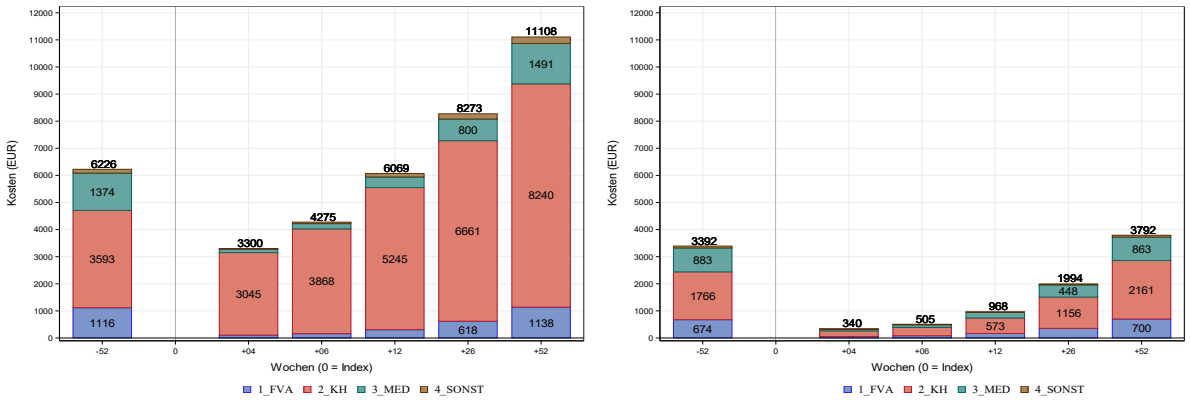

Abbildung 2: Abbildung 3: Aufteilung der kumulativen Gesamtkosten auf die Kostenkomponenten (ambulant (FVA), stationär (KH), Arzneimittel (Med), Sonstige (Krankengeld und Rehabilitation in Euro)) für Fälle (links) und Kontrollen (rechts). Entnommen aus dem Abschlussbericht zum Projekt *Beckenfrakturen in der älteren und betagten Bevölkerung.* Daten enthalten in (Andrich et al. 2021). Abdruck mit freundlicher Genehmigung von Springer Nature.

Im Zeitverlauf zeigten die adjustierten Modelle insgesamt, für stationär und ambulante behandelte sowie für schwere und leichte Beckenfrakturen hohe Mehrkosten: Die CRs sanken von 10,7 [10,2-11,1] innerhalb der ersten 4 Wochen auf 1,3 [1,2-1,4] innerhalb der Woche 49-52. Die Mehrkosten waren bei stationär behandelten Frakturen höher als bei ambulant behandelten (CRs von 13,4 [12,9-13,9] und 2,3 [2,0-2,6] in Woche 1-4). CRs sanken für schwere Beckenfrakturen von 11,9 [11,4-12,4] innerhalb der Woche 1-4 auf 1,2 [1,1-1,4] in Woche 49-52. Für leichte Beckenfrakturen lagen sie in Woche 1-4 bei 8,5 [7,9-9,1] und in Woche 49-52 bei 1,3 [1,1-1,5].

Zusammengefasst waren ein starker Anstieg der Inanspruchnahme der stationären Versorgung und deutliche Mehrkosten bei älteren Menschen im ersten Jahr nach einer Beckenfraktur im Vergleich zu einer Population ohne Beckenfraktur – letzteres sogar nach Adjustierung von relevanten Drittvariablen – festzustellen. Die Mehrkosten waren in den ersten Monaten besonders hoch und hauptsächlich auf die stationäre Behandlung zurückzuführen. Subgruppenanalysen, in denen nach Schweregrad stratifiziert wurde, ergaben, dass Mehrkosten auch für Personen mit leichten Beckenfrakturen anfielen. Die durch die Studie erzielten Ergebnisse liefern spezifische Erkenntnisse und sollten für eine angemessene Planung und Zuweisung von Ressourcen im Gesundheitswesen Berücksichtigung finden.

3.4 Nutzung von GKV-Daten zur Auswertung von Non-Response in einer Querschnittsstudie zur Rolle der Depression bei Menschen mit Diabetes

Linnenkamp, U.; Gontscharuk, V.; Brüne, M.; Chernyak, N.; Kvitkina, T.; Arend, W.; Fiege, A.; Schmitz-Losem, I.; Kruse, J.; Evers, S. M. A. A.; Hiligsmann, M.; Hoffmann, B.; **Andrich, S.**; Icks, A. (2020). Using statutory health insurance data to evaluate non-response in a cross-sectional study on depression among patients with diabetes in Germany. *Int J Epidemiol* 49 (2):629–637. geteilte Letztautorenschaft

Die vierte Arbeit kann als Beispiel für die Durchführung einer Non-Responderanalyse auf Basis von Sekundärdaten dienen. Dabei wurden Daten der Pronova BKK zur Auswertung der Nicht-Teilnahme (Non-Response) an einer Querschnitts-Befragungsstudie zu Depression bei Menschen mit Diabetes im Jahr 2013 und zur Abschätzung eines damit einhergehenden Bias verwendet. Als Studienteilnehmende kamen alle bei der Pronova BKK versicherten Personen mit Diabetes in Frage. Das Vorhandensein einer Diabetes-Erkrankung wurde nach den Kriterien von Hauner festgelegt (Hauner et al. 2003). Eine Zufallsstichprobe von 4.053 Personen wurde zur Teilnahme an der Befragungsstudie eingeladen (multi-modaler Kontaktaufbau). Von den letztlich 3.642 zulässigen Studienteilnehmende sendeten 1.860 Personen den ausgefüllten Fragebogen mit einer unterschriebenen Einverständniserklärung zurück (Rücklauf 51,1%); entsprechend gab es 1.782 Nicht-Teilnehmende (Non-Responder).

Für die Non-Responder-Analyse stellte die Pronova BKK auf individueller Ebene Daten aus dem Jahr vor der Basiserhebung (2012) sowohl für Responder als auch Non-Responder zur Verfügung, die operationalisiert und weiter aufbereitet wurden. Um Vergleiche zwischen Respondern und Non-Respondern anzustellen wurden folgende Variablen betrachtet: Alter, Geschlecht, Behandlung mit Insulin, Verwendung oraler Antihyperglykämika (OAD), Depressionsdiagnose, Anzahl der Krankenhausaufenthalte, Anzahl der verschriebenen Medikamente und Komorbiditäten (hier als Anzahl der Diagnosen aus dem sogenannten morbiditätsorientierten Risikostrukturausgleich erfasst). Neben Gruppenvergleichen wurden logistische Regressionen zur Berechnung von Odds Ratios (OR [95 %-KI]) durchgeführt, um zu prüfen, ob die genannten Variablen mit der Teilnahme assoziiert waren.

Im Regressionsmodell zeigte sich für die Anzahl der verschriebenen Medikamente (OR 1,29 [1,10-1,51]), eine Behandlung mit Insulin (OR 1,73 [1,36-2,21]), eine Behandlung mit OAD (OR 1,77 [1,49-2,09]) und eine Behandlung sowohl mit Insulin als auch OAD (OR 1,91 [1,51-2,43]) ein Zusammenhang mit der Teilnahme. Eine Depressionsdiagnose (OR 0,99 [0,82-1,2]), die

Anzahl der Komorbiditäten (1,17 [1,00-1,37]) und die Anzahl der Krankenhauseinweisungen (1,09 [0,93-1,28]) waren nicht mit der Teilnahme assoziiert. Für Frauen war die Chance an der Studie teilzunehmen geringer als für Männer (0,72 [0,58-0,88]). Personen jünger als 50 Jahre hatten eine geringere Chance teilzunehmen (0,53 [0,39-0,73]). Allerdings ließ sich eine Interaktion zwischen Geschlecht und Altersgruppe für die Gruppe der Personen unter 50 Jahren beobachten (β=0,68 mit p-Wert 0,01): Frauen, die jünger als 50 Jahre waren, schienen etwas häufiger teilzunehmen als Männer derselben Altersgruppe.

Abschließend lässt sich zusammenfassen, dass die Analysen Unterschiede in Bezug auf Alter, Geschlecht, Diabetesbehandlung und Medikamenteneinnahme zwischen Respondern und Non-Respondern verdeutlichten, die die Ergebnisse der Studie verfälschen könnten. Die identifizierten Merkmale können je nach Fragestellung in zukünftigen Auswertungen berücksichtigt werden (z.B. durch Adjustierung im Rahmen von Zusammenhangsanalysen). Responder und Non-Responder unterschieden sich nicht hinsichtlich des Vorhandenseins einer Depression, dem Hauptoutcome der DiaDec-Studie. Dies ist ein wichtiges Ergebnis, da ein Bias, der das interessierende Outcome betrifft, kritisch auszulegen wäre. Grundsätzlich ist festzuhalten, dass die Nutzung von GKV-Daten im Rahmen einer Non-Responderanalyse wesentliche Vorteile aufweist, da die Bewertung einer potentiellen Verzerrung durch Non-Response umfassend erfolgen kann und Angaben auch für Subgruppen vorliegen, die möglicherweise nicht an einer Studien teilnehmen würden. Bei der Durchführung ähnlicher Studien sollte ein solches Vorgehen konzeptionell bedacht werden.

3.5 Datenlinkage – Gegenüberstellung von verschiedenen Methoden zur Erfassung einer depressiven Störung bei Menschen mit Diabetes mittels Verknüpfung von Befragungs- und longitudinalen GKV-Daten

Linnenkamp, U.; Gontscharuk, V.; Ogurtsova, K.; Brüne, M.; Chernyak, N.; Kvitkina, T.; Arend, W.; Schmitz-Losem, I.; Kruse, J.; Hermanns, N.; Kulzer, B.; Evers, S. M. A. A.; Hiligsmann, M.; Hoffmann, B.; Icks, A.; Andrich, S. (2023). PHQ-9, CES-D, health insurance data-who is identified with depression? A Population-based study in persons with diabetes. *Diabetol Metab Syndr* 15 (1):54. geteilte Letztautorenschaft

Die fünfte für die Habilitationsschrift berücksichtigte Arbeit thematisiert die Erfassung einer depressiven Störung bei Menschen mit Diabetes mithilfe von verschiedenen Methoden sowie die Charakterisierung der identifizierten Populationen. Bei der zugrundeliegenden Studienpopulation handelt es sich wie bei der vierten Arbeit um das Pronova BKK-Versichertenkollektiv mit Diabetes, für die im Jahr 2013 im Querschnitt Befragungsdaten erhoben und mit longitudinalen GKV-Daten verknüpft wurden, die für den Zeitraum von vier Quartalen vor und nach dem Quartal der Primärdatenerhebung vorlagen. Drei Methoden wurden zur Identifizierung einer depressiven Störung eingesetzt: die Centre for Epidemiological Studies Depression Scale (CES-D), der Patient Health Questionnaire-9 (PHQ-9) und das Heranziehen von spezifischen Depressionsdiagnosen aus GKV-Daten.

Für 1.308 Personen waren vollständige Daten vorhanden. Auf Basis der durch die Methoden erzielten Ergebnisse wurden die Versicherten in acht Gruppen eingeteilt: Beispielsweise wies Gruppe 1 eine depressive Symptomatik laut PHQ-9 und CES-D auf und hatte eine Diagnose in den GKV-Daten. Gruppe 8 wies weder eine depressive Symptomatik in den Fragebögen noch

eine Diagnose auf. Die anderen sechs Gruppen setzten sich aus den verschiedenen möglichen Ausprägungen (abhängig vom Vorhandensein einer depressiven Symptomatik respektive Vorliegen einer Diagnose) zusammen.

Neben deskriptiven Analysen zur Beschreibung der Studienpopulation wurden Gruppenvergleiche durchgeführt. Wir entschieden uns dafür, die Gruppe ohne Depression/depressiver Symptomatik (d. h. Gruppe 8) als Referenzgruppe zu wählen. Dadurch konnten wir in einem Many-to-One-Ansatz einen Vergleich der sieben Gruppen, die eine depressive Störung aufwiesen, mit der Referenzgruppe vornehmen. Die Gruppenzugehörigkeit wurde durch eine multinomiale logistische Regression (Schätzung von Odds Ratios) dargestellt, bei der die logarithmische Wahrscheinlichkeit, zu einer Gruppe zu gehören, im Vergleich zur Referenzgruppe als lineare Kombination von Einflussvariablen modelliert wurde. In das endgültige Modell gingen folgende Einflussvariablen ein: Alter, Geschlecht, Insulineinnahme, frühere Depression, Einnahme von Antidepressiva, Anzahl der Komorbiditäten, gesundheitsbezogene Lebensqualität (HRQoL) und der sogenannte PAID-Score (Problem Areas in Diabetes). Diese wurden entweder auf Basis der GKV-Daten abgeleitet oder waren selbstberichtete Angaben (HRQoL und PAID).

Eine depressive Störung/Depression wurde unter Verwendung mindestens einer der genannten Methoden bei knapp einem Drittel (n=521, 33,0 %) unserer Analysestichprobe identifiziert. Mit allen Methoden wurden 79 Personen (5,0 %) als depressiv identifiziert (s. Abbildung 3).

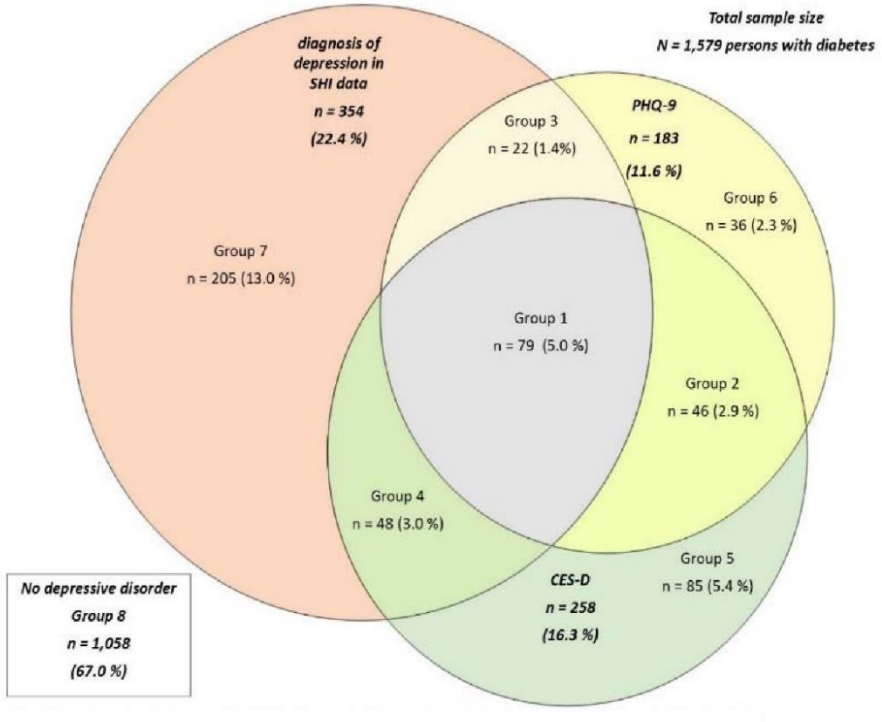

Abbildung 4: Venn Diagramm zur Darstellung der resultierenden Gruppenbildung auf Basis der mit verschiedenen Methoden identifizierten Personen aus (Linnenkamp et al. 2023). Abdruck mit freundlicher Genehmigung von Springer Nature.

In den multivariaten Analysen (logistischen Regressionen) ließen sich Unterschiede zwischen den unabhängigen Variablen und der Gruppenzugehörigkeit beobachten, die mit der gewählten Methode zur Identifizierung einhergehen könnten. Beispielsweise war die Wahrscheinlichkeit einer Person, die Antidepressiva einnahm, im Vergleich zu einer Person, die keine Antidepressiva einnahm, 12-mal (bzw. 9-, 8- und 7-mal) höher zur Gruppe 3 (Gruppe 1, 7 bzw. 4) zu gehören (die korrespondierenden Odds Ratios (OR) waren 12,00, 8,94, 8,31 bzw. 7,25). Alle diese Gruppen weisen eine Diagnose in den GKV-Daten auf. Im Gegensatz dazu waren die Wahrscheinlichkeiten für die Zugehörigkeit zu den übrigen Gruppen (ohne GKV-Diagnose) für eine Person, die Antidepressiva einnahm, im Vergleich zu einer Person, die keine Antidepressiva einnahm, deutlich geringer und für die Gruppen 5 und 6 (nur depressive Symptomatik gemäß CES-D und PHQ-9) nicht signifikant. Ein recht ähnliches Muster zeigte sich auch für die Variablen frühere Depression und Anzahl der Komorbiditäten (die ebenfalls beide anhand von GKV-Daten operationalisiert wurden und in den Gruppen mit GKV-Diagnose wahrscheinlicher waren). Zudem waren Frauen häufiger in der Gruppe mit alleiniger GKV-Diagnose (Gruppe 7) vertreten als in der Referenzgruppe. Hinsichtlich des Alters ließ sich beobachten, dass die Wahrscheinlichkeit in die Referenzgruppe (Gruppe ohne Depression) zu gehören mit dem Alter zunahm. Dieses Ergebnis war für die Gruppen mit GKV-Diagnose signifikant. Im Hinblick auf die Wahl der Methode zeigte sich ein analoges Muster für die Gruppen, die keine GKV-Diagnose aufwiesen. Für die gesundheitsbezogene Lebensqualität – und hier insbesondere für den psychischen Summenscore – deutete sich an, dass Personen mit niedrigeren psychischen Summenscore-Werten eine höhere Wahrscheinlichkeit hatten, zu den Gruppen zu gehören, bei denen die depressive Symptomatik sowohl durch den PHQ-9 als auch durch den CES-D belegt wurden (Gruppe 1 und 2). Ferner unterschieden sich diejenigen Personen, die nur anhand einer Diagnose in den GKV-Daten identifiziert wurden, in ihrer HRQoL nicht von denjenigen, die keine Depression hatten (Referenzgruppe). Die Ergebnisse zum PAID-Score erlauben eine ähnliche Auslegung.

Als Fazit lässt sich konstatieren, dass die verschiedenen Methoden nicht dieselben Personen mit depressiver Störung identifizierten. Obwohl es Überschneidungen gab, fielen diese gering aus. Das bedeutet im Umkehrschluss, dass je nach verwendeter Methode bestimmte Personen übersehen werden könnten. Letztlich konnte kein klares Muster zwischen den Charakteristika der identifizierten Personen und den verwendeten Methoden festgestellt werden, wenngleich Zusammenhänge mit individuellen und klinischen Merkmalen sichtbar waren. Zudem ergaben sich Hinweise darauf, dass die Wahl der Methode mit spezifischen zugrundeliegenden Merkmalen in der untersuchten Population einhergehen könnte.

Bezugnehmend auf unsere Ergebnisse sollten weitere Studien auf Basis größerer Datensätze durchgeführt werden, um diese zu überprüfen und perspektivisch Empfehlungen abzuleiten, welches Screening-Instrument für welchen Zweck geeignet erscheint. Darüber hinaus stärkt unsere Studie die Anwendung des Datenlinkages bei methodischen Fragestellungen.

4. Diskussion

4.1 Zusammenfassung

Die in dieser Habilitationsschrift vorgestellten Arbeiten belegen, dass GKV-Daten sowohl zur Schätzung der Inzidenz von Ereignissen und Mortalität nach Ereignissen herangezogen werden können als auch zur Bewertung der medizinischen Leistungsinanspruchnahme der Versichertenpopulation und der damit einhergehenden Kosten. Darüber hinaus lassen sich durch die Verknüpfung von verschiedenen Datenquellen (Datenlinkage) gewinnbringende Synergieffekte erzielen. Es wurde demonstriert, dass GKV-Daten in Studien, in denen eine Verknüpfung mit Daten aus Primärerhebungen stattfindet, ideal für die Analyse der Non-Response geeignet sind, da sie Angaben sowohl für Teilnehmende als auch Nicht-Teilnehmende enthalten, die sich in den Primärdaten nicht oder nur stark eingeschränkt wiederfinden. Zudem ist es möglich, Informationen, die in den verschiedenen Datenquellen enthalten sind – beispielsweise zum Vorliegen einer Erkrankung (hier Depression) –, gegenüberzustellen, um einen Erkenntnisgewinn zu erlangen.

Die vorgestellten Arbeiten erweitern zum einen durch ihre methodische Herangehensweise, d.h. die Nutzung umfangreicher GKV-Daten verschiedener Krankenkassen und des Datenlinkages von GKV- und individuell erhobenen Befragungsdaten, und zum anderen durch die erbrachten Ergebnisse den Wissensstand der *Alterstraumatologischen Versorgungsforschung* ebenso wie den Forschungsstand zur *psychischen Komorbidität des Diabetes*. Die Arbeiten zeigen, dass die Nutzung von GKV-Daten und ihre Verknüpfung mit Befragungsdaten zur Beantwortung epidemiologischer, versorgungsbezogener und methodischer Fragestellungen sehr vielfältig, gut handhabbar und erkenntnisorientiert möglich ist. Wichtig ist dabei das Wissen um die Dateninhalte, die Datenqualität, die Möglichkeiten der Operationalisierung und Datenaufbereitung sowie die Anwendung statistischer Methoden zur Auswertung.

4.2 Stärken und Limitationen von GKV-Daten

Die grundsätzlichen Stärken bei der Nutzung von GKV-Daten, die auch für die vorgestellten Arbeiten zutrafen, liegen in der umfassenden sektorübergreifenden, längsschnittlichen, personenbezogenen sowie populationsbasierten Datenbasis und den damit einhergehenden ausreichenden Fallzahlen, die es erlauben valide Schätzungen epidemiologischer Maßzahlen zu erhalten. Zudem ist es aufgrund der vorliegenden Daten möglich, die untersuchten Ereignisse (hier waren es Beckenfrakturen und Diabetes) sehr genau zu erfassen, Leistungsinanspruchnahme und Kosten umfänglich darzustellen und viele weitere Drittvariablen, wie zum Beispiel Komorbidität, zu berücksichtigen (Schubert et al. 2008; Hoffmann et al. 2008b; Glaeske et al. 2009; Swart et al. 2014a). Durch die Verwendung von GKV-Daten im Rahmen der Non-Responderanalyse ergibt sich ein Datensatz mit vorliegenden Angaben zu allen Personen, die für die Teilnahme an einer Studie in Frage kommen. So können die vorliegenden Daten zur Beschreibung der gesamten Stichprobe der eingeladenen Personen im Hinblick auf demografische Merkmale, aber auch im Hinblick auf relevante gesundheitsbezogene Merkmale, die für viele Studien von primärem Interesse sind, herangezogen werden.

Bei der Nutzung von GKV-Daten waren für die zugrundeliegenden Arbeiten die folgenden Limitationen zu berücksichtigen, die auch für zukünftige Projekte zu beachten sind: Die GKV-Daten enthielten neben den Diagnosen für Beckenfrakturen keine Angaben zum Ausmaß der assoziierten Traumata oder zu den Ursachen der Verletzungen. Bezüglich der Arbeiten zur psychischen Komorbidität ist zu beachten, dass nur allgemein das Vorhandensein von depressiver Störung/Depression analysiert wurde, jedoch nicht zwischen den verschiedenen Arten von Depressionen unterschieden werden konnte, die sich zwischen den Befragten und denjenigen, die nicht an der Studie teilgenommen haben, unterschiedlich dargestellt haben könnten. Zudem sind in GKV-Daten keine klinischen Daten oder Angaben zu Gewicht, Rauchen, zum Alkoholkonsum, zu körperlicher Aktivität, zur Ernährung, zur Bestimmung der sozialen Schichtzugehörigkeit oder zu patienten-berichtete Angaben (PROs) bzw. subjektiven Einschätzungen enthalten, was die Darstellung der Studienpopulationen und die Interpretation der Ergebnisse einschränken könnte (Schubert 2022; Schubert et al. 2008; Glaeske et al. 2009).

Grundsätzlich wichtig ist es, sich zu vergegenwärtigen, dass es sich um Abrechnungsdaten handelt, die genau zu diesem Zweck erhoben werden. Das bedeutet konkret, dass nicht bei der GKV abrechenbare Leistungen, wie z.B. selbständig gekaufte Arzneimittel oder Medikamentengabe im stationären Sektor, nicht in den Daten enthalten sind. Vielmehr gelten die Aussagen für die Versicherten-Population, die das Gesundheitssystem in Anspruch genommen hat. Auch Erkrankungen, die unterdiagnostiziert sind, wie Stewart et al. (2021) es zum Beispiel für Migräne berichten, sind aus den Daten nicht umfänglich zu entnehmen (Stewart et al. 2021). Des Weiteren ist zu bedenken, dass es möglicherweise zu Abrechnungsstrategien oder Kodierfehlern kommen könnte (Glaeske et al. 2009; Schubert et al. 2008; Hoffmann et al. 2008b). Eine Prüfung der Datenqualität sowie die Durchführung von Studien zur internen oder externen Validierung sollen diesen Limitationen entgegenwirken und Aufschluss über die Vollständigkeit, Richtigkeit und Eignung der Daten geben (Hoffmann et al. 2008a; Horenkamp-Sonntag et al. 2014b). Bei der internen Validierung werden die zu hinterfragenden Dateninhalte (z.B. Diagnosen) mit anderen in den GKV-Daten enthaltenen Angaben gegenübergestellt bzw. ergänzt (s. Diabetes-Algorithmus, Originalpublikation 4). Die interne Validierung gilt als „deutlich weniger aufwendig, aber z.T. «reduziert» valide“ (Horenkamp-Sonntag et al. 2014b, S. 318). Externe Validierungsstudien basieren neben der Berücksichtigung von GKV-Daten als Grundlage auf weiteren Datenquellen, wie beispielsweise Arzneimitteldaten, Patientenakten, Krankenhausentlassungsbriefen, radiologischen Befunden (z.B. zur möglichen Validierung von Fraktur-Diagnosen) oder Arzt- und Patientenbefragungen (wie im vorliegenden Fall zur Erfassung depressiver Symptomatik), die den zu hinterfragenden Inhalten in GKV-Daten gegenübergestellt werden. Externe Validierungsstudien sind somit Studien, die ein Datenlinkage erfordern. Sie werden als „max. aufwendig, aber «höchst» valide“ beschrieben (Horenkamp-Sonntag et al. 2014b, S. 318).

Für viele mit GKV-Daten durchgeführte Analysen greift die Problematik der Linkszensierung, die dadurch zustande kommt, dass es einen definierten Beginn des Beobachtungszeitraums oder der jeweilige Versicherungszeit gibt und Daten nicht rückwirkend in der Lebenszeitperspektive ausgewertet werden können. Aussagen über Diagnosen oder Ereignisse vor Beginn des Beobachtungszeitraums bzw. der jeweiligen Versicherungsperiode sind somit nicht möglich. Es wäre daher denkbar, dass es sich nicht um ein erstes Ereignis,

sondern ein Folgeereignis (z.B. eine Folgebehandlung eines vorausgegangenen Ereignisses außerhalb des Beobachtungszeitraums) im Beobachtungszeitraum handelt, so dass die Gefahr der Überschätzung von Ereignissen vor allem zu Beginn des Beobachtungszeitraums besteht (Wagner 2014). Für die Auswertung von Inzidenzen im Beobachtungszeitraum können deshalb verschiedene Annahmen getroffen werden, z.B. Ansetzung eines ereignisfreien Zeitintervalls als Grundbedingung oder Erfassung von ersten Ereignisse pro Person pro Jahr, um diese Limitation zu adressieren (Abbas et al. 2012; Claessen et al. 2018).

Ebenso ist die Frage der Übertragbarkeit der Studienergebnisse für alle GKV-Datenanalysen relevant. Wenn beispielsweise wie in den Arbeiten dieser Schrift nur Personen einer GKV an der Studie teilnehmen, könnte dies die Ergebnisse beeinflussen, da diese bestimmte Merkmale aufweisen könnten, die sich von anderen Populationen unterscheiden. In diesem Zusammenhang ist zu berücksichtigen, dass bereits beschrieben wurde, dass Versicherte der AOK nicht repräsentativ für die gesamte deutsche Bevölkerung sind (Hoffmann und Icks 2012). So ließ sich in der Studie von Hoffmann und Icks aus dem Jahr 2012 beobachten, dass sie im Vergleich zu Mitgliedern anderer Krankenkassen (hier wurden sowohl GKV als PKV eingeschlossen) älter und häufiger sozial benachteiligt sind. Im Hinblick auf die Prävalenz chronischer Erkrankungen zeigten die Daten erhebliche Unterschiede zwischen den verschiedenen Krankenkassen. Um Unterschiede in den Populationen auszugleichen bzw. Abweichungen zu bereinigen, wird in der Regel eine Alters- und Geschlechtsstandardisierung auf die deutsche Bevölkerung vorgenommen. Nichtsdestotrotz muss die Verallgemeinerbarkeit der Ergebnisse für andere Bevölkerungsgruppen hinterfragt werden, wenn Daten nur einer GKV vorliegen.

4.3 Stärken und Limitationen des Datenlinkages

Ein wesentlicher Vorteil der Verknüpfung von GKV- mit Befragungsdaten ist die Möglichkeit der detaillierteren Beschreibung (hier der identifizierten Personen mit depressiver Störung/Depression), die bei Verwendung nur einer der beiden Datenquellen begrenzt wäre, da Angaben fehlen oder nicht vollständig in einer Datenquelle enthalten sind. Aufgrund einer Verknüpfung lassen sich selbstberichtete Angaben mit Abrechnungsdaten für ein vollständigeres Bild kombinieren und somit fehlende Angaben ergänzen, aber auch gegenseitig validieren. Dadurch kann eine Einschätzung beispielsweise zur Nutzbarkeit der Daten gewonnen werden. Weitere Vorteile sind, dass durch ein Datenlinkage der Befragungsaufwand minimal gehalten und dem Prinzip der Datensparsamkeit Folge geleistet werden kann (Stallmann et al. 2015; Glaeske et al. 2009).

Im Hinblick auf die im Rahmen dieser Habilitationsschrift vorgestellte Arbeit zum Datenlinkage ist konkret als Limitation zu benennen, dass eine Diskrepanz bezüglich des entsprechenden Zeitpunkts der Erhebung der vorliegenden Angaben, die gegenübergestellt wurden, existiert. So wurden die Befragungsdaten zur depressiven Symptomatik im Querschnitt (im Jahr 2013) erhoben, während die GKV-Daten für den Zeitraum von vier Quartalen vor und nach dem Quartal der Primärdatenerhebung (insgesamt neun Quartale) vorlagen und somit den gesamten Studienzeitraum abdeckten. Dies kann als eine Erklärung herangezogen werden, warum die in den GKV-Daten beobachtete Prävalenz der Depression höher ist als die durch die Screening-Instrumente ermittelte Prävalenz. Eine weitere Diskrepanz könnte sich

hinsichtlich der Aussagekraft der erhobenen Angaben ergeben, da die Ergebnisse der CES-D und des PHQ-9 keine klinischen Diagnosen darstellen, sondern Ergebnisse eines Screenings für depressive Symptomatik sind und eine Diagnose in den GKV-Daten nicht als Screening-Ergebnis zu verstehen ist.

Ganz allgemein betrachtet besteht die größte Herausforderung eines individuellen Datenlinkages – externe Validierungsstudien eingeschlossen – im Aufwand, der dafür betrieben werden muss, beispielsweise hinsichtlich der datenschutzrechtlichen Grundlagen (insbesondere bei einem personenbezogenen Datenlinkage), finanzieller und personeller Ressourcen sowie der Planung und Durchführung des Projektes (March et al. 2019; March et al. 2014b; Stallmann et al. 2015). Insbesondere bei den Abstimmungen zum Datenfluss – z.B. welche Datenbestände gibt es, wer erhält welche Daten und wo werden Daten verknüpft – und ggf. der Einrichtung einer Vertrauensstelle handelt es sich um wichtige datenschutzrechtliche und organisatorische Aspekte, die nicht zu unterschätzen sind (March et al. 2019). Grundlegend kommt der Verknüpfung der Datenquellen anhand eindeutiger Schlüsselvariablen und der korrekten Umsetzung bzw. Fehleranfälligkeit des Linkageverfahrens eine entscheidende Rolle zu. Aus diesem Grund werden Arten des Datenlinkages beschrieben und die Machbarkeit der Verknüpfung überprüft (March et al. 2018; March et al. 2019; Druschke et al. 2020; Bobeth et al. 2023; Domhoff et al. 2022). Ferner ist zu bedenken, dass zunächst die Limitationen der jeweiligen zu verknüpfenden Datenquelle gelten, die dann durch das Linkage ausgeglichen werden sollen. Es gibt aber auch Limitationen, die dann ebenso für Datenlinkagestudien greifen könnten, wie beispielsweise ein Selektionsbias hinsichtlich der Zustimmung zur Verknüpfung personenbezogener Daten auf Basis von Einverständniserklärungen (March et al. 2019; Stallmann et al. 2017; Hutchings et al. 2021; Weissman et al. 2016).

5. Schlussfolgerung und Ausblick

Die vorliegende Habilitationsschrift widmet sich zentralen Fragen der Epidemiologie und der Versorgungsforschung. Dabei liegt der Fokus auf der Nutzung von GKV-Daten und ihrer Verknüpfung. Im Rahmen dieser Habilitationsschrift wird untermauert, dass GKV-Daten für vielfältige Fragestellungen herangezogen werden können. Die Möglichkeiten der Nutzung werden aufgezeigt und es wird Anschlusspotential für ähnliche oder weiterführende Fragestellungen angeboten. Es ist davon auszugehen, dass die Nutzung von GKV-Daten zukünftig – auch durch die Bereitstellung eines umfassenden Datenpools von GKV-Daten durch das Forschungsdatenzentrum Gesundheit – noch weiter ausgebaut wird. Des Weiteren besteht auch zukünftig ein Bedarf an externen Validierungsstudien, da sie spezifisch für die jeweilige Fragestellung unternommen werden sollten. Darüber hinaus wird das Datenlinkage zunehmend an Bedeutung gewinnen. Es erscheint für die Versorgungsforschung unerlässlich, da relevante Fragestellungen, die sowohl auf patientenberichtete Outcomes als auch auf Versorgungsprozesse und -outcomes abzielen, auf Basis des Datenlinkages bestmöglich untersucht werden können. Perspektivisch können neue Quellen für Sekundärdatenanalysen erschlossen werden, beispielsweise Daten aus der Telemedizin, dem Telemonitoring, Gesundheitsapplikationen oder digitale Gesundheitsanwendungen (Slagman et al. 2023), die durch eine Verknüpfung mit weiteren Datenquellen zu einem umfassenderen Verständnis im Rahmen der gesundheitswissenschaftlichen Forschung beitragen können.

Die vorliegende Habilitationsschrift unterstreicht den Wert von Sekundärdaten für die Epidemiologie und für die Versorgungsforschung. Durch die Bandbreite der in den vorgestellten Arbeiten beleuchteten Forschungsfragen und die eingängige Schilderung ihrer methodischen Umsetzung erweitert die Habilitationsschrift den bisherigen inhaltlichen wie auch methodischen Kenntnisstand. Sie trägt zu einem tiefergehenden Verständnis bei, wie insbesondere GKV-Daten und ihre Verknüpfung genutzt werden können, um epidemiologische, versorgungsbezogene und methodische Fragestellungen zu beantworten. Auch wenn weitere Forschung notwendig bleibt, sind die Arbeiten der Habilitationsschrift – insbesondere vor dem Hintergrund, dass die Nutzung von bereits vorliegenden umfassenden GKV-Daten und das individuelle Datenlinkage auch in Zukunft eine elementare Rolle im Forschungsprozess spielen werden – ein wertvoller Beitrag für das Forschungsfeld.

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7. Abbildungsverzeichnis

8. Abkürzungsverzeichnis

AGENS	Arbeitsgruppe Erhebung und Nutzung von Sekundärdaten
ATC	Anatomisch-Therapeutisch-Chemische Klassifikation
BMBF	Bundesministerium für Bildung und Forschung
CES-D	Center of Epidemiological Studies-Depression Scale
CR	Cost Ratios
DDD	verordnete Tagesdosis (Defined Daily Dose)
DIMDI	Deutsches Institut für Medizinische Dokumentation und Information
DGEpi	Deutsche Gesellschaft für Epidemiologie
DGSMP	Deutsche Gesellschaft für Sozialmedizin und Prävention
DMP	Disease-Management-Programm
DSG	Datenschutzgesetz
DSGVO	Datenschutz-Grundverordnung
DSM	Diagnostisches und Statistisches Manual Psychischer Störungen
DVG	Digitale-Versorgung-Gesetz
EBM	Einheitlicher Bewertungsmaßstab
FKZ	Förderkennzeichen
G-BA	Gemeinsamer Bundesausschuss
GEP	Gute Epidemiologische Praxis
GKV	Gesetzliche Krankenversicherung
GPD	Gute Praxis Datenlinkage
GPS	Gute Praxis Sekundärdatenanalyse
HR	Hazard Ratios
HRQoL	Gesundheitsbezogene Lebensqualität (Health-Related Quality of Life)
ICD	Internationale statistische Klassifikation der Krankheiten und verwandter Gesundheitsprobleme
InEK	Institut für das Entgeltsystem im Krankenhaus
IR	Inzidenzrate
KI	Konfidenzintervall
OPS	Operationen- und Prozedurenschlüssel

OR	Odds Ratios
PAID	Problem Areas in Diabetes
PHQ-9	Patient Health Questionnaire-9
PJ	Personenjahre
PRO	patienten-berichtete Angaben (Patient-reported Outcomes)
PZN	Pharmazentralnummer
RKI	Robert Koch-Institut
RR	Relatives Risiko
SCID	Strukturiertes Klinisches Interview
SGB	Sozialgesetzbuch
Zi	Zentralinstitut für die kassenärztliche Versorgung in der Bundesrepublik Deutschland

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10. Eidesstattliche Erklärung

Hiermit erkläre ich, Dr. Silke Brunhild Andrich, geboren am 12.11.1979 in Düsseldorf, an Eides statt, dass

- Die von mir vorgelegte schriftliche Habilitationsleistung eigenständig und nur unter Verwendung der angegebenen Hilfsmittel und Quellen angefertigt wurde;
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- An keiner anderen Hochschule ein Habilitationsverfahren von mir eingeleitet oder erfolglos beendet wurde.

Düsseldorf, den 27.08.2023 Dr. rer. medic. Silke Brunhild Andrich

11. Anlagen Originalarbeiten

Der Anhang der eigenen Originalarbeiten erfolgt mit freundlicher Genehmigung der Verlage.

Originalarbeit 1

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RESEARCH ARTICLE

Epidemiology of Pelvic Fractures in Germany: Considerably High Incidence Rates among Older People

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Abstract

Epidemiological data about pelvic fractures are limited. Until today, most studies only analyzed inpatient data. The purpose of this study was to estimate incidence rates of pelvic fractures in the German population aged 60 years or older, based on outpatient and inpatient data. We conducted a retrospective population-based observational study based on routine data from a large health insurance company in Germany. Age and sex-specific incidence rates of first fractures between 2008 and 2011 were calculated. We also standardized incidence rates with respect to age and sex in the German population. Multiple Poisson regression models were used to evaluate the association between the risk of first pelvic fracture as outcome and sex, age, calendar year and region as independent variables. The total number of patients with a first pelvic fracture corresponded to 8,041 and during the study period 5,978 insured persons needed inpatient treatment. Overall, the standardized incidence rate of all first pelvic fractures was 22.4 [95% CI 22.0–22.9] per 10,000 person-years, and the standardized incidence rate of inpatient treated fractures 16.5 [16.1–16.9]. Our adjusted regression analysis confirmed a significant sex (RR 2.38 [2.23–2.55], $p < 0.001$, men as reference) and age effect (higher risk with increasing age, $p < 0.001$) on first fracture risk. We found a slight association between calendar year (higher risk in later years compared to 2008, $p = 0.0162$) and first fracture risk and a further significant association with region (RR 0.92 [0.87–0.98], $p = 0.006$, Westfalen-Lippe as reference). The observed incidences are considerably higher than incidences described in the international literature, even if only inpatient treated pelvic fractures are regarded. Besides which, non-inclusion of outpatient data means that a relevant proportion of pelvic fractures are not taken into account. Prevention of low energy trauma among older people remains an important issue.

role in study design, data collection and analysis, decision to publish, or preparation of the manuscript. The AOK NORDWEST was responsible for the salary for Elke Neuhaus and Kathrin Neidert, but did not have any additional role in the study design, data collection and analysis, decision to publish, or preparation of the manuscript. mediStatistica was responsible for the salary for Burkhard Haastert, but did not have any additional role in the study design, data collection and analysis, decision to publish, or preparation of the manuscript. The specific roles of these authors are articulated in the 'author contributions' section.

Competing Interests: The authors have the following interests: Elke Neuhaus and Kathrin Neidert are employed by AOK NordWest, and Burkhard Haastert by mediStatistica. There are no patents, products in development or marketed products to declare. This does not alter the authors' adherence to all the PLoS ONE policies on sharing data and materials.

Introduction

Pelvic fractures are one of the main results of low energy trauma such as falls, particularly in older individuals [1–4]. Due to the increase of the older population worldwide [5] the burden of pelvic fractures will become highly relevant for society in general and in particular for our healthcare systems. Consequently, low energy fractures are assumed to affect a growing number of individuals and an increase of pelvic fracture incidences has already been reported [3, 6–10]. Pelvic fractures are associated with significant morbidity and mortality [2, 11–13]; for instance, one year mortality after pelvic fractures is reported to be fairly substantial, ranging from about 8%-27% [2, 11, 12, 14, 15]. In addition, pelvic fractures will result in rising healthcare costs due to the requirement of hospital and follow-up care [7, 16–18]. In comparison to hip fractures, which have been thoroughly investigated, pelvic fractures have as yet only been analyzed to some extent. Even more striking, incidences of pelvic fractures show opposing trends in the older population compared with rates of hip fractures: while absolute numbers of hip fractures increase due to the aging of the population, age-standardized incidence rates are levelling off or even declining in a number of countries [19–23]. In contrast, age-standardized rates of pelvic fractures have also been found to increase in the last decades. There is sufficient evidence that incidences of pelvic fractures increase with age and are more common in women than in men. However, most of the available studies have focused on inpatient data, e.g. hospital admission or discharge diagnoses, but it can be assumed that a significant proportion of individuals with pelvic fracture are treated as outpatients [12, 24, 25]. Furthermore, most studies had no access to individual patient data and hence could not avoid double counting which may occur not only due to further fractures, but also due to hospital changes or readmissions because of complications. The aim of this study was to estimate incidence rates of pelvic fractures in the German population aged 60 years or older based on outpatient and inpatient data from a statutory health insurance. We further evaluated the association between the risk of first pelvic fracture as the dependent variable and sex, age, calendar year and region as independent variables.

Methods

Ethics Statement

The study was approved by the ethics committee of the Faculty of Medicine, Heinrich-Heine University Düsseldorf. The survey and utilization of secondary health administration data was conducted retrospectively and in compliance with the applicable standards and legal rules on data protection. All procedures performed were in accordance with the Declaration of Helsinki and comparable ethical standards (e.g., Good Epidemiologic Practice (GEP) [26] and Good Practice of Secondary Data Analysis (GPS) [27]). The data were analyzed anonymously; informed patient consent is not required.

Study Design, data source and population

The study is a retrospective population-based observational study. Routine data for outpatient and inpatient care was provided by a large statutory health insurance company in Germany, the AOK NordWest. Overall, the AOK NordWest covers about 2.8 million insured people in two regions Schleswig-Holstein (700,000 insured) and Westfalen-Lippe (2.1 Million insured), of whom about 29% count 60 years or older. We included all people aged minimum 60 years who were continuously insured for at least one year between January 1, 2007 and December 31, 2011. The selection process is presented in detail below. Most persons were insured during the whole study period with the AOK NordWest.

Ascertainment of pelvic fracture events

Pelvic fractures along with the exact date of occurrence were identified in inpatient and outpatient data according to the 10th revision of the International Classification of Diseases (ICD-10). A fracture event is defined by the ICD 10 codes S32.1 (fracture of sacrum), S32.2 (fracture of coccyx), S32.3 (fracture of ilium), S32.4 (fracture of acetabulum), S32.5 (fracture of pubis), S32.81 (fracture of ischium), S32.83 (fracture of pelvis unspecified) and S32.89 (multiple and other fractures of pelvis). Only first fractures defined by an event-free period of at least one year prior to the event were included. Therefore, data for insured persons with pelvic fractures in the first study/observation year were excluded. Furthermore, data of insured persons with first fractures marked as a follow-up diagnosis of a former fracture were excluded. For the ascertainment of first fractures we distinguished between exclusively outpatient and at some point inpatient treated fractures. First pelvic fractures, which led to hospital treatment during the whole study period, were counted as inpatient treated pelvic fractures. The decision for this classification was made with regard to the comparability to the international literature, which relies mostly on inpatient databases.

Ascertainment of person-years

We calculated person-years for the individual observation periods. Person-years were summed up for all insured persons aged minimum 60 years being at risk of having a first pelvic fracture, as predefined. According to the definition, all person-years in the first year of observation were excluded. Furthermore, person-years after first pelvic fracture events were deleted. The selection process of the study population (individuals with pelvic fractures and person years) is illustrated as a flow chart in Fig 1. For the entire study population aggregated persons-times, also stratified by year, sex, age and region are provided in Table 1.

Further variables

We also assessed individual patient data, e.g. start and end of the period of insurance, month and year of birth and, if applicable, month and year of death, and included the following variables as possible predictors of a first pelvic fracture: age, sex, and insurance region as an approximation for the insured's residence (Schleswig-Holstein or Westfalen-Lippe).

Statistical analyses

Incidence rates (IR) of first pelvic fracture were calculated for the total of outpatient and inpatient events and also for inpatient treated pelvic fractures only. We estimated incidence rates (IR) per 10,000 person-years (pyrs) along with 95% confidence intervals [95% CI] by dividing the number of first fractures by the total number of person-years, overall and stratified by sex and age (5-year age groups). We also standardized incidence rates with respect to age and sex to the German population in 2009. Population data were taken from official statistics (National Office of Statistics). The association between the risk of first pelvic fracture as outcome and sex, age, calendar year and region as independent variables was examined using multiple Poisson regression, controlling for each of the aforementioned variables. We calculated estimates of relative risks (RR) along with 95% confidence intervals and corresponding p-values. To take overdispersion into account, we performed all analyses with dscale adjustment [28].

All analyses were performed using the Statistical Analysis Systems SAS (SAS for X64_8PRO, Release 9.4, SAS Institute Inc. Cary, NC, USA).

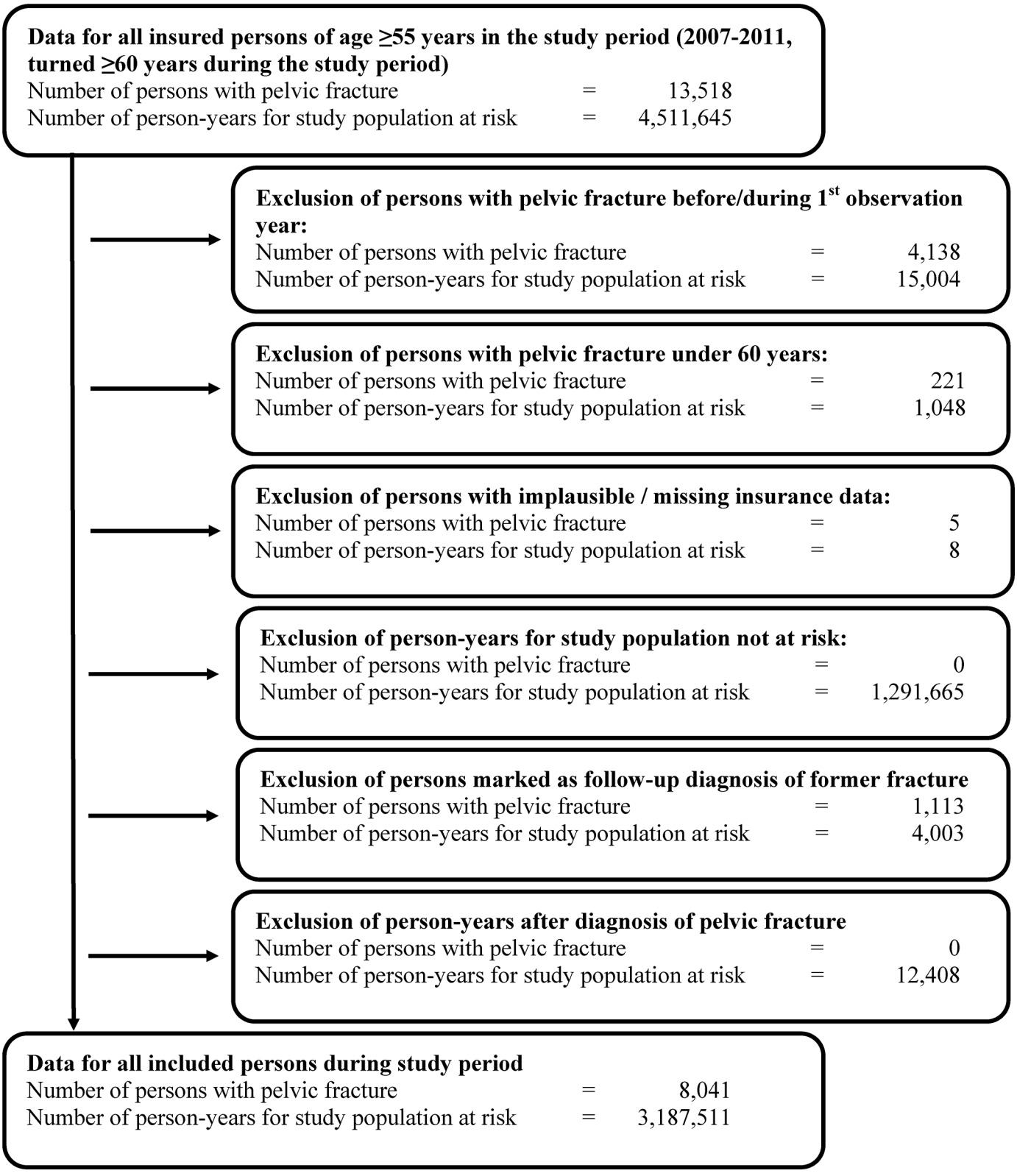

Fig 1. Selection process of the study population.

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Results

Numbers and incidence rates of all first pelvic fractures and inpatient treated pelvic fractures

During the study period, we identified 8,041 insured persons, mostly women (82%), with first pelvic fractures. The mean age of affected insured persons was 80.3 ± 8.7 years. A total of 5,978 (74%) insured persons needed inpatient care due to pelvic fracture during the whole study period. Table 2 describes selected characteristics of persons with first pelvic fractures.

Table 3 shows crude incidence rates of all first fractures identified from inpatient and outpatient data and crude incidence rates for inpatient treated fractures. The crude incidence rate of all first pelvic fractures was 25.2 [95% confidence interval 24.7–25.8] per 10,000 person-years. For inpatient treated pelvic fractures the crude incidence rate corresponds to 18.8 [18.3–19.2] per 10,000 pyrs.

Standardized incidence rates of all first pelvic fractures and inpatient treated pelvic fractures

Table 3 also displays standardized incidence rates. The standardized incidence rate of all first fractures was 22.4 [22.0–22.9] per 10,000 pyrs. It was significantly higher in women than in men: 28.7 [28.0–29.4] vs. 12.1 [11.5–12.8] per 10,000 pyrs respectively ($p < 0.001$). The standardized incidence of all inpatient treated fractures was 16.5 [16.1–16.9] per 10,000 pyrs (age standardized using the whole German population in 2009, using the same basis for women and men).

Table 1. Aggregated persons-time, also stratified by year, sex, age and region.

	Person-years at risk
Total [N (%)]	3,187,511 (100.0)
Calendar year [N (%)][a]	
2008	812,797 (25.5)
2009	798,620 (25.1)
2010	790,964 (24.8)
2011	785,129 (24.6)
Sex	
Women [N (%)]	1,879,167 (59.0)
Men [N (%)]	1,308,344 (41.0)
Age in 5-year age groups [N (%)][a]	
60–64 years	568,665 (17.8)
65–69 years	616,229 (19.3)
70–74 years	733,587 (23.0)
75–79 years	546,177 (17.1)
80–84 years	393,674(12.4)
85–89 years	228,937 (7.2)
≥90 years	100,241 (3.1)
Insured's region[b]	
Schleswig-Holstein	937,746 (29.4)
Westfalen-Lippe	2,249,764 (70.6)

N = Number of person-years

[a]small differences from rounding of person-years might occur

[b]1 insured person in both regions, at time of first fracture in Westfalen-Lippe, counted in Westfalen-Lippe

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Table 2. Characteristics of persons with first pelvic fractures.

	Persons with first pelvic fracture
Total [N (%)]	8,041 (100.0)
Women [N (%)]	6,617 (82.3)
Men [N (%)]	1,424 (17.7)
Age (yrs) [Mean, SD]	80.3±8.7
Age in 5-year age groups [N (%)]	
60–64 years	388 (4.8)
65–69 years	610 (7.6)
70–74 years	1,136 (14.1)
75–79 years	1,372 (17.1)
80–84 years	1,733(21.6)
85–89 years	1,702 (21.2)
≥90 years	1,100 (13.7)
Outpatient treatment [N (%)]	2,063 (25.7)
Insured's region[a]	
Schleswig-Holstein	2,210 (27.5)
Westfalen-Lippe	5,831 (72.5)

N = Number of participants; yrs = Years; SD = standard deviation

[a]1 insured person in both regions, at time of first fracture in Westfalen-Lippe, counted in Westfalen-Lippe

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Age- and sex-specific incidence rates of all first pelvic fractures and inpatient treated pelvic fractures

The incidence rates of all first pelvic fractures and of inpatient treated pelvic fractures, stratified by sex and age, are illustrated in Fig 2. As expected, we found higher incidence rates in women than in men. These differences were observed in all age groups, but in particular for women in the higher age groups. Incidence rates of all first pelvic fractures and inpatient treated pelvic fractures, stratified by sex and age, are also tabulated in Table 4.

Table 3. Crude and standardized pelvic fracture incidence rates: Incidence rate per 10,000 person-years at risk and [95% confidence Interval], overall and sex-specific.

Total population aged ≥ 60years				
	Number of fractures	Person-years at risk	Pelvic fractures/10,000 pyrs [95% CI]	Standardized Incidence rate[b]
All first pelvic fractures	8,041	3,187,511	25.2 [24.7–25.8]	22.4 [22.0–22.9]
Inpatient treated pelvic fractures[a]	5,978	3,187,511	18.8 [18.3–19.2]	16.5 [16.1–16.9]
Women				
All first pelvic fractures	6,617	1,879,167	35.2 [34.4–36.1]	28.7 [28.0–29.4]
Inpatient treated pelvic fractures[a]	4,937	1,879,167	26.3 [25.5–27.0]	20.7 [20.1–21.3]
Men				
All first pelvic fractures	1,424	1,308,344	10.9 [10.3–11.4]	12.1 [11.5–12.8]
Inpatient treated pelvic fractures[a]	1,041	1,308,344	8.0 [7.5–8.4]	9.0 [8.4–9.6]

CI = Confidence Interval; pyrs = Person-years

[a]First fractures leading to hospital treatment

[b]Standard: German population 2009

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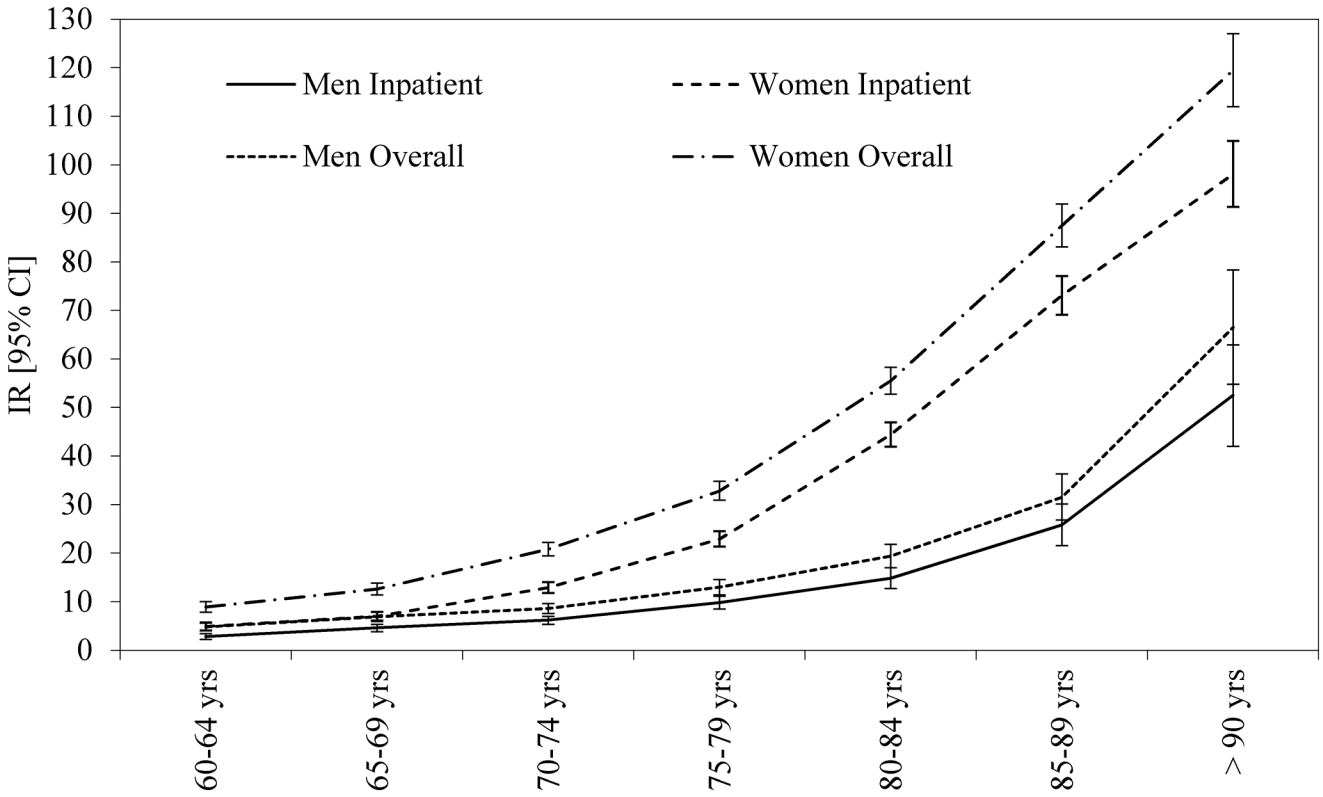

Fig 2. Age adjusted incidence rates of pelvic fractures per 10,000 pyrs in men and women 60 years or older (all first pelvic fractures and inpatient treated pelvic fractures).

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Possible predictors of a first pelvic fracture

As expected, the adjusted Poisson regression analysis showed a significant sex and age effect on first fracture risk (Table 5). Women had a considerably higher risk of first pelvic fracture than men (adjusted RR 2.38 [2.23–2.55], $p < 0.001$). The fracture risk was highest in persons aged 90 years or older (compared to those aged 60 to 64 years; adjusted RR 12.76 [11.13–14.63], $p < 0.001$). We found a slight association between calendar year and first fracture risk, indicating an increase of the incidence of pelvic fracture during the observation period, adjusted for age, sex and insured's region. An additional model using trend variables for age and year showed significance for trend (adjusted RR = 1.04 [1.01–1.06], $p = 0.003$ per calendar year). In addition, there was a significant association with region showing higher incidences in Westfalen-Lippe; the effect, however, was small.

Discussion

Main findings

In this retrospective population-based observational study we found a considerable risk of pelvic fractures in the German population aged 60 years and older. As expected, we observed a clear age and sex effect on the incidence of pelvic fractures in older persons. A total of 5,978 (74%) patients received hospital treatment, with a higher percentage of inpatient treatment in older people. That means that when only inpatient data is used, a relevant proportion of pelvic fractures are not taken into account and the proportion differs with age. The most important finding of our study is that the reported incidences are considerably higher than incidences

Table 4. Incidence rates of all first pelvic fractures and inpatient treated pelvic fractures, stratified by sex and age.

	Women			Men		
	Number of fractures	Person-years at risk	Pelvic fractures/10000 pyrs [95% CI]	Number of fractures	Person-years at risk	Pelvic fractures/10000 pyrs [95% CI]
All first fractures (in total)						
Age (yrs)						
60–64	251	281,770	8.9 [7.8–10.0]	137	286,895	4.8 [4.0–5.6]
65–69	409	324,697	12.6 [11.4–13.8]	201	291,532	6.9 [5.9–7.8]
70–74	861	413,325	20.8 [19.4–22.2]	275	320,262	8.6 [7.6–9.6]
75–79	1,097	334,228	32.8 [30.9–34.8]	275	211,950	13.0 [11.4–14.5]
80–84	1,490	268,349	55.5 [52.7–58.3]	243	125,325	19.4 [17.0–21.8]
85–89	1,532	175,042	87.5 [83.1–91.9]	170	53,895	31.5 [26.8–36.3]
≥ 90	977	81,756	119.5 [112.0–127.0]	123	18,485	66.5 [54.8–78.3]
Inpatient treatment						
Age (yrs)						
60–64	138	281,770	4.9 [4.1–5.7]	81	286,895	2.8 [2.2–3.4]
65–69	227	324,697	7.0 [6.1–7.9]	133	291,532	4.6 [3.8–5.3]
70–74	534	413,325	12.9 [11.8–14.0]	197	320,262	6.2 [5.3–7.0]
75–79	766	334,228	22.9 [21.3–24.5]	208	211,950	9.8 [8.5–11.1]
80–84	1,191	268,349	44.4 [41.9–46.9]	186	125,325	14.8 [12.7–17.0]
85–89	1,279	175,042	73.1 [69.1–77.1]	139	53,895	25.8 [21.5–30.1]
≥ 90	802	81,756	98.1 [91.3–104.9]	97	18,485	52.5 [42.0–62.9]

CI = confidence interval; pyrs = Person-years; yrs = years

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described in the international literature, even if only inpatient pelvic fractures are evaluated. Our data indicate that pelvic fractures increased in Germany during calendar years 2008–2011, and that regional differences exist.

Comparison to previous studies

In past studies over the last decades, several authors have found increasing incidences. For example, a study to determine trends of pelvic fracture-related hospitalizations among older people (population aged 65 years and older) in the Netherlands (1986–2011) found an increase of 39.7% in the age-adjusted incidence rate for women and an increase of 30.0% for men (1986: women 6.82 per 10,000 persons, men 2.83 per 10,000 persons vs. 2011: women 9.53 per 10,000 persons, men 3.68 per 10,000 persons) [6]. A trend analysis of osteoporotic pelvic fractures in Finland (1970–1997) based on data of the National Hospital Discharge Register reported the relative increase in the age-adjusted incidence of osteoporotic pelvic fractures as being 232% in women and 192% in men (1970: women 31 per 100,000 persons, men 13 per 100,000 persons vs. 1997: women 103 per 100,000 persons, men 38 per 100,000 persons) in the population aged 60 years and older [3]. In Germany, data about trends of pelvic fracture incidences are lacking, in contrast to data about trend of hip fractures [21, 29, 30].

Benzinger et al. provided recent data (from AOK Bavaria) on pelvic fracture rates in people with and without disability living both in the community and in nursing homes in Germany. However, the authors analyzed pelvic fracture cases based on hospital admission data [1]. As in our study, age and sex-specific incidence rates were considerably higher than incidence rates in other countries.

Table 5. Possible predictors of a first pelvic fracture: Relative Risk (RR) and [95% confidence Interval] estimated by a multiple Poisson regression model.

Variable	Relative Risk [95% CI]	*p* value
Sex		
Male	1.00 (Reference)	
Female	2.38 [2.23–2.55]	<0.001
Age (years)		
60–64	1.00 (Reference)	
65–69	1.43 [1.23–1.66]	<0.001
70–74	2.16 [1.88–2.47]	<0.001
75–79	3.36 [2.95–3.84]	<0.001
80–84	5.60 [4.92–6.38]	<0.001
85–89	8.95 [7.86–10.20]	<0.001
≥ 90	12.76 [11.13–14.63]	<0.001
Calendar year		
2008	1.00 (Reference)	
2009	1.01 [0.94–1.09]	0.771
2010	1.08 [1.01–1.17]	0.029
2011	1.10 [1.02–1.18]	0.009
Region		
Westfalen-Lippe	1.00 (Reference)	
Schleswig-Holstein	0.92 [0.87–0.98]	0.006

CI = Confidence Interval

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Previous international studies have documented overall incidences ranging from 1.0 to 9.2 per 10,000 person-years respectively [2, 3, 6, 7, 12, 31]. The obvious question is why are higher incidences reported for German populations? One reason might be that the higher incidence corresponds with a higher detection rate. Diagnostic procedures have improved considerably in the last two decades; there are an increasing number of computer tomography and MRI devices available and more examinations are performed [32–35]. Therefore, a combined effect of actually increasing incidence rates as well as an increasing awareness and improvements in diagnosis could be hypothesized. In 2008, 78% of all hospitals in Germany were able to carry out computer tomography examinations [34]. Lower incidence rates in other countries could partly be explained by the varying availability of computer tomography examinations [34, 36]. For the same year, a considerably larger number of CT devices were available in German hospitals (n = 1374; 16.73 per million population) in comparison to the Netherlands (n = 163; 9.91 per million population) or Spain (n = 677; 14.73 per million population) [36]. The exact reasons for the differences in incidence rates for different countries cannot fully be disentangled. It may be that different risk patterns exist in different populations. Moreover, it cannot be ruled out that methodological differences between studies account for variations in reported incidence rates.

Implications

Pelvic fracture incidence rates turned out to be considerably higher than expected, which is a worrying sign. The predicted increase will have major effects on both individual and societal burden, on the one hand causing deterioration in mobility and increased dependency for the individual and on the other hand resulting in rising healthcare costs due to the need for hospital and follow-up care. Our results emphasize the need for preventive measures aimed at

stopping the increase and stimulating a levelling off or even a decrease in pelvic fracture incidence rates, as has been reported for the occurrence of hip fractures in a number of countries. Further analyses and studies are needed to explore the factors (if any) related to different fractures or to find out which falls and fracture prevention programs are best suited. Future research should also focus on the trends of incidence rates. Monitoring of prevention programs will help to target prevention strategies.

Strengths and limitations

Our study incorporates several important strengths. For one, we used longitudinal health insurance data of a large population-based sample in order to get valid estimates of epidemiological measures. Furthermore, health insurance data provide information of treatment in routine care. Because we had personalized individual data, we were able to describe first pelvic fractures and hence avoid overestimation due to double counting. This also meant that, when estimating predictors, bias could be prevented, which may occur since subsequent fractures are highly predicted by a previous one. After the first pelvic fracture, it is rather difficult to distinguish follow-up pelvic fractures from the follow-up therapies of the first fracture mentioned in the data. Furthermore, the risk after the first fracture might change because of successful or unsuccessful therapy or behaviour of the insured person. Therefore, other risk factors might weaken the results because of additional inhomogeneity of the data.

Several limitations have to be considered: We used only specific ICD 10 coding for pelvic fracture, since clinical expertise suggests, that codings for external causes of morbidity and mortality are not very reliable in Germany. Therefore, level of associated trauma and causes of injury were not assessed. However, we assume that in older individuals pelvic fractures are in most cases caused by low energy trauma like simple falls. In addition, with the definition of pelvic fracture according to ICD coding used in our study, we used a comparable approach as the only other German publication regarding incidence of pelvic fractures [1]. Only individual case data for the persons with pelvic fractures was provided. Person-years were aggregated for all insured persons aged 60 years or older and at risk of having a first pelvic fracture. Most persons were continuously insured with the AOK NordWest, which is in line with results of a study conducted by Hoffmann and Icks [37]. Therefore, person-years per calendar year should resemble persons in a very adequate manner. A first fracture was defined by an event-free period of one year. It has to be assumed that prior fractures may have occurred. However, the number should be small. In addition, due to the uncertainty about how long the treatment of a single pelvic fracture may last, some fractures defined as those receiving outpatient treatment may have later been treated in an inpatient setting. However, according to clinical experience misclassification may be low. Moreover, it has to be taken into account that AOK members are not representative for the whole German population. They have been found to be older and more likely to be socially deprived compared to members of other health insurances [38]. In this study by Hoffmann and Icks structural differences between statutory health insurance companies and their impact on health service research were assessed. With regard to the prevalence of chronic diseases, the data showed considerable differences between the various German health insurance companies. However, in our study we standardized the incidence rates for the German population, adjusting partially for age and sex deviations from the general German population. Nevertheless, the generalization of our findings for other populations has to be proven.

Conclusions

We estimated incidence rates of pelvic fractures in the German population aged 60 years or older based on outpatient and inpatient data from a health insurance company. Incidence rates

are considerably higher than incidences described in the international literature. If data is available, inpatient and outpatient events should be analyzed; otherwise a relevant proportion of pelvic fractures are not taken into account. We further evaluated the association between the risk of first pelvic fracture as outcome and sex, age, calendar year and region as independent variables and found that the considerably high incidences observed were significantly influenced by sex and age. There may be an increase in the risk of pelvic fractures due to calendar years and regional differences. The latter has to be confirmed in future studies.

Our study results are highly relevant for policy makers who have to make decisions on health service planning and prevention, such as fall prevention programs.

Author Contributions

Conceived and designed the experiments: AI CO JW BH EN. Performed the experiments: KN BH SA AV WA. Analyzed the data: BH. Wrote the paper: SA. Data collection and management: KN AV SA BH CO JG. Data interpretation: BH SA AI GR PJ. Revising manuscript critically for important intellectual content: AI BH GR PJ JW EN KN AV WA CO JG. Approving final version of manuscript: SA AI BH GR PJ JW EN KN AV WA CO JG.

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ORIGINAL ARTICLE

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Excess Mortality After Pelvic Fractures Among Older People

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ABSTRACT

The study aimed to estimate excess mortality in patients aged 60 years or older up to 1 year after pelvic fracture compared with a population without pelvic fracture. In this retrospective population-based observational study, we use routine data from a large health insurance in Germany. For each patient with a first pelvic fracture between 2008 and 2010 ($n = 5685$ cases, 82% female, mean age 80 ± 9 years), about 34 individuals without pelvic fracture ($n = 193{,}159$ controls) were frequency matched by sex, age at index date, and index month. We estimated survival probabilities in the first year after the index date separated for cases (further stratified into inpatient/outpatient treated or minor/major pelvic fractures) and controls using Kaplan-Meier curves. Additionally, time-dependent hazard ratios (HRs) measuring excess mortality in 4-week intervals up to 52 weeks were estimated by fitting Cox regression models including adjustment for relevant confounders. Twenty-one percent of cases and 11% of controls died within 1 year. HRs (95% confidence intervals) decreased from 3.9 (3.5–4.5) within the first 4 weeks to 1.4 (1.1–1.9) within weeks 49 to 52 after the index date. After full adjustment, HRs lowered substantially (3.0 [2.6–3.4] and 1.0 [0.8–1.4]) but were still significantly increased up to week 32. Adjusted HRs in women were lower than in men: 2.8 (2.4–3.2) and 1.0 (0.7–1.4) versus 3.8 (2.9–5.0) and 1.2 (0.6–2.3). We found a clear excess mortality among older people in the first 8 months after pelvic fracture even after full adjustment. Excess mortality was higher among men in the beginning as well as for inpatient-treated persons. Absence of excess mortality was noticed for outpatient-treated persons within the first 3 months. When broken down into site-specific data, excess mortality was no longer significant for most pelvic fractures classified as minor. The only exception was fracture of pubis within the first 4 weeks. © 2017 American Society for Bone and Mineral Research.

KEY WORDS: EPIDEMIOLOGY; HEALTH SERVICES RESEARCH; PELVIC FRACTURE; EXCESS MORTALITY; POPULATION-BASED STUDY; INPATIENT TREATMENT; OUTPATIENT TREATMENT

Introduction

A main result of simple falls are low-energy pelvic fractures, particularly among older people.[1–4] The pelvic fracture–related burden will become highly relevant for society in general and in particular for our health care systems because of the worldwide demographic change and an aging population.[5] Consequently, low-energy fractures are assumed to affect a growing number of individuals, and an increase of the incidence of pelvic fracture has already been reported.[3,6–10] In Germany, the incidence of pelvic fractures was found to be even higher when compared with other countries.[11] Even though pelvic fractures are assumed to be associated with a significant increase in mortality, up to now data are limited.[2,12,13] Studies report the 1-year mortality after pelvic fractures to be fairly considerable, ranging from 8% up to 27%.[2,12,14,15] Mortality in the older population is in general high; hence, to evaluate differences in mortality in vulnerable populations, more data regarding excess mortality would be helpful. To the best of our knowledge, only three studies analyzed excess mortality in older people after pelvic fracture. All three studies found an increased risk of mortality for individuals with pelvic fracture compared with those without. However, the studies had limitations, and the results were conflicting.[16–18] The aim of this study was to estimate excess mortality in patients aged 60 years or older after a pelvic fracture compared with people without pelvic fracture in Germany, based on data from a large statutory health insurance.

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Materials and Methods

Study design, data source, and population

The study is a retrospective population-based observational study. Routine data for outpatient and inpatient care was provided by a large statutory health insurance in Germany, the AOK NordWest. Overall, the AOK NordWest covers around 2.8 million people in two regions, Schleswig-Holstein (700,000 people) and Westfalen-Lippe (2.1 million people), of whom about 29% are 60 years or older. We included all people aged 60 years or older who were continuously insured for at least 1 year between January 1, 2007, and December 31, 2011 (4,511,645 person-years under risk). The selection process is presented in detail elsewhere.[11] Most persons were insured during the whole study period with the AOK NordWest.

Ascertainment of cases with pelvic fracture events and controls without pelvic fracture

All insured persons with a first pelvic fracture between 2008 and 2010 were identified. In brief, pelvic fractures along with the exact week of occurrence were identified in inpatient and outpatient data according to the 10th revision of the International Classification of Diseases (ICD-10). A fracture event was defined by the following ICD-10 codes and later classified into a major or minor pelvic fracture: S32.1 (fracture of sacrum, major), S32.2 (fracture of coccyx, minor), S32.3 (fracture of ilium, major), S32.4 (fracture of acetabulum, major), S32.5 (fracture of pubis, minor), S32.81 (fracture of ischium, minor), S32.83 (fracture of pelvis unspecified, minor), and S32.89 (multiple and other fractures of pelvis, major). Only first fractures defined by an event-free period of at least 1 year before the event were included. Therefore, data of persons with pelvic fractures in the first study/observation year were excluded. Furthermore, data of persons with a first fracture marked as a follow-up diagnosis of a former fracture were excluded. For further analyses, we distinguished between at first outpatient-treated (whether or not the case was hospitalized in the long run) and acutely inpatient-treated pelvic fracture. First pelvic fractures, which led to hospital treatment during the first week, were considered as acutely inpatient-treated pelvic fractures. Moreover, a secondary analysis concerning survival depending on minor or major pelvic fractures (compared with controls) was conducted. A pelvic fracture was classified as a major pelvic fracture if at least one major ICD-10 code occurred during the index week. To ensure complete cost data, needed for further analyses, the following additional criterion was introduced: The first year after the pelvic fracture had to be included in the insurance period of each person with the only exception of death during this time. Since older people are known to not frequently change their insurance, this criterion should not be very restrictive. In fact, compared with all incident first cases between 2008 and 2010,[11] 4.4% were excluded because of this criterion.

For every person with a first pelvic fracture in 2008 to 2010 ("case"), controls without pelvic fractures during the whole study period were frequency matched by sex, age (in integer years, one class for age $\geq$100 years) and index month. The index date was the date of the first pelvic fracture for cases and was randomly selected in the insurance period of the controls. The requirement of continuously insured time periods for the controls was the same as for cases: Controls had to be insured 1 year before and after the index date, the only exception being death during the first year after the index date. In the end, the sample comprised 5685 cases with and 193,159 controls without a pelvic fracture, equivalent to a mean matching rate of 1 to 34. No further selection of the controls was performed. This implies more precise estimates in controls and simplifies subgroup analyses. The overall power is limited by the number of cases.

Date of death and further variables

All data were derived from the statutory health insurance. For insured persons who died during the observation period, we assessed the week of death. The following variables were included as possible confounders: age, sex, insurance region, level of care, comorbidity, health care cost, and type of pelvic fracture. Age was considered at index date and also classified in 5-year age groups. The insurance region is used as an approximation for the residence of the insured person (Schleswig-Holstein or Westfalen-Lippe). Level of care according to the German legislation on social care insurance[19] is divided into four stages depending on the amount of care needed (zero = none, and one to three). In brief, the level of care documents the limitation of the ability of a person to function in daily life. The levels refer to a considerable (I), intensive (II), or highly intensive (III) need of care, with regard to a person's need for assistance with personal hygiene, eating, and mobility. Within the different care levels, help is required for at least 90 minutes, 3 hours, or 5 hours per day. Moreover, a hardship clause for cases who require an extraordinarily high level of care is included in the framework of Care Level III.[20] The maximum level of care reached in the period before ($\leq$) the index week is taken into account. Comorbidity-related overall disease burden was assessed using the enhanced Charlson comorbidity algorithm for ICD-10 codes.[21,22] Adapting approaches of previous studies,[23–26] we calculated the Charlson comorbidity index based on inpatient diagnoses 52 weeks before ($<$) the index week and outpatient diagnoses four quarters before ($<$) the index quarter. We summed up a score variable, which was then categorized from 0, 1, 2–3, 4–5, 6+ weighted comorbidities. Health care costs accumulated in the year before the index week consisted of inpatient and outpatient care, medications, rehabilitation, and sickness benefit. Health care costs in euro were categorized in approximate quintile classes (€ 0–499, 500–999, 1000–1999, 2000–4999, 5000+). Type of pelvic fracture was defined by the corresponding ICD-10 codes listed above.

Statistical analyses

Patient characteristics at index date were described by frequency tables, means $\pm$ standard deviations, and mean 95% BCA bootstrap confidence intervals,[27] and corresponding statistical tests were used (chi square, *t*, Wilcoxon test). If a person died within 52 weeks after the index week, data were evaluated as "events" (deaths). The corresponding survival time is the duration between index week and the week of death. Death in the first week was counted as 1-week survival time. If an individual survived the 52 weeks after the index week, survival time is 52 weeks, evaluated as "censored."

Time-dependent survival probabilities for cases and controls were estimated by Kaplan-Meier curves including pointwise 95% confidence intervals (CI) between 1 and 52 weeks after the index week. The proportional hazard assumption was investigated graphically based on empirical cumulative hazard curves (Nelson-Aalen plots) and Cox test on interaction between time and risk case/control.[28,29] Because survival curves did not meet the proportional hazard assumption and time-dependent

Table 1. Characteristics of the Study Population

	Persons with first pelvic fracture ($n = 5685$)			Persons without pelvic fracture ($n = 193,159$)		
	All	Men ($n = 996$)	Women ($n = 4689$)	All	Men ($n =$ 38,199)	Women ($n = 154,960$)
Mean age (years) ± SD	80.3 ± 8.7	76.9 ± 9.3	81.0 ± 8.4	79.1 ± 8.4	76.2 ± 8.7	79.8 ± 8.2
Age (years) (%)						
60–64	4.9	9.1	4.0	5.2	9.1	4.3
65–69	8.9	15.4	7.5	10.5	17.2	8.8
70–74	14.5	20.6	13.2	16.5	20.9	15.4
75–79	17.5	20.0	16.9	20.0	20.4	19.9
80–84	22.0	16.3	23.3	21.5	15.8	23.0
85–89	19.7	10.5	21.7	17.2	10.5	18.8
>90	12.5	8.1	13.5	9.1	6.1	9.9
Region (%) in Westfalia	72.7	72.4	72.7	70.9	69.7	71.2
Level of care (%)						
Level of care 0	60.7	68.8	59.0	76.2	84.4	74.2
Level of care 1	23.4	17.9	24.6	12.1	7.9	13.1
Level of care 2	14.1	12.1	14.5	8.7	5.9	9.4
Level of care 3	1.8	1.3	1.9	3.0	1.7	3.4
Comorbidity (%)						
Charlson 0	16.7	15.4	17.0	26.5	27.3	26.3
Charlson 1	19.3	16.6	19.9	21.3	18.5	22.0
Charlson 2–3	31.0	29.4	31.4	28.7	27.3	29.0
Charlson 4–5	17.7	18.4	17.5	14.0	14.9	13.7
Charlson 6–	15.3	20.3	14.3	9.6	12.0	9.0
Mean cost	6226	6590	6148	3392	3600	3341
(95% CI[a])	(5974–6493)	(6002–7254)	(5892–6456)	(3368–3424)	(3534–3685)	(3311–3369)
52 weeks before index date						

[a]BCA bootstrap 95% confidence intervals.

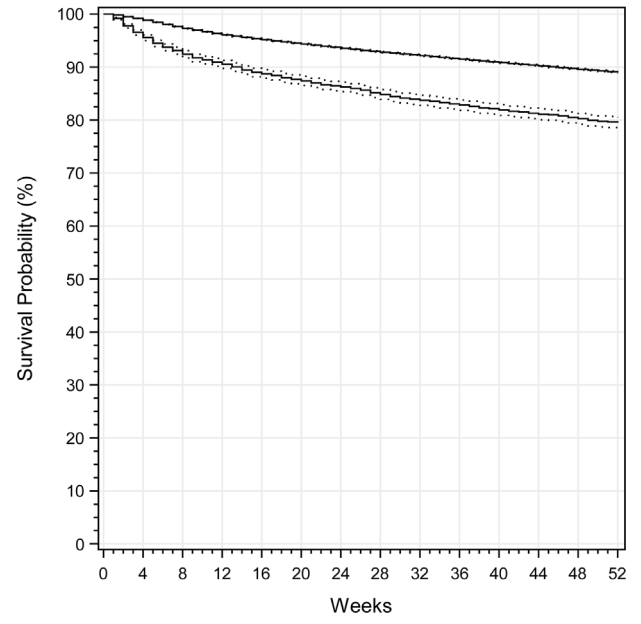

Fig. 1. Kaplan-Meier curves. Cases with pelvic fractures (lower curve), controls (upper curve); pointwise 95% confidence intervals (hardly visible for upper curve because of large sample size).

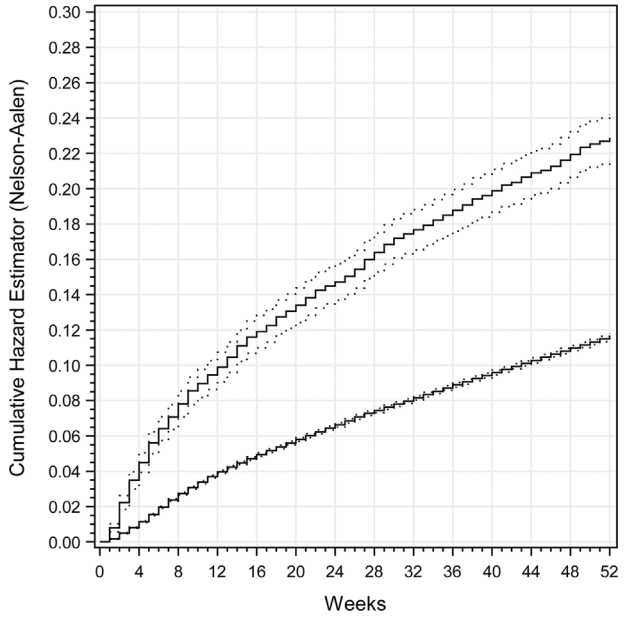

Fig. 2. Nelson-Aalen plots (empirical cumulative hazard curve). Cases with pelvic fractures (upper curve), controls (lower curve); pointwise 95% confidence intervals (hardly visible for lower curve because of large sample size).

hazard ratios were observed, Cox regression models were performed using case/control indicator variables corresponding to 4-week survival time intervals (1–4, 5–8, 9–12, 13–16, and so on, up to 49–52 weeks). Time-dependent hazard ratios (HRs) along with 95% CIs, with and without adjustment for the above-mentioned confounders at the index week (baseline), were estimated as a measure of excess mortality. We use the term excess mortality to describe an increase of mortality risk that may be directly or indirectly related to pelvic fracture. Adjustment for pelvic fracture type was done by including single dichotomous ICD-10 indicator variables as independent variables in the model (reference: S32.89; controls: all indicators equal to 0). The estimated time-dependent HRs compare S32.89 fractures with controls. ICD-adjusted time-dependent overall HRs for all cases versus controls were estimated by multiplying the time-dependent HRs for S32.89 with the time-independent HRs of the other ICD-10 codes accounting for their weights in the data. Additional Cox regression models were fitted in a similar way but assuming differences between the time courses of the different pelvic fracture types. The HR of each ICD-10 code was estimated time dependently in intervals of 4 weeks as before (Supplemental Table S1). Furthermore, the described main analyses were conducted for different risk groups by splitting cases into at first outpatient treated and acutely inpatient treated or into minor and major pelvic fractures (reference group: controls). Additionally, two sensitivity analyses were performed concerning the duration of the event-free period before the event and the accurate estimation of mortality

Table 2. Hazard Ratios Estimated in Cox Regression Models (Overall, Men, Women)

	Week of death	Non-adjusted HR (95% CI)	Fully adjusted HR (95% CI)[a]
Overall			
	01–04	3.94 (3.45–4.48)	2.93 (2.57–3.35)
	05–08	2.09 (1.79–2.43)	1.58 (1.35–1.83)
	09–12	1.69 (1.40–2.05)	1.27 (1.04–1.53)
	13–16	2.07 (1.70–2.53)	1.54 (1.26–1.88)
	17–20	1.74 (1.38–2.19)	1.29 (1.02–1.62)
	21–24	1.59 (1.24–2.04)	1.17 (0.91–1.50)
	25–28	2.05 (1.64–2.57)	1.49 (1.19–1.87)
	29–32	1.81 (1.40–2.34)	1.32 (1.02–1.70)
	33–36	1.49 (1.13–1.97)	1.08 (0.82–1.42)
	37–40	1.59 (1.20–2.09)	1.14 (0.87–1.51)
	41–44	1.48 (1.11–1.98)	1.06 (0.79–1.42)
	45–48	1.49 (1.12–1.99)	1.06 (0.79–1.42)
	49–52	1.44 (1.06–1.95)	1.02 (0.75–1.38)
Men			
	01–04	5.56 (4.26–7.25)	3.83 (2.92–5.01)
	05–08	2.92 (2.14–3.97)	2.07 (1.52–2.83)
	09–12	1.98 (1.30–3.00)	1.41 (0.92–2.14)
	13–16	3.23 (2.21–4.71)	2.28 (1.56–3.33)
	17–20	1.90 (1.11–3.24)	1.35 (0.79–2.30)
	21–24	1.90 (1.09–3.30)	1.35 (0.77–2.35)
	25–28	2.84 (1.76–4.58)	2.00 (1.24–3.23)
	29–32	1.04 (0.46–2.33)	0.72 (0.32–1.63)
	33–36	1.73 (0.92–3.25)	1.20 (0.64–2.26)
	37–40	1.63 (0.84–3.17)	1.13 (0.58–2.21)
	41–44	0.97 (0.40–2.36)	0.67 (0.28–1.63)
	45–48	2.26 (1.30–3.95)	1.55 (0.89–2.71)
	49–52	1.79 (0.92–3.49)	1.23 (0.63–2.39)
Women			
	01–04	3.59 (3.09–4.17)	2.73 (2.35–3.17)
	05–08	1.91 (1.61–2.27)	1.46 (1.23–1.74)
	09–12	1.64 (1.32–2.03)	1.24 (0.99–1.53)
	13–16	1.83 (1.44–2.31)	1.37 (1.09–1.74)
	17–20	1.71 (1.32–2.21)	1.27 (0.99–1.65)
	21–24	1.53 (1.16–2.02)	1.13 (0.86–1.50)
	25–28	1.90 (1.47–2.45)	1.39 (1.08–1.79)
	29–32	1.97 (1.51–2.58)	1.45 (1.10–1.89)
	33–36	1.44 (1.06–1.96)	1.05 (0.77–1.44)
	37–40	1.58 (1.16–2.14)	1.15 (0.85–1.56)
	41–44	1.58 (1.16–2.15)	1.14 (0.84–1.55)
	45–48	1.32 (0.95–1.86)	0.95 (0.68–1.34)
	49–52	1.37 (0.97–1.92)	0.98 (0.69–1.38)

[a]Adjusted for age, sex, insurance region, level of care, comorbidity, health care cost, and pelvic fracture ICD-10 codes. No missings in the covariables.

because of incomplete documentation of death in the data (both subgroup analyses). All analyses were performed separately for men and women. Differences between male and female HRs (case/control) were compared using an interaction model for the whole population. For the statistical analyses, the software package SAS was used (SAS for X64_8PRO, Release 9.4, SAS Institute Inc., Cary, NC, USA).

Results

Numbers of death, survival curves, and empirical cumulative hazard curves

The study cohort comprised 5685 persons (996 men, 4689 women) with a first pelvic fracture between 2008 and 2010, as well as 193,159 persons (38,199 men, 154,960 women) without pelvic fracture. The mean age (± standard deviation) was 79.1 ± 8.4 years (79.8 ± 8.2 years in women and 76.2 ± 8.7 years in men). Characteristics are shown in Table 1. More than three-quarters of the persons had only one documented ICD-10 code during their index week. Most frequently coded ICD-10 codes were S32.89 (multiple and other fractures of pelvis) with 43.7%, S32.5 (fracture of pubis) with 26.2%, and S32.83 (fracture of pelvis unspecified) with 13.6% (data not shown in table). Twenty-one percent of the study population with pelvic fracture and 11% of the population without pelvic fracture died during the 1-year follow-up period (women cases and controls: 19% and 11%; men cases and controls: 26% and 11%). The survival curves demonstrate increased mortality of persons with pelvic fractures particularly during the first months after the event (Fig. 1). The differences between cases and controls seemed larger in men compared with women (Supplemental Figs. S1 and S2). Survival probabilities for male and female controls were similar, male controls being on average 3.6 years younger than the female controls. The empirical cumulative hazard curves (Aalen-Nelson plots) in Fig. 2 illustrate higher mortality risks (= slope of hazard curve) in the first weeks after the pelvic fracture compared with controls. Clearly, the proportional hazard assumption is not fulfilled ($p < 0.0001$ for the Cox test of interaction between time and case/control hazard).

Excess mortality (Cox regression models and hazard ratios)

Table 2 shows the HRs for the 4-week periods up to 52 weeks, crude as well as adjusted for age, sex, region, comorbidity, level of care, classified health care cost, and type of pelvic fracture. Non-adjusted HRs decreased from 3.9 (3.5–4.5) in the first 4 weeks to 1.4 (1.1–1.9) 49–52 weeks after the index date. After full adjustment, the HRs lowered substantially during 1 year (2.9 [2.6–3.4] and 1.0 [0.8–1.4]). Significant excess mortality (HRs >1) is only observed until week 32, except in weeks 21–24. In

Table 3. Characteristics of at First Outpatient-Treated and Acutely Inpatient-Treated Persons as Well as Patients With Minor and Major Pelvic Fractures

	Persons with first pelvic fracture ($n = 5685$)					
	Outpatient ($n = 2340$)	Inpatient ($n = 3345$)	Test outpatient/ inpatient	Minor ($n = 2039$)	Major ($n = 3646$)	Test minor/major
Sex (%)						
Women	82.9	82.2	$p = 0.480$	84.9	81.1	$p = 0.0003$
Men	17.1	17.8		15.1	18.9	
Mean age (years) ± SD	78.8 ± 8.9	81.3 ± 8.4	$p < 0.0001$	79.5 ± 8.9	80.7 ± 8.5	$p < 0.0001$
Age (years) (%)						
60–64	6.5	3.8		5.9	4.3	
65–69	11.4	7.1		10.5	8.0	
70–74	17.7	12.3	$p < 0.0001$	15.9	13.7	$p < 0.0001$
75–79	18.3	16.8		17.4	17.5	
80–84	19.6	23.7		21.3	22.4	
85–89	15.9	22.4		17.4	21.0	
>90	10.6	13.9		11.6	13.0	
Region (%) in Westfalia	72.5	72.8	$p = 0.773$	75.0	72.4	$p = 0.0035$
Level of care (%)						
Level of care 0	65.0	57.7		63.1	59.4	
Level of care 1	21.3	24.9	$p < 0.0001$	21.9	24.3	$p = 0.0342$
Level of care 2	12.0	15.5		13.5	14.4	
Level of care 3	1.8	1.9		1.5	2.0	
Comorbidity (%)						
Charlson 0	17.8	16.0		16.9	16.6	
Charlson 1	20.2	18.6	$p = 0.129$	19.4	19.2	$p = 0.9461$
Charlson 2–3	29.9	31.8		30.5	31.4	
Charlson 4–5	17.1	18.1		17.6	17.7	
Charlson 6–	15.0	15.5		15.7	15.1	
Mean cost (95% CI[a]) 52 weeks before index date	5916 (5574–6316)	6442 (6108–6801)	$p = 0.098$[b]	6291 (5893–6707)	6189 (5895–6507)	$p = 0.7691$[b]

[a]BCA bootstrap 95% confidence intervals.
[b]Wilcoxon test.

women, the non-adjusted HRs decreased from 3.6 (3.1–4.2) to 1.4 (0.97–1.9), fully adjusted from 2.7 (2.4–3.2) to 1.0 (0.7–1.4). In men, excess mortality after pelvic fracture was more evident than for women as non-adjusted HRs decreased from 5.6 (4.3–7.3) to 1.8 (0.9–3.5) and fully adjusted from 3.8 (2.9–5.0) to 1.2 (0.6–2.4). A fully adjusted model including additional interaction terms between sex and time-dependent case/control indicators concludes significant interaction only in weeks 13–16 (1–4 weeks: $p = 0.053$; 5–8 weeks: $p = 0.08$; 9–12 weeks: $p = 0.50$; 13–16 weeks: $p = 0.01$; 17–20 weeks: $p = 0.89$; corresponding HR estimates for interactions female versus male were between 0.7 and 1.0).

Numbers of death and survival curves for at first outpatient-treated and acutely inpatient-treated persons

Of 5685 persons with pelvic fracture, 3345 (59%) were acutely treated inpatient. Mean age was higher for acutely inpatient-treated individuals ($p < 0.0001$). Level of care was higher among persons treated inpatient compared with outpatient-treated individuals ($p < 0.0001$). Table 3 shows selected characteristics.

Individuals with acutely inpatient-treated pelvic fractures had a higher 1-year mortality than individuals with at first outpatient-treated pelvic fracture (inpatient/outpatient/controls: 25% versus 14% versus 11%; women: 24% versus 13% versus 11%; men: 31% versus 18% versus 11%). The survival curves (Figs. 3 and 4) for at first outpatient-treated and acutely inpatient-treated persons follow the same pattern for men and women, which means that a higher mortality is found for acutely inpatient-treated persons. However, within the first 4 weeks, the mortality risk for inpatient-treated men was higher compared with women (significant interaction, cf. below).

Excess mortality (Cox regression models and hazard ratios) for at first outpatient-treated and acutely inpatient-treated persons

HRs for the 4-week periods up to 52 weeks, non-adjusted and adjusted for the same relevant variables as named above, are tabulated in Table 4. HRs show excess mortality for acutely inpatient-treated men and women when compared with those without pelvic fracture, especially in the first weeks after admission to hospital. For women, non-adjusted HRs in weeks 1–4 were 5.9 (5.0–6.8) and fully adjusted HRs in weeks 1–4 resulted in 4.1 (3.5–4.8). Men showed non-adjusted HRs in weeks 1–4 of 8.7 (6.6–11.5) and fully adjusted HRs of 6.0 (4.5–8.0). In the non-adjusted model, the HRs for women were significantly increased (HR >1) until week 44. In men, the non-adjusted HRs among those compared with those without pelvic fracture were significantly >1 until week 40 (with exceptions in weeks 17–20 and 29–32). Fully adjusted, the HRs were significantly elevated for the first 4 month in women and men when compared with those without pelvic fracture. In contrast, women who were at first outpatient treated had significantly lower HRs (HR <1) in the first 4 weeks compared with women without a pelvic fracture (fully adjusted HR: 0.4 [0.2–0.8]). Yet, also significant excess mortality was found for outpatient-treated women in weeks 17–20 (fully adjusted HR: 1.8 [1.3–2.5]) and weeks 29–32 (fully adjusted HR: 1.7 [1.1–2.5]). Overall, absence of excess mortality was noticed for outpatient-treated persons within the first 3 months. Including additional interaction terms between sex and time-dependent risk group indicators in the fully adjusted model, significant interaction was only found for inpatients in the first 4 weeks (HR: 0.7 [0.5–0.98], $p = 0.037$).

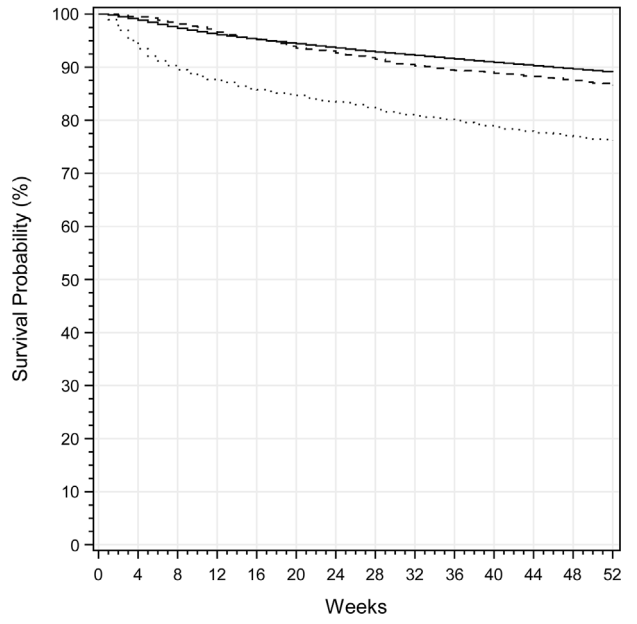

Fig. 3. Kaplan-Meier curves for females. Acutely inpatient-treated cases (dotted curve), outpatient-treated cases (dashed curve), controls (solid curve).

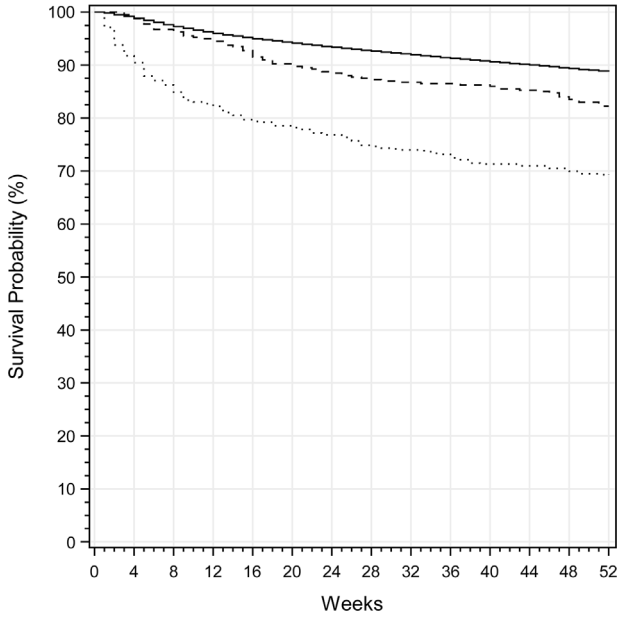

Fig. 4. Kaplan-Meier curves for males. Acutely inpatient-treated cases (dotted curve), outpatient-treated cases (dashed curve), controls (solid curve).

Secondary analysis: survival depending on minor or major pelvic fractures (numbers of death, survival curves, Cox regression models, and hazard ratios)

Of 5685 persons with pelvic fracture, 3646 (64%) had a major pelvic fracture. Mean age was 80.7 ± 8.5 years in cases with major pelvic fractures and 79.5 ± 8.9 years in cases with minor pelvic fractures. Level of care was in cases with major pelvic fractures (0-1-2-3) 59%, 24%, 14%, 2%, and in cases with minor pelvic fractures 63%, 22%, 14%, 2%, respectively. A higher percentage of major pelvic fractures were inpatient treated (67%). Still, a considerable percent of minor pelvic fractures were also inpatient treated (44%). Inpatient treated major pelvic fractures seem to be more pronounced for men, with 69% compared with 40% of minor pelvic fractures inpatient treated (women: 66% major pelvic fractures inpatient treated, 45% minor pelvic fractures inpatient treated). Table 3 shows selected characteristics. Individuals with a major pelvic fracture had a slightly higher 1-year mortality than individuals with a minor pelvic fracture (major/minor/controls: 22% versus 17% versus 11%; women: 21% versus 17% versus 11%; men: 28% versus 19% versus 11%). The survival curves for women and men (Figs. 5 and 6) relating to the severity of fracture (versus female and male controls) show slight differences between major and minor cases. The risk of death is considerably higher even in the minor cases compared with controls. Non-adjusted and adjusted HRs for the 4-week periods up to 52 weeks are given in Table 5 and briefly discussed in the following. HRs show excess mortality for cases with minor and major pelvic fractures when compared with persons without a pelvic fracture. Fully adjusted, in women, the HRs were significantly elevated for minor pelvic fractures during the first 4 weeks (HR: 2.4 [1.9–3.2]) and again at a later stage. However, during weeks 41–48, fully adjusted HRs were significantly decreased compared with women without pelvic fracture. Fully adjusted HRs for major pelvic fractures in women were significantly increased during the first 2 months (weeks 1–4 HR: 3.0 [2.5–3.5]; weeks 5–8 HR: 1.6 [1.3–2.0]) and at a later stage. Men showed increased HRs for minor pelvic fractures in weeks 1–4 (fully adjusted HR: 2.1 [1.2–3.9]) and at a later stage. Excess mortality was most pronounced in men with major pelvic fracture: During the first 4 months, the fully adjusted HRs were high and decreased from 4.6 (3.5–6.2) to 2.7 (1.8–4.1). To gain more insight into the different types of minor and major pelvic fractures, we cautiously evaluated site-specific fracture data. Table 6 displays HRs for S32.89 multiple and other fractures of pelvis (major) versus controls estimated in the overall Cox regression model. This is the basis for the fully adjusted overall model of Table 2 (HRs for additional confounders from patient characteristics are only not shown). As expected, significant excess mortality for S32.89 can be noticed (weeks 1–4 HR: 3.0 [2.6–3.5]) up to weeks 17–20 HR: 1.3 [1.1–1.7], weeks 25–28 HR: 1.5 [1.2–2.0], and weeks 29–32 HR: 1.4 [1.1–1.8]). Additionally, time-independent HRs for all remaining ICD-10 codes are given (reference S32.89). In comparison to S32.89, we observed significantly lower HRs for both minor fractures S32.2 fracture of coccyx (fully adjusted HR: 0.6 [0.4–0.9]) and S32.83 fracture of pelvis unspecified (fully adjusted HR: 0.8 [0.6–0.9]). In this analysis, the HR for S32.5 fracture of pubis (minor) and S32.81 fracture of ischium (minor) indicate comparable risks as found for S32.89 multiple and other fractures of pelvis (HR S32.5: 1.0 [0.9–1.1] and S32.81: 0.9 [0.8–1.1]). As anticipated, HRs were >1 for all major ICD-10 codes (S32.1, S32.3, and S32.4). The HR for S32.3 fracture of ilium (major) was significantly increased (HR: 1.6 [1.2–2.2]) in comparison to S32.89. Furthermore, the time-dependent HRs for the different major ICD-10 codes revealed significant excess mortality in the beginning (Supplemental Table S1), whereas excess mortality was no longer significant for most pelvic fractures classified as minor. The only exception was S32.5 fracture of pubis. Here we found significant excess mortality for S32.5 within the first 4 weeks (HR: 1.5 [1.1–2.0], Supplemental Table S1). In this more sophisticated model, S32.81 fracture of ischium did not show a significantly increased risk in the beginning (only later in weeks 13–16).

Discussion

Main findings

We found a clear excess mortality in older people in the first year after pelvic fracture even after adjustment for several confounders. The HRs between cases and controls were high in the beginning, lower in later weeks, and not far from 1 after 33 weeks. High excess mortality was observed in the beginning, in particular for men. Furthermore, excess mortality was higher for inpatient-treated persons, which was somewhat expected. Interestingly, in the first month after the fracture, men had a higher excess mortality for inpatient-treated pelvic fractures compared with women. In contrast, surprisingly, women who were at first outpatient treated showed a significant HR <1 corresponding to lower mortality risk in women with pelvic fracture in the first 4 weeks. We suggest that the lower risk of women during the first month could be explained by an excellent health status before the event (pelvic fracture may have occurred within the scope of an active lifestyle). Doctors decide after risk assessment that they can be treated in an outpatient setting based on special characteristics. Excess mortality was detected for cases with minor and major pelvic fractures when compared with persons without a pelvic fracture. However, when broken down into site-specific data, excess mortality was no longer significant for most pelvic fractures classified as minor, with fracture of pubis being the only exception. Fracture of pubis is one of the most frequently coded ICD-10 codes during the index week (26%), which may explain why we find a significant excess mortality looking at the classified/summarized minor pelvic fractures. When interpreting these results, one should keep in mind that the size of the male subpopulation is low compared with females. This implies lower power to detect differences or associations among males. Overall, results without adjustment are dominated by the larger female subpopulation.

Comparison to previous studies

We found only three studies analyzing excess mortality in older people after pelvic fracture. In a German study, HRs after pelvic fracture were 1.52 to 2.95, whereas excess mortality was observed for men in the first month and for women in the first 2 months after the event.[16] We also found that excess mortality was more evident in men than excess mortality in women. The reasons for this are only partially understood. The higher susceptibility to specific causes of death like coronary heart disease, infections, or complications after the event of a pelvic fracture could be discussed as an explanation for higher excess mortality observed among men. Up to now, evidence has only been evaluated in studies analyzing sex differences in mortality after hip fracture.[30–32] Nonetheless, the German study was restricted to residents from nursing homes and patients with

Table 4. Hazard Ratios Estimated in Cox Regression Models (Inpatient/Outpatient Treated, Stratified for Overall, Men, and Women)

	Week of death	Non-adjusted HR (95% CI)	Fully adjusted HR (95% CI)[a]
Overall			
Acutely inpatient treated	01–04	6.36 (5.56–7.27)	4.40 (3.83–5.04)
	05–08	2.93 (2.48–3.47)	2.06 (1.74–2.44)
	09–12	1.99 (1.57–2.51)	1.38 (1.09–1.74)
	13–16	2.33 (1.82–2.99)	1.59 (1.24–2.04)
	17–20	1.49 (1.07–2.07)	1.01 (0.72–1.40)
	21–24	1.84 (1.35–2.49)	1.23 (0.91–1.68)
	25–28	2.40 (1.82–3.15)	1.59 (1.21–2.09)
	29–32	1.88 (1.35–2.62)	1.24 (0.89–1.73)
	33–36	1.74 (1.24–2.45)	1.14 (0.81–1.61)
	37–40	2.19 (1.60–3.01)	1.43 (1.05–1.97)
	41–44	1.82 (1.28–2.58)	1.18 (0.83–1.68)
	45–48	1.45 (0.99–2.14)	0.94 (0.64–1.39)
	49–52	1.33 (0.87–2.02)	0.85 (0.56–1.30)
Outpatient treated	01–04	0.56 (0.34–0.93)	0.49 (0.29–0.81)
	05–08	0.98 (0.70–1.36)	0.84 (0.61–1.17)
	09–12	1.32 (0.95–1.82)	1.13 (0.81–1.56)
	13–16	1.75 (1.27–2.41)	1.50 (1.09–2.07)
	17–20	2.06 (1.50–2.83)	1.77 (1.29–2.44)
	21–24	1.28 (0.85–1.94)	1.10 (0.73–1.66)
	25–28	1.62 (1.11–2.35)	1.37 (0.94–2.00)
	29–32	1.73 (1.17–2.54)	1.47 (0.999–2.17)
	33–36	1.17 (0.73–1.86)	1.00 (0.63–1.59)
	37–40	0.83 (0.47–1.46)	0.70 (0.40–1.24)
	41–44	1.06 (0.64–1.77)	0.90 (0.54–1.49)
	45–48	1.53 (1.01–2.34)	1.29 (0.84–1.96)
	49–52	1.58 (1.02–2.43)	1.32 (0.86–2.03)
Men			
Acutely inpatient treated	01–04	8.71 (6.61–11.47)	6.03 (4.53–8.02)
	05–08	3.90 (2.75–5.54)	2.78 (1.95–3.97)
	09–12	2.43 (1.48–4.00)	1.73 (1.05–2.86)
	13–16	3.36 (2.07–5.46)	2.38 (1.46–3.89)
	17–20	1.68 (0.80–3.56)	1.18 (0.56–2.50)
	21–24	2.07 (1.03–4.18)	1.45 (0.71–2.93)
	25–28	3.65 (2.09–6.36)	2.51 (1.44–4.40)
	29–32	1.24 (0.46–3.32)	0.84 (0.31–2.27)
	33–36	2.79 (1.43–5.42)	1.90 (0.97–3.70)
	37–40	2.29 (1.08–4.86)	1.57 (0.74–3.35)
	41–44	0.70 (0.18–2.83)	0.48 (0.12–1.94)
	45–48	1.88 (0.84–4.23)	1.28 (0.57–2.88)
	49–52	1.43 (0.53–3.85)	0.97 (0.36–2.62)
Outpatient treated	01–04	1.08 (0.45–2.62)	0.78 (0.32–1.89)
	05–08	1.59 (0.85–2.97)	1.18 (0.63–2.21)
	09–12	1.39 (0.66–2.92)	1.03 (0.49–2.18)
	13–16	3.05 (1.72–5.43)	2.25 (1.26–4.01)
	17–20	2.18 (1.03–4.61)	1.64 (0.77–3.48)
	21–24	1.67 (0.69–4.05)	1.28 (0.53–3.09)
	25–28	1.81 (0.75–4.37)	1.38 (0.57–3.35)
	29–32	0.79 (0.20–3.16)	0.59 (0.15–2.38)
	33–36	0.39 (0.06–2.79)	0.29 (0.04–2.09)
	37–40	0.81 (0.20–3.27)	0.60 (0.15–2.42)
	41–44	1.31 (0.42–4.09)	0.96 (0.31–3.01)
	45–48	2.73 (1.29–5.79)	1.99 (0.94–4.22)
	49–52	2.24 (0.92–5.43)	1.62 (0.67–3.95)
Women			
Acutely inpatient treated	01–04	5.87 (5.03–6.84)	4.07 (3.48–4.76)
	05–08	2.72 (2.25–3.30)	1.92 (1.58–2.33)
	09–12	1.89 (1.45–2.47)	1.31 (1.003–1.71)
	13–16	2.11 (1.58–2.81)	1.44 (1.08–1.93)

Table 4. (*Continued*)

	Week of death	Non-adjusted HR (95% CI)	Fully adjusted HR (95% CI)[a]
	17–20	1.45 (1.001–2.09)	0.98 (0.68–1.42)
	21–24	1.79 (1.27–2.51)	1.20 (0.85–1.69)
	25–28	2.15 (1.57–2.95)	1.43 (1.04–1.96)
	29–32	2.01 (1.42–2.86)	1.33 (0.94–1.90)
	33–36	1.53 (1.03–2.28)	1.01 (0.68–1.50)
	37–40	2.17 (1.54–3.07)	1.42 (1.003–2.01)
	41–44	2.03 (1.41–2.91)	1.32 (0.91–1.89)
	45–48	1.36 (0.88–2.12)	0.88 (0.57–1.37)
	49–52	1.30 (0.82–2.08)	0.84 (0.52–1.33)
Outpatient treated	01–04	0.45 (0.24–0.84)	0.41 (0.22–0.76)
	05–08	0.85 (0.58–1.25)	0.75 (0.51–1.11)
	09–12	1.30 (0.91–1.87)	1.14 (0.79–1.64)
	13–16	1.46 (0.99–2.16)	1.29 (0.87–1.90)
	17–20	2.04 (1.44–2.90)	1.79 (1.26–2.54)
	21–24	1.21 (0.76–1.92)	1.05 (0.66–1.67)
	25–28	1.58 (1.04–2.38)	1.36 (0.90–2.05)
	29–32	1.92 (1.28–2.87)	1.67 (1.11–2.50)
	33–36	1.32 (0.82–2.14)	1.16 (0.72–1.87)
	37–40	0.83 (0.45–1.55)	0.72 (0.39–1.34)
	41–44	1.02 (0.57–1.79)	0.87 (0.49–1.55)
	45–48	1.28 (0.77–2.13)	1.10 (0.66–1.83)
	49–52	1.44 (0.88–2.37)	1.24 (0.75–2.03)

[a]Adjusted for age, sex, insurance region, level of care, comorbidity, health care cost, and pelvic fracture ICD-10 codes. No missings in the covariables.

inpatient-treated pelvic fractures, and the adjustment for comorbidity was limited, considering only the level of care. Lower HRs reported by Rapp and colleagues[16] compared with our study may be because of a population that is older and worse off (elevated baseline risk of mortality among controls).

In a Spanish study, excess mortality (adjusted HR 2.5 [2.1–3.1]) was elevated up to 3 years after the fracture event.[17] The study of Prieto-Alhambra and colleagues[17] was community based and differentiated between inpatient and outpatient treatment. However, it did not adjust for comorbidities but only for BMI.

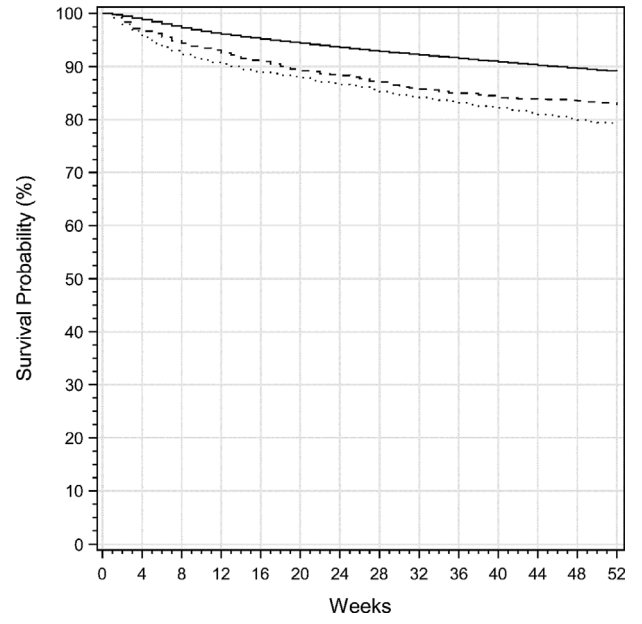

Fig. 5. Kaplan-Meier curves for females. Cases with major pelvic fractures (dotted curve), cases with minor pelvic fractures (dashed curve), controls (solid curve).

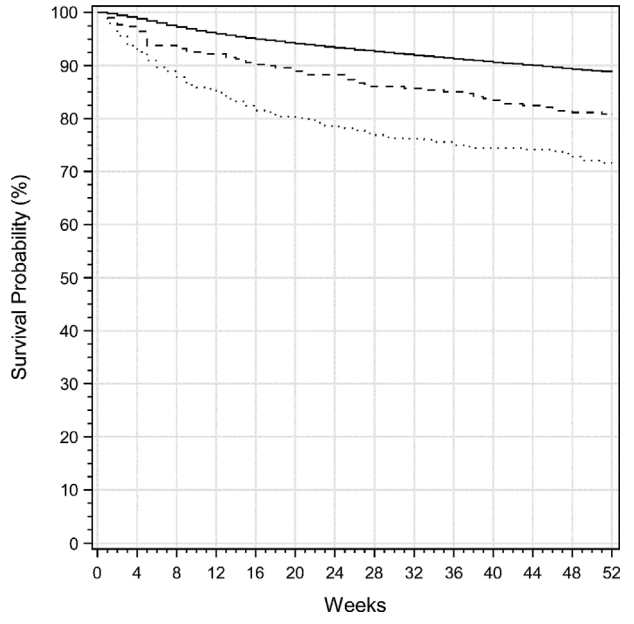

Fig. 6. Kaplan-Meier curves for males. Cases with major pelvic fractures (dotted curve), cases with minor pelvic fractures (dashed curve), controls (solid curve).

Table 5. Hazard Ratios Estimated in Cox Regression Models (Minor/Major Pelvic Fractures, Stratified for Overall, Men, and Women)

	Week of death	Non-adjusted HR (95% CI)	Fully adjusted HR (95% CI)[a,b]
Overall			
Minor	01–04	2.96 (2.32–3.76)	2.37 (1.86–3.02)
	05–08	1.58 (1.19–2.09)	1.27 (0.96–1.69)
	09–12	1.53 (1.10–2.12)	1.22 (0.87–1.69)
	13–16	1.81 (1.28–2.56)	1.43 (1.02–2.02)
	17–20	2.21 (1.58–3.09)	1.74 (1.24–2.43)
	21–24	1.14 (0.70–1.83)	0.89 (0.55–1.44)
	25–28	2.00 (1.39–2.89)	1.55 (1.08–2.24)
	29–32	1.91 (1.28–2.86)	1.47 (0.98–2.21)
	33–36	1.17 (0.70–1.95)	0.90 (0.54–1.50)
	37–40	1.66 (1.06–2.58)	1.27 (0.82–1.98)
	41–44	0.68 (0.34–1.37)	0.52 (0.26–1.05)
	45–48	0.75 (0.39–1.45)	0.57 (0.30–1.10)
	49–52	1.17 (0.68–2.02)	0.87 (0.51–1.51)
Major	01–04	4.49 (3.86–5.22)	3.28 (2.82–3.81)
	05–08	2.38 (1.99–2.83)	1.75 (1.47–2.09)
	09–12	1.79 (1.42–2.26)	1.31 (1.04–1.65)
	13–16	2.23 (1.75–2.83)	1.62 (1.27–2.05)
	17–20	1.46 (1.07–2.00)	1.06 (0.77–1.45)
	21–24	1.86 (1.39–2.47)	1.33 (1.00–1.77)
	25–28	2.08 (1.58–2.74)	1.47 (1.12–1.94)
	29–32	1.75 (1.27–2.42)	1.24 (0.90–1.72)
	33–36	1.68 (1.21–2.32)	1.18 (0.85–1.64)
	37–40	1.55 (1.09–2.20)	1.08 (0.76–1.54)
	41–44	1.95 (1.42–2.68)	1.36 (0.99–1.86)
	45–48	1.92 (1.40–2.64)	1.33 (0.97–1.83)
	49–52	1.60 (1.11–2.30)	1.11 (0.77–1.59)
Men			
Minor	01–04	3.15 (1.73–5.72)	2.14 (1.18–3.90)
	05–08	2.13 (1.14–3.98)	1.52 (0.81–2.84)
	09–12	0.80 (0.26–2.47)	0.56 (0.18–1.74)
	13–16	2.03 (0.91–4.55)	1.40 (0.62–3.13)
	17–20	1.63 (0.61–4.38)	1.12 (0.42–3.01)
	21–24	0.88 (0.22–3.52)	0.61 (0.15–2.46)
	25–28	3.31 (1.57–7.02)	2.28 (1.07–4.82)
	29–32	0.52 (0.07–3.68)	0.35 (0.05–2.50)
	33–36	1.03 (0.26–4.15)	0.70 (0.17–2.82)
	37–40	2.70 (1.11–6.54)	1.82 (0.75–4.42)
	41–44	1.76 (0.56–5.49)	1.19 (0.38–3.73)
	45–48	2.10 (0.78–5.64)	1.42 (0.53–3.83)
	49–52	0.60 (0.08–4.24)	0.40 (0.06–2.86)
Major	01–04	6.68 (5.00–8.92)	4.61 (3.45–6.16)
	05–08	3.28 (2.31–4.66)	2.32 (1.63–3.29)
	09–12	2.54 (1.63–3.98)	1.80 (1.15–2.81)
	13–16	3.81 (2.50–5.81)	2.67 (1.75–4.07)
	17–20	2.03 (1.08–3.81)	1.42 (0.76–2.67)
	21–24	2.40 (1.32–4.39)	1.67 (0.92–3.05)
	25–28	2.61 (1.43–4.76)	1.79 (0.98–3.27)
	29–32	1.30 (0.54–3.15)	0.88 (0.36–2.14)
	33–36	2.08 (1.03–4.21)	1.41 (0.70–2.84)
	37–40	1.09 (0.41–2.93)	0.74 (0.27–1.98)
	41–44	0.58 (0.15–2.35)	0.39 (0.10–1.57)
	45–48	2.34 (1.21–4.56)	1.56 (0.80–3.03)
	49–52	2.39 (1.18–4.85)	1.60 (0.79–3.23)
Women			
Minor	01–04	2.92 (2.25–3.81)	2.42 (1.86–3.15)
	05–08	1.48 (1.08–2.03)	1.22 (0.89–1.68)
	09–12	1.67 (1.19–2.36)	1.36 (0.97–1.93)
	13–16	1.78 (1.21–2.60)	1.45 (0.99–2.12)

Table 5. (*Continued*)

	Week of death	Non-adjusted HR (95% CI)	Fully adjusted HR (95% CI)[a,b]
	17–20	2.32 (1.62–3.31)	1.87 (1.31–2.68)
	21–24	1.18 (0.71–1.97)	0.95 (0.57–1.58)
	25–28	1.78 (1.16–2.71)	1.41 (0.92–2.15)
	29–32	2.17 (1.43–3.28)	1.71 (1.13–2.59)
	33–36	1.19 (0.69–2.06)	0.94 (0.55–1.63)
	37–40	1.47 (0.88–2.45)	1.16 (0.69–1.92)
	41–44	0.50 (0.21–1.20)	0.39 (0.16–0.94)
	45–48	0.50 (0.21–1.21)	0.39 (0.16–0.93)
	49–52	1.27 (0.72–2.24)	0.97 (0.55–1.71)
Major	01–04	3.99 (3.34–4.76)	2.95 (2.47–3.52)
	05–08	2.17 (1.77–2.66)	1.62 (1.32–1.99)
	09–12	1.61 (1.23–2.12)	1.19 (0.90–1.56)
	13–16	1.85 (1.39–2.48)	1.36 (1.01–1.81)
	17–20	1.34 (0.93–1.92)	0.97 (0.68–1.40)
	21–24	1.74 (1.25–2.41)	1.25 (0.90–1.74)
	25–28	1.97 (1.44–2.69)	1.41 (1.03–1.92)
	29–32	1.85 (1.31–2.62)	1.33 (0.94–1.88)
	33–36	1.59 (1.10–2.30)	1.13 (0.78–1.64)
	37–40	1.64 (1.13–2.39)	1.16 (0.80–1.69)
	41–44	2.23 (1.60–3.09)	1.56 (1.13–2.17)
	45–48	1.83 (1.27–2.63)	1.28 (0.89–1.84)
	49–52	1.43 (0.93–2.18)	1.00 (0.65–1.52)

[a]Adjusted for age, sex, insurance region, level of care, comorbidity, and health care cost.
[b]No additional adjustment for ICD-10 codes due to overadjustment.
No missings in the covariables.

Mortality was higher for inpatient-treated patients compared with outpatient-treated persons, and hospital admission was associated with excess mortality (adjusted HR 1.8 [1.2–2.6]). Mortality in non-admitted versus admitted was 2.4% versus 6.8% by 3 months. Our result regarding outpatient-treated persons is comparable with a non-adjusted mortality probability from Kaplan–Meier curves after 12 weeks of 3.8% (3.1%–4.6%). However, we found a higher mortality in acutely inpatient-treated persons of 13.5% (12.3–14.7).

In a Scottish study, excess mortality was present up to 5 years after fracture (HR 1.8 [1.5–2.1]).[18] In multiple logistic regression, the effect of age, sex, dementia, the level of mobility, and residential status before injury was analyzed with age and dementia being predictive of mortality ($p < 0.05$), although no adjustment was made for comorbidities. Furthermore, the study included only patients with a fracture of the pubic rami, one control group was age-matched, a second group consisted of patients with a hip fracture, and the study group as such was small. In contrast, with regard to the population that is likely to experience a fracture (mostly older women), we conducted a frequency matching by index month, age, and sex. Rapp and colleagues[16] and Prieto-Alhambra[17] and colleagues also used sex and age for their matching procedure expanded by further matching variables.

Up until now, this is the first study to report excess mortality in such a detail. To our knowledge, no other study has compared at first outpatient-treated and acutely inpatient-treated persons (versus controls) and survival depending on minor, major, and site-specific pelvic fractures (versus controls).

Implications

As we have already shown, pelvic fracture incidence rates in Germany are high.[11] Furthermore, an increase has been predicted, which will not only have major effects on both individual and societal burden but will also be accompanied by a high risk of mortality. Most importantly, mortality risk is higher than expected. Our results underline once more the importance of preventive measures and of further analyses and community-based studies to explore trends of mortality rates. In particular, patients with inpatient treatment after pelvic fracture should be addressed.

Limitations and strengths

Several limitations need to be considered: First, we used specific ICD-10 coding for pelvic fracture because clinical expertise suggests that coding for external causes of morbidity and mortality is not very reliable in Germany. Therefore, level of associated trauma and causes of injury were not assessed. However, we assume that in older individuals pelvic fractures are in most cases caused by low-energy trauma like simple falls. Second, it has to be taken into account that AOK members are not representative for the whole German population. They were found to be older and more likely to be socially deprived and to have a higher prevalence of chronic diseases compared with members of other health insurances.[33] Therefore, the generalization of our findings for other populations has to be proven. It should be mentioned that we did not have appropriate information/data on socioeconomic status and were therefore not able to adjust for it. Third, including first fractures defined by an event-free period of at least 1 year before the event might result in overestimation since earlier fractures may have occurred. In a subgroup analysis including only insured persons with an event-free period of 2 years, the results were very similar (data not shown). Beyond, from a clinical point of view, misclassification as a first pelvic fracture was considered to be low. Fourth, there might be an underestimation of mortality

Table 6. Hazard Ratios Estimated in Cox Regression Model Overall (Including Confounders)

	Week of death	HR (95% CI)
Overall		
S32.89 multiple and other fractures of pelvis, major vs. control	01–04	3.04 (2.63–3.51)
	05–08	1.63 (1.39–1.92)
	09–12	1.31 (1.07–1.60)
	13–16	1.60 (1.30–1.97)
	17–20	1.33 (1.05–1.69)
	21–24	1.21 (0.94–1.56)
	25–28	1.54 (1.22–1.95)
	29–32	1.36 (1.05–1.77)
	33–36	1.12 (0.84–1.48)
	37–40	1.18 (0.89–1.57)
	41–44	1.10 (0.82–1.48)
	45–48	1.10 (0.82–1.48)
	49–52	1.06 (0.77–1.44)
Other ICD confounders (vs. S32.89)[a]		
S32.1 fracture of sacrum, major		1.03 (0.84–1.26)
S32.2 fracture of coccyx, minor		0.61 (0.43–0.85)
S32.3 fracture of ilium, major		1.64 (1.24–2.16)
S32.4 fracture of acetabulum, major		1.16 (0.98–1.37)
S32.5 fracture of pubis, minor		0.99 (0.87–1.13)
S32.81 fracture of ischium, minor		0.93 (0.78–1.11)
S32.83 fracture of pelvis unspecified, minor		0.77 (0.64–0.92)

[a]Other confounders (HRs not shown): age, sex, insurance region, level of care, comorbidity, and health care cost.

owing to incomplete documentation of death in the data. However, a sensitivity analysis excluding a subgroup that has insurance coverage through their family members showed similar results. Furthermore, this bias should be similar in cases and controls. Fifth, a selection bias might be induced by the conditions on continuous insurance and a period of at least 1 year without pelvic fracture before the index date. However, a very high proportion of cases and controls were continuously insured with the AOK NordWest. This finding is well in line with results of a study conducted by Hoffmann and Icks.[34] Sixth, no adjustment for multiple testing was performed. Some significant tests might be inflated by chance. Seventh, the interpretation of the site-specific fracture data should be carried out with caution. Different pelvic fracture types might result in different time dependencies of mortality risks. But the sample size (number of events in time intervals) was too low to fit the corresponding more complicated models on each subgroup. Furthermore, multiple fractures were documented during the study period. Therefore, a strict separation of the site-specific results as presented in the supplemental material should be cautiously interpreted. Still, misclassification for minor and major pelvic fractures seems very unlikely. At last, although we adjusted for comorbidities in a reasonable way, there are other patient or clinical characteristics along with further effects of hospitalization for a pelvic fracture that could play a role, such as lifestyle factors (smoking, alcohol intake, physical activity) and operative or postoperative complications.

Our study has several strengths: First, we were able to analyze a very large sample and adjust for a number of important confounders. We used longitudinal health insurance data of a large population-based sample in order to get valid estimates of epidemiological measures. Because personalized individual data was available, we were able to follow all insured persons. Furthermore, we performed an accurate assessment of fracture events for outpatient-and inpatient-treated cases. Few studies are able to describe excess mortality based on inpatient and outpatient data. In our study, our mean matching rate corresponds to 1 to 34, which is higher compared with the matched cases and controls of two other studies on excess mortality after pelvic fracture.[16,17] This frequency-matching procedure was applied to reach high comparability between both groups. We further adjusted for comorbidities because patient characteristics and coexisting medical conditions are very important with regard to mortality. The Charlson comorbidity index is known as the most widely used algorithm and has been validated in different patient populations.[35] Although there are no studies to assess the performance of the Charlson comorbidity index in predicting mortality among patients with pelvic fracture, there are some studies that reported valid results for predicting mortality after hip fracture.[23,36,37]

Conclusions

Our study presents comprehensive results on excess mortality after pelvic fracture. It shows a high excess mortality. Therefore, further studies are needed to identify treatment improvements to reduce mortality.

Disclosures

All authors state that they have no conflicts of interest.

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Originalarbeit 3

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ORIGINAL ARTICLE

Health care utilization and excess costs after pelvic fractures among older people in Germany

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Abstract

Summary Our study demonstrates a strong increase in utilization of inpatient health care and clear excess costs in older people in the first year after pelvic fracture, the latter even after adjustment for several confounders. Excess costs were particularly high in the first few months and mainly attributable to inpatient treatment.

Introduction We aimed to estimate health care utilization and excess costs in patients aged minimum 60 years up to 1 year after pelvic fracture compared to a population without pelvic fracture.

Methods In this retrospective population-based observational study, we used routine data from a large statutory health insurance (SHI) in Germany. Patients with a first pelvic fracture between 2008 and 2010 (n=5685, 82% female, mean age 80±9 years) were frequency matched with controls (n=193,159) by sex, age at index date, and index month. We estimated health care utilization and mean total direct costs (SHI perspective) with 95% confidence intervals (CIs) using BCA bootstrap procedures for 52 weeks before and after the index date. We calculated cost ratios (CRs) in 4-week intervals after the index date by fitting mixed two-part models including adjustment for possible confounders and repeated measurement. All analyses were further stratified for men/women, in-/outpatient-treated, and major/minor pelvic fractures.

Results Health care utilization and mean costs in the year after the index date were higher for cases than for controls, with inpatient treatment being particularly pronounced. CRs (95% CIs) decreased from 10.7 (10.2–11.1) within the first 4 weeks to 1.3 (1.2–1.4) within week 49–52. Excess costs were higher for inpatient than for outpatient-treated persons (CRs of 13.4 (12.9–13.9) and 2.3 (2.0–2.6) in week 1–4). In the first few months, high excess costs were detected for both persons with major and minor pelvic fracture.

Conclusion Pelvic fractures come along with high excess costs and should be considered when planning and allocating health care resources.

Keywords Epidemiology · Excess costs · Health services research · Health care utilization · Pelvic fracture

Introduction

Low-energy pelvic fractures, which are mainly a result of simple falls among older people [1–4], are assumed to affect a growing number of individuals. In line, an increase of the incidence of pelvic fracture has already been reported [4–8]. In Germany, the incidence of pelvic fractures among older people was estimated to be even higher when compared to

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other countries [9]. For the same study population, excess mortality was found in the first 8 months after pelvic fracture even after adjustment for age, sex, insurance region, level of care, comorbidity, health care cost, and type of pelvic fracture [10]. Due to the worldwide demographic change and an aging population, pelvic fractures will gain increasing relevance for the society in general and for the German health care system in particular [11]. In addition to developing and monitoring prevention programs, it is necessary to describe health care utilization and determine the burden of pelvic fractures in monetary terms. This knowledge is, for example, needed for planning and allocating health care resources. It is well known that hip fractures are the most expensive fractures on a per-patient basis [12–15]. In comparison, there is only little evidence regarding the financial burden of pelvic fractures, although there are hints that pelvic fractures contribute to high costs as well [13, 14, 16]. Up to now, we have not identified any study that evaluated fracture severity, i.e., major or minor pelvic fractures. The aim of this study was to estimate health care utilization and excess costs in patients aged 60 years or older after a pelvic fracture compared to people without a pelvic fracture in Germany, based on data from a large statutory health insurance company (SHI). In sex-stratified analyses, particular attention was paid to the treatment setting and severity of fracture.

Material and methods

Study Design, data source, and population

The study is a retrospective population-based observational study. Routine data on health care provision was provided by a large SHI in Germany, the AOK NordWest. Overall, the AOK NordWest covers around 2.8 million people in two regions—Schleswig-Holstein (700,000 people) and Westfalen-Lippe (2.1 million people)—of whom about 29% are 60 years or older. We included all people aged 60 years or older who were continuously insured for at least 1 year between January 1, 2007, and December 31, 2011 (4,511,645 person-years at risk). The selection process is presented in detail elsewhere [9].

Ascertainment of cases with pelvic fracture events and controls without pelvic fracture

All insured persons with a first pelvic fracture between 2008 and 2010 were identified. In brief, pelvic fractures along with the exact week of occurrence were identified in inpatient and outpatient data according to the 10th revision of the International Classification of Diseases (ICD-10). A fracture event was defined by the following ICD-10 codes and classified into a major or minor pelvic fracture according to clinicians' decision: S32.1 (fracture of sacrum, major), S32.2 (fracture of coccyx, minor), S32.3 (fracture of ilium, major), S32.4 (fracture of acetabulum, major), S32.5 (fracture of pubis, minor), S32.81 (fracture of ischium, minor), S32.83 (fracture of pelvis unspecified, minor), and S32.89 (multiple and other fractures of pelvis, major). Only persons with a first fracture defined by an event-free period of at least 1 year prior to the event were included. For further analyses, we distinguished between persons with exclusively outpatient-treated and at some point inpatient-treated pelvic fracture within 1 year after the event. First pelvic fractures were considered inpatient-treated fractures, when insured persons had at least one hospital admission with a diagnosis of a pelvic fracture during the whole study period in line with a previous study conducted by the authors [9]. A pelvic fracture was classified as a major pelvic fracture if at least one major ICD-10 code occurred during the index week. To ensure complete cost data, we excluded persons who were not insured at least one complete year after the first fracture, with the only exception of death during this time (exclusion 4.4% of all persons with a fracture between 2008 and 2010) [9]. Persons with a first pelvic fracture in 2008–2010 ("case") and controls without pelvic fractures during the whole study period were frequency matched by sex, age (in integer years, one class for age ≥100 years), and index month. The index date was the date of the first pelvic fracture for cases and was randomly selected in the insurance period of the controls. The requirement of continuously insured time periods for the controls was the same as for cases. In the end, the sample comprised 5685 cases with and 193,159 controls without a pelvic fracture, equivalent to a mean matching rate of 1 to 34. No further selection of the controls was done. This implies more precise estimates in controls and simplifies subgroup analyses. The overall power is limited by the number of cases.

Assessment of health care utilization and costs

Health care utilization considering place and type of service, namely, inpatient care, outpatient care, outpatient drug prescriptions, rehabilitation, and received sickness benefit, was assessed. Direct net costs from the perspective of the SHI were assessed in total and separately for inpatient care, outpatient care, prescribed outpatient medication, and rehabilitation. Copayments from the patients are not included. All costs were assessed in euro (€). Additionally, sickness benefit was considered as transfer payment and stratified for cases and controls. Since our base year was 2011, all costs were adjusted to 2011 using the general consumer price index. Mean total costs included (a) inpatient costs: total costs of treatment of each hospitalization excluding costs for outpatient hospital services; (b) outpatient costs: costs of outpatient consultations, which are expressed as fees for all outpatient services, including extra-budgetary services and costs of dialysis treatment;

(c) medication costs: costs of each outpatient medication; (d) total costs of rehabilitation; and (e) total costs of sickness benefit. Outpatient costs were available only quarterly (as in Germany most outpatient services are reimbursed once in a quarter) and equally distributed over the weeks of the quarter.

Assessment of further variables

The following variables were included as possible confounders and are already described in full detail elsewhere [10]: age in 5-year age groups, sex, index year, insurance region as an approximation for the residence of the insured person, level of care according to the German legislation on social care insurance [17], comorbidity assessed by using the enhanced Charlson comorbidity algorithm for ICD-10 codes [18–23], health care cost consisting of inpatient and outpatient care, medications, rehabilitation, and sickness benefit accumulated in the year before the index week, death, and observation/survival time. For people who died during the observation period, the corresponding week of death was recorded. Additionally, observation time was considered, which equals survival time in weeks since the index week. Our selection of confounders was based on literature evidence [14, 24, 25] and clinical experience.

Statistical analyses

Patient characteristics in the index week were described by frequency tables, means ± standard deviations. Analyses were stratified by cases (all, inpatient-/outpatient-treated fractures, minor/major fractures) with controls as reference. The frequency matching ensured an adequate overall adjustment regarding age and gender. Frequency matching was not stratified for the different subgroups (e.g., for inpatient and outpatient cases) to avoid different control populations. However, in the fully adjusted models, adjustment was performed for confounders including sex and age. Prevalence of health care utilization as well as mean values for health care utilization for cases and controls were estimated along with 95% BCA bootstrap confidence intervals [26] to compare cases and controls 52 weeks before and after the index date. Mean total costs were calculated cumulatively for a total of 52 weeks before the index date. Health care costs 52 weeks before the index date were categorized in approximate quintile classes (€ 0–499, 500–999, 1000–1999, 2000–4999, 5000+) to get more robust results from the adjusted models (described below). After the index date, costs were on the one hand cumulated for 52 weeks and on the other hand proportionally divided in 13 time intervals of 4 weeks, in order to investigate the development of costs for cases and controls more closely. In each time interval, only data of surviving patients were included. There are alternative methods to describe excess costs (please see also *Comparison to previous studies*). One way is to calculate cost differences by subtracting the mean cost of controls from the mean cost of cases, as done in this manuscript for instance, to provide an estimate along with a 95% BCA bootstrap confidence interval for the absolute mean difference of annual total costs between cases and controls. Since the relation between costs for cases and controls is easier to understand and in order to facilitate interpretation of the data and improve legibility, excess costs were expressed as cost ratios and not as differences (subtracted costs). Cost outcomes were investigated by fitting uncorrelated mixed multiple two-part models [27] as follows: Firstly, in small but non-negligible (about 9%) percentages, there were zero values of costs for patients without a pelvic fracture in the follow-up intervals of 4 weeks and also for some cases in the time course after the pelvic fracture. In the first part of the model, the probability of "health care utilization" was used as a binary outcome, and relative risks (RRs) were estimated for independent variables (per unit change). Instead of a log-binomial model, a Poisson model with robust variance estimation was used to get stable results [28]. In the second part, a gamma model with log-link was fitted on the subpopulation with positive costs estimating CRs for unit changes of independent variables [29]. Both parts of the model were assumed to be approximately independent because of low percentages of zero costs. However, a valid estimation of correlations between all random effects in a correlated two-part model cannot be expected taking into account the efforts to get stable results in the first part of the model. A joint model was derived by multiplication of the RR and CR to get a joint CR corresponding to the overall means for the unit change of each independent variable. Variances and confidence intervals of the CRs in the joint model were calculated using log transformation. Independent variables were case (all or inpatient/outpatient or major/minor cases) versus control, time, and interaction time * case/control. Furthermore, adjusted models were fitted comprising the above named prespecified possible confounders including an interaction term for health care costs in the year before * case/control. Furthermore, high costs because of death were adjusted by including the confounder death and survival time. Adjustment for repeated measurement was performed by covariance patterns [30]. All analyses were performed separately for men and women. For the statistical analyses the software package SAS was used (SAS for X64_10PRO, Release 9.4, SAS Institute Inc. Cary, NC, USA).

Results

Characteristics of the study population

The study cohort comprised 5685 persons (n=4689 (82.5%) women) with a first pelvic fracture between 2008 and 2010, as well as 193,159 persons (n=154,960

(80.2%) women) without a pelvic fracture. The mean age (± standard deviation) was 80.3±8.7 (81.0±8.4 in women and 76.9±9.3 in men) for cases and 79.1 ± 8.4 years (79.8 ± 8.2 years in women and 76.2 ± 8.7 years in men) for controls. Further characteristics for cases and controls are summarized in Table 1. Overall, of 5685 persons with pelvic fracture, 4214 (74.1%) were at some point inpatient treated (for pelvic fracture within 1 year after the event), and 3646 (64.1%) had a major pelvic fracture. About 82.7% of major pelvic fractures were at some point inpatient treated. Yet, more than half of the minor pelvic fractures (58.8%) were at some point inpatient treated, too. Table 2 shows selected characteristics in more detail.

Health care utilization 1 year before the index date and in the year after

Table 3 shows health care utilization 52 weeks before and after the index date for the whole sample and stratified for men and women. Hospitalization, outpatient care, and prescriptions were frequently used, whereas rehabilitation and payment of sickness benefit for cases and controls did not contribute much to the overall health care utilization. In the year before the index date, health care use was higher in cases than in controls, particularly hospitalization. In the year after the index date, occurrence of inpatient care rose to almost 90% for cases, while it stayed almost the same for controls. No large difference was seen for outpatient care compared to the year before, although prevalence for cases was slightly lower than in the year before (but still > 98%). The number of outpatient drug prescriptions increased for cases and did not alter much for controls. Although a slight increase in occurrence of rehabilitation and payment of sickness benefit could be observed, the overall impact was still small. Comparing all components for cases, the largest change was seen in inpatient treatment. For controls, the development of health care utilization in the year after the index date was without striking deviations. There was only a small difference between cases and controls for men and women. However, the number of prescribed outpatient drugs was slightly higher for women—again higher for female cases than female controls—and increased in the year after the index date for the female cases. Table 4 reports health care utilization for at some point inpatient and exclusively outpatient-treated persons as well as patients with major and minor pelvic fractures. In the year before the index date, almost similar results were observed. Health care utilization in the year after the index date was clearly higher in inpatients compared to outpatients, in particular hospitalization.

Table 1 Characteristics of the study population

	Persons with first pelvic fracture (*n*=5685)			Persons without pelvic fracture (n=193,159)		
	All	Men (*n*=996)	Women (*n*=4689)	All	Men (*n*=38,199)	Women (*n*=154,960)
Mean age ± SD	80.3±8.7	76.9±9.3	81.0±8.4	79.1±8.4	76.2±8.7	79.8±8.2
Age (%)						
60–64	4.9	9.1	4.0	5.2	9.1	4.3
65–69	8.9	15.4	7.5	10.5	17.2	8.8
70–74	14.5	20.6	13.2	16.5	20.9	15.4
75–79	17.5	20.0	16.9	20.0	20.4	19.9
80–84	22.0	16.3	23.3	21.5	15.8	23.0
85–89	19.7	10.5	21.7	17.2	10.5	18.8
≥ 90	12.5	8.1	13.5	9.1	6.1	9.9
Region (%) in Westfalia	72.7	72.4	72.7	70.9	69.7	71.2
Level of care (%)						
Level of care 0	60.7	68.8	59.0	76.2	84.4	74.2
Level of care 1	23.4	17.9	24.6	12.1	7.9	13.1
Level of care 2	14.1	12.1	14.5	8.7	5.9	9.4
Level of care 3	1.8	1.3	1.9	3.0	1.7	3.4
Comorbidity (%)						
Charlson 0	16.7	15.4	17.0	26.5	27.3	26.3
Charlson 1	19.3	16.6	19.9	21.3	18.5	22.0
Charlson 2–3	31.0	29.4	31.4	28.7	27.3	29.0
Charlson 4–5	17.7	18.4	17.5	14.0	14.9	13.7
Charlson 6	15.3	20.3	14.3	9.6	12.0	9.0

Table 2 Characteristics of at some point inpatient-treated and exclusively outpatient-treated persons as well as patients with major and minor pelvic fractures

	Persons with first pelvic fracture (*n*=5685)			
	Inpatient (*n*=4214)	Outpatient (*n*=1471)	Major (*n*=3646)	Minor (*n*=2039)
Sex (%)				
Men	17.4	17.7	18.9	15.1
Women	82.6	82.3	81.1	84.9
Mean age ± SD	81.3 ± 8.3	77.3±9.0	80.7 ± 8.5	79.5 ± 8.9
Age (%)				
60–64	3.4	9.0	4.3	5.9
65–69	7.3	13.5	8.0	10.5
70–74	12.6	19.9	13.7	15.9
75–79	16.9	19.2	17.5	17.4
80–84	23.8	16.9	22.4	21.3
85–89	22.2	12.6	21.0	17.4
≥ 90	13.9	8.8	13.1	11.6
Region (%) in Westfalia	72.2	74.0	71.4	75.0
Level of care (%)				
Level of care 0	57.1	71.2	59.4	63.1
Level of care 1	25.7	16.9	24.3	21.9
Level of care 2	15.5	10.1	14.4	13.5
Level of care 3	1.8	1.8	2.0	1.5
Comorbidity (%)				
Charlson 0	15.4	20.5	16.6	16.9
Charlson 1	18.4	21.8	19.2	19.4
Charlson 2–3	31.8	29.0	31.4	30.5
Charlson 4–5	18.2	16.1	17.7	17.6
Charlson 6	16.3	12.6	15.1	15.7

Table 3 Health care utilization and costs, 52 weeks before and after index date, overall, men, and women

	Persons with first pelvic fracture			Persons without pelvic fracture		
	All (*n*=5685)	Men (*n*=996)	Women (*n*=4689)	All (*n*=193,159)	Men (*n*=38,199)	Women (*n*=154,960)
Health care utilization[a]						
52 weeks before index date						
Inpatient care (%)	49.6 (48.2–50.9)	48.2 (45.0–51.3)	49.8 (48.4–51.3)	30.8 (30.6–31.0)	30.4 (30.0–30.9)	30.9 (30.7–31.1)
Outpatient care (%)	99.4 (99.1–99.6)	99.0 (98.2–99.5)	99.5 (99.2–99.7)	94.9 (94.9–95.0)	91.8 (91.5–92.1)	95.7 (95.6–95.8)
Rehabilitation (%)	4.24 (3.73–4.80)	3.92 (2.80–5.31)	4.31 (3.74–4.93)	2.22 (2.15–2.28)	1.89 (1.75–2.03)	2.30 (2.22–2.37)
Sickness benefit (%)	0.09 (0.03–0.21)	0.10 (0.00–0.56)	0.09 (0.02–0.22)	0.13 (0.11–0.14)	0.35 (0.29–0.41)	0.07 (0.06–0.09)
Outpatient drug prescriptions (mean)	22.8 (22.4–23.3)	20.2 (19.1–21.3)	23.4 (22.9–23.8)	16.9 (16.8–17.0)	14.5 (14.3–14.7)	17.5 (17.4–17.6)
52 weeks after index date						
Inpatient care (%)	87.6 (86.7–88.4)	88.2 (86.0–90.1)	87.5 (86.5–88.4)	34.7 (34.5–34.9)	35.1 (34.6–35.6)	34.6 (34.4–34.8)
Outpatient care (%)	99.2 (99.0–99.5)	98.3 (97.3–99.0)	99.4 (99.2–99.6)	95.2 (95.1–95.3)	92.1 (91.8–92.4)	96.0 (95.9–96.1)
Rehabilitation (%)	6.82 (6.18–7.51)	7.13 (5.61–8.91)	6.76 (6.06–7.52)	2.10 (2.03–2.16)	1.90 (1.76–2.04)	2.15 (2.08–2.22)
Sickness benefit (%)	0.28 (0.16–0.46)	0.60 (0.22–1.31)	0.21 (0.10–0.39)	0.13 (0.12–0.15)	0.38 (0.32–0.45)	0.07 (0.06–0.08)
Outpatient drug prescriptions (mean)	25.9 (25.4–26.4)	22.2 (20.9–23.7)	26.7 (26.2–27.3)	16.7 (16.6–16.8)	14.4 (14.2–14.5)	17.3 (17.2–17.3)
Mean costs (€)[b]						
52 weeks before index date						
Total costs	6226 (5974–6493)	6590 (5965–7344)	6148 (5909–6436)	3392 (3368–3424)	3600 (3524–3672)	3341 (3312–3373)
Inpatient care	3593 (3413–3771)	3801 (3371–4373)	3549 (3382–3752)	1766 (1746–1788)	1907 (1851–1961)	1731 (1709–1754)
Outpatient care	1116 (1045–1220)	1254 (1039–1574)	1086 (1003–1184)	674 (668–682)	716 (695–738)	664 (656–671)
Rehabilitation	139 (118–163)	145 (103–214)	137 (117–163)	65 (63–67)	59 (53–65)	67 (64–70)
Sickness benefit	4.2 (1.1–12.3)	11.2 (0.0–33.5)	2.7 (0.6–7.8)	4.3 (3.6–5.3)	14.7 (11.2–18.8)	1.8 (1.3–2.4)
Outpatient drug prescriptions	1374 (1301–1470)	1379 (1220–1571)	1373 (1297–1492)	883 (874–892)	903 (881–930)	878 (868–889)
52 weeks after index date						
Total costs	11,108 (10,756–11,453)	12,965 (12,004–14,057)	10,714 (10,379–11,074)	3792 (3762–3823)	4234 (4147–4327)	3683 (3652–3717)
Inpatient care	8240 (7941–8513)	10,078 (9236–11,127)	7850 (7584–8167)	2161 (2136–2187)	2527 (2459–2603)	2071 (2045–2097)
Outpatient care	1138 (1066–1225)	1241 (1046–1525)	1116 (1041–1202)	700 (693–706)	743 (722–764)	689 (682–697)
Rehabilitation	227 (203–257)	213 (165–278)	230 (203–264)	61 (59–64)	60 (55–67)	61 (59–64)
Sickness benefit	11.3 (5.1–22.0)	34.3 (7.2–104.9)	6.5 (2.4–14.4)	6.7 (5.6–8.0)	22.7 (18.1–28.8)	2.8 (2.1–3.6)
Outpatient drug prescriptions	1491 (1414–1586)	1399 (1250–1611)	1511 (1425–1620)	863 (854–872)	881 (861–905)	858 (849–868)

[a] Data on health care utilization is given as prevalence (%) or mean number (for outpatient drug prescriptions) including 95% confidence intervals (Pearson-Clopper for prevalences, BCA bootstrapping for mean numbers)

[b] Mean costs including 95% confidence intervals (BCA bootstrapping)

Table 4 Health care utilization and costs, 52 weeks before and after index date, inpatient-outpatient, major-minor

	Persons with first pelvic fracture (*n*=5685)			
	Inpatient (*n*=4214)	Outpatient (*n*=1471)	Major (*n*=3646)	Minor (*n*=2039)
Health care Utilization[a]				
52 weeks before index date				
Inpatient care (%)	51.5 (50.0–53.0)	44.0 (41.4–46.6)	49.9 (48.2–51.5)	49.0 (46.8–51.2)
Outpatient care (%)	99.2 (98.9–99.5)	99.9 (99.5–100.0)	99.3 (99.0–99.5)	99.6 (99.2–99.8)
Rehabilitation (%)	4.08 (3.50–4.72)	4.69 (3.67–5.90)	4.14 (3.52–4.84)	4.41 (3.56–5.40)
Sickness benefit (%)	0.07 (0.01–0.21)	0.14 (0.02–0.49)	0.05 (0.01–0.20)	0.15 (0.03–0.43)
Outpatient drug prescriptions (mean)	23.5 (23.0–24.0)	20.8 (20.0–21.7)	23.0 (22.4–23.5)	22.6 (21.9–23.3)
52 weeks after index date				
Inpatient care (%)	100.0[b]	52.1 (49.5–54.7)	92.2 (91.3–93.1)	79.4 (77.5–81.1)
Outpatient care (%)	99.0 (98.6–99.3)	100.0 (99.7–100.0)	99.2 (98.8–99.4)	99.4 (98.9–99.7)
Rehabilitation (%)	7.64 (6.86–8.48)	4.49 (3.49–5.67)	7.35 (6.52–8.25)	5.89 (4.90–7.00)
Sickness benefit (%)	0.14 (0.05–0.31)	0.68 (0.33–1.25)	0.25 (0.11–0.47)	0.34 (0.14–0.71)
Outpatient drug prescriptions (mean)	26.7 (26.0–27.2)	23.7 (22.7–24.7)	26.1 (25.5–26.8)	25.6 (24.7–26.4)
Mean costs (€)[b]				
52 weeks before index date				
Total costs (€)	6539 (6244–6826)	5327 (4942–5800)	6189 (5894–6506)	6291 (5923–6727)
Inpatient care	3851 (3645–4062)	2853 (2572–3151)	3633 (3423–3886)	3522 (3231–3813)
Outpatient care	1130 (1035–1248)	1075 (960–1250)	1062 (971–1164)	1211 (1083–1405)
Rehabilitation	136 (113–161)	146 (111–198)	134 (110–166)	147 (114–187)
Sickness benefit	4.2 (0.3–14.2)	4.1 (0.0–14.7)	1.8 (0.0–7.2)	8.4 (1.7–34.5)
Outpatient drug prescriptions	1418 (1329–1532)	1249 (1123–1434)	1358 (1276–1504)	1402 (1283–1578)
52 weeks after index date				
total costs	12773 (12359–13229)	6339 (5826–6844)	11747 (11339–12203)	9965 (9433–10550)
Inpatient care	9907 (9557–10308)	3466 (3110–3830)	8937 (8575–9297)	6994 (6584–7573)
Outpatient care	1107 (1024–1210)	1227 (1098–1422)	1061 (973–1158)	1276 (1136–1447)
Rehabilitation	262 (228–298)	129 (97–167)	252 (218–294)	182 (152–225)
Sickness benefit	8.9 (2.5–24.8)	18.5 (7.4–43.2)	13.3 (4.2–30.6)	7.8 (2.2–23.2)
Outpatient drug prescriptions	1489 (1413–1587)	1498 (1347–1787)	1483 (1383–1629)	1505 (1388–1677)

[a] Data on health care utilization is given as prevalence (%) or mean number (for outpatient drug prescriptions) including 95% confidence intervals (Pearson-Clopper for prevalences, BCA bootstrapping for mean numbers); costs including 95% confidence intervals (BCA bootstrapping)

[b] All inpatient-treated persons used inpatient care, such that a confidence interval would not be meaningful

Inpatient care increased to over 90% for major pelvic fractures and about 80% for minor pelvic fractures.

Mean costs 1 year before the index date and in the year after

Mean total costs for the whole sample and stratified for men and women are also shown in Table 3. The observed overall pattern was similar to that described for health care utilization. Previous-year costs were higher in cases. While the mean total costs for the cases were nearly doubled compared to the previous year, the mean total costs for controls almost stayed the same. The absolute mean difference of total costs between cases and controls (95% CIs) in the year after the index date was €7317 (6992–7691). Thus, a disproportionate increase in the cost of cases compared to controls was observed, mainly driven by costs for inpatient care. Unadjusted absolute mean differences of different costs and subgroups can be calculated from the estimates in Tables 3 and 4.

In the year before and after the index date, the costs in total and all cost components were generally higher for men than for women in cases and controls. An exception were costs for outpatient drug prescriptions and rehabilitation which were higher for female cases.

Table 4 also displays mean total costs for at some point inpatient and exclusively outpatient-treated persons as well

as patients with major and minor pelvic fractures. In contrast to the year after the index date, mean total costs and their cost components did not differ considerably for inpatient-treated and outpatient-treated persons in the year before. However, costs for inpatients were already a bit higher than for outpatients. In the year after the index date, costs for inpatient-treated cases were twice as high as for outpatient-treated cases, again driven by costs for hospitalization. Mean costs for outpatient care and outpatient drug prescriptions were slightly lower for inpatients than for outpatients.

In the year before the index date, the mean total costs for persons with major and minor fractures were almost the same. In total and for some components costs were slightly higher for persons with minor fracture. In the year after the index date, the mean total costs for major fractures exceeded the costs for minor fractures. The largest increase in costs was attributable to inpatient care, where costs almost doubled for minor pelvic fractures and were about 2.5 times higher for major pelvic fractures compared to the year before.

Excess costs after pelvic fracture (two-part models and cost ratios)

Table 5 shows the fully adjusted CRs (95% CI) for the 4-week periods up to 52 weeks for the total sample and for at some point inpatient-treated and exclusively outpatient-treated persons. Overall, significant excess costs were observed until 52 weeks after the index date. CRs decreased during the 52 weeks from 10.7 (10.2–11.1) in week 1–4 to 1.3 (1.2–1.4) in week 49–52. Excess costs in men and women were quite similar.

Moreover, fully adjusted CRs were elevated until week 52 for inpatient-treated persons and until week 44 for outpatient-treated persons. For inpatient-treated persons, the fully adjusted CR was 13.4 (12.9–13.9) in week 1–4. Outpatient-treated persons showed a fully adjusted CR of 2.3 (2.0–2.6) in week 1–4 weeks after pelvic fracture.

Table 5 also contains fully adjusted CRs (95% CI) for the 4-week periods up to 52 weeks for persons with major and minor pelvic fractures. CRs express excess costs for persons with major and minor pelvic fractures when compared with persons without a pelvic fracture. Fully adjusted CRs for persons with major pelvic fracture were 11.9 (11.4-12.4) in the first 4 weeks and 1.2 (1.1-1.4) in week 49-52 after the index date. Excess costs (CRs) for minor pelvic fractures were high (but not comparable) in the beginning, too: From 8.5 (7.9–9.1) in the fully adjusted model in week 1–4, they lowered to 1.3 (1.1–1.5) in week 49–52.

Discussion

Main findings

By using longitudinal SHI data from a large population-based sample, we were able to assess health care utilization and costs in great detail and provide accurate estimates. Our results are broadly in line with our expectations: It was found that in the year after the index date, health care utilization of persons with pelvic fracture increased compared to the year before, with utilization of inpatient treatment being particularly noticeable. Accordingly, our study showed high costs with a disproportionate increase in the year after pelvic fracture, especially for inpatient care. However, it has to be taken into account that already in the year before the index date, health care use and costs were higher in cases than in controls. This leads to the conclusion that cases were sicker than the controls. Excess costs (adjusted for confounders) were observed in the complete year after a pelvic fracture—which was somewhat surprising—with a fairly similar pattern in men and women. Excess costs were particularly high in the first 4 weeks after pelvic fracture and lowered substantially in later weeks. Already in weeks 5–8, they were only about half as high as in the first period, with the only exception of excess costs for outpatient-treated persons (which were rather low in comparison). Excess costs were highest for inpatient-treated persons. In the first few months, high excess costs were detected for persons with major and persons with minor pelvic fracture (when compared with persons without a pelvic fracture), although excess costs for minor fractures occurred to a lesser extent.

Comparison to previous studies

The comparison with existing studies is limited due to differences in study design, study period, study population, and methods used for cost analysis. Since most studies are carried out in the USA, a comparison with German data is considerably limited due to the different health care and insurance systems. Overall, we identified no study which analyzed excess cost in time intervals of 4 weeks in the year after the index date. However, there were three studies that examined direct medical costs in older people after a pelvic fracture based on administrative data using different approaches [13, 14, 16]. Ohsfeldt et al. [13] provided estimates of fracture-related direct medical costs and data on health care utilization in a managed care setting for patients with a mean age of 70 years with a primary diagnosis for a fragility non-vertebral fracture, including pelvic fracture, during the first year following the event. They analyzed cost per fracture for the first month

Table 5 Cost ratios for the total sample, inpatient-/outpatient-treated, and major/minor fractures, stratified for overall, men, and women

	Week after index date	Fully adjusted CR (95% CI)[a]				
		Total sample	Inpatient treated	Outpatient treated	Major	Minor
Overall	01–04	10.65 (10.24–11.06)	13.39 (12.91–13.90)	2.30 (2.04–2.59)	11.87 (11.37–12.39)	8.46 (7.86–9.10)
	05–08	5.22 (4.95–5.49)	6.28 (5.95–6.62)	2.07 (1.80–2.38)	5.83 (5.48–6.20)	4.10 (3.77–4.46)
	09–12	3.15 (2.94–3.37)	3.62 (3.37–3.90)	1.83 (1.55–2.15)	3.43 (3.15–3.73)	2.63 (2.37–2.90)
	13–16	2.11 (1.96–2.27)	2.38 (2.19–2.59)	1.38 (1.18–1.62)	2.21 (2.02–2.43)	1.91 (1.70–2.15)
	17–20	1.86 (1.72–2.01)	2.02 (1.85–2.22)	1.48 (1.26–1.73)	1.81 (1.64–2.00)	1.91 (1.69–2.17)
	21–24	1.63 (1.51–1.77)	1.80 (1.64–1.97)	1.30 (1.10–1.54)	1.70 (1.53–1.88)	1.49 (1.33–1.68)
	25–28	1.51 (1.40–1.63)	1.68 (1.53–1.84)	1.16 (1.00–1.33)	1.57 (1.43–1.74)	1.38 (1.22–1.56)
	29–32	1.46 (1.35–1.58)	1.59 (1.46–1.74)	1.24 (1.05–1.47)	1.52 (1.38–1.67)	1.36 (1.20–1.54)
	33–36	1.39 (1.28–1.51)	1.44 (1.31–1.58)	1.29 (1.06–1.56)	1.38 (1.25–1.51)	1.40 (1.19–1.64)
	37–40	1.35 (1.24–1.48)	1.39 (1.26–1.55)	1.29 (1.08–1.54)	1.34 (1.19–1.50)	1.37 (1.20–1.57)
	41–44	1.37 (1.26–1.48)	1.41 (1.28–1.56)	1.22 (1.05–1.41)	1.35 (1.22–1.50)	1.37 (1.20–1.55)
	45–48	1.30 (1.19–1.41)	1.37 (1.25–1.51)	1.09 (0.94–1.26)	1.30 (1.17–1.44)	1.28 (1.11–1.47)
	49–52	1.26 (1.16–1.37)	1.34 (1.22–1.47)	1.04 (0.90–1.20)	1.22 (1.11–1.35)	1.30 (1.12–1.50)
Men	01–04	10.93 (9.90–12.07)	13.50 (12.29–14.84)	2.64 (1.94–3.59)	12.33 (11.08–13.71)	7.45 (6.16–9.03)
	05–08	5.14 (4.46–5.93)	6.18 (5.33–7.16)	1.96 (1.41–2.72)	5.81 (4.94–6.83)	3.67 (2.82–4.78)
	09–12	3.25 (2.72–3.88)	3.69 (3.06–4.45)	1.74 (1.22–2.47)	3.77 (3.07–4.62)	2.06 (1.57–2.71)
	13–16	2.06 (1.73–2.45)	2.18 (1.83–2.60)	1.76 (1.10–2.81)	2.26 (1.83–2.78)	1.62 (1.21–2.16)
	17–20	1.82 (1.54–2.15)	2.06 (1.71–2.48)	1.44 (1.00–2.08)	1.83 (1.50–2.22)	1.82 (1.34–2.46)
	21–24	1.85 (1.49–2.29)	2.08 (1.64–2.64)	1.50 (0.88–2.56)	2.20 (1.70–2.84)	1.14 (0.84–1.55)
	25–28	1.56 (1.27–1.91)	1.82 (1.43–2.32)	1.12 (0.74–1.69)	1.66 (1.28–2.15)	1.33 (0.97–1.83)
	29–32	1.54 (1.26–1.88)	1.76 (1.39–2.23)	1.20 (0.81–1.78)	1.70 (1.33–2.18)	1.28 (0.94–1.74)
	33–36	1.29 (1.07–1.56)	1.30 (1.06–1.61)	1.41 (1.00–1.99)	1.30 (1.04–1.62)	1.33 (0.96–1.84)
	37–40	1.21 (1.00–1.48)	1.21 (0.96–1.52)	1.31 (0.95–1.81)	1.29 (1.01–1.64)	1.10 (0.79–1.52)
	41–44	1.18 (0.99–1.41)	1.20 (0.99–1.46)	1.19 (0.78–1.82)	1.20 (0.97–1.48)	1.17 (0.88–1.56)
	45–48	1.33 (1.11–1.59)	1.47 (1.19–1.80)	1.22 (0.80–1.85)	1.36 (1.09–1.70)	1.31 (0.98–1.75)
	49–52	1.11 (0.92–1.35)	1.13 (0.90–1.41)	1.08 (0.72–1.63)	1.06 (0.84–1.32)	1.20 (0.86–1.67)
Women	01–04	10.55 (10.12–10.99)	13.31 (12.79–13.84)	2.23 (1.95–2.54)	11.71 (11.18–12.26)	8.56 (7.92–9.26)
	05–08	5.21 (4.93–5.50)	6.27 (5.92–6.64)	2.09 (1.79–2.43)	5.81 (5.44–6.21)	4.16 (3.81–4.54)
	09–12	3.12 (2.90–3.35)	3.60 (3.33–3.90)	1.82 (1.53–2.17)	3.34 (3.04–3.66)	2.71 (2.43–3.02)
	13–16	2.12 (1.95–2.31)	2.42 (2.20–2.66)	1.32 (1.12–1.54)	2.21 (1.98–2.45)	1.96 (1.72–2.22)
	17–20	1.87 (1.71–2.04)	2.02 (1.83–2.24)	1.49 (1.25–1.77)	1.82 (1.62–2.04)	1.93 (1.68–2.21)
	21–24	1.60 (1.47–1.74)	1.74 (1.58–1.92)	1.28 (1.08–1.52)	1.61 (1.44–1.79)	1.56 (1.37–1.77)
	25–28	1.51 (1.39–1.64)	1.65 (1.49–1.82)	1.19 (1.02–1.39)	1.57 (1.41–1.74)	1.39 (1.22–1.59)
	29–32	1.45 (1.33–1.57)	1.56 (1.42–1.72)	1.26 (1.05–1.52)	1.48 (1.34–1.64)	1.38 (1.20–1.58)
	33–36	1.41 (1.28–1.55)	1.47 (1.32–1.63)	1.27 (1.02–1.58)	1.39 (1.25–1.55)	1.41 (1.19–1.68)
	37–40	1.38 (1.25–1.53)	1.43 (1.27–1.60)	1.29 (1.06–1.58)	1.34 (1.18–1.53)	1.43 (1.23–1.66)
	41–44	1.40 (1.28–1.54)	1.45 (1.30–1.61)	1.23 (1.05–1.44)	1.38 (1.23–1.55)	1.41 (1.23–1.62)
	45–48	1.29 (1.17–1.42)	1.35 (1.21–1.51)	1.08 (0.93–1.27)	1.29 (1.15–1.44)	1.28 (1.09–1.50)
	49–52	1.29 (1.17–1.41)	1.38 (1.25–1.53)	1.03 (0.88–1.20)	1.26 (1.13–1.41)	1.32 (1.12–1.54)

[a] Adjusted for age, sex, index year, insurance region, care level, comorbidity, previous year's costs, death, survival time, and previous year's costs * case/control (interaction term). No missings in the covariables.

separately. Results were stratified for outpatient, inpatient, long-term care, and other. However, by using this approach, no excess/incremental costs were reported. Kilgore et al. [16] conducted a retrospective, person-level, and pre-/post-fracture analysis among a sample of Medicare beneficiaries aged 65 years or older and presented incremental and attributable payments in the 6 months after the fracture event for various closed fractures, among other pelvic fractures. In their study,

costs for drug prescription and institutional care are missing. Pike et al. [14] described resource use, as well as direct and indirect costs for Medicare patients at age 65 or older in the first year after a fracture. Osteoporotic fracture cases, including patients with pelvic fracture, were matched randomly on age, sex, geographic region, and race to controls with osteoporosis and no fractures. Cost differences between patients and controls were calculated as excess costs. It has to be kept in mind that this study only included patients with diagnosed osteoporosis, which might lead to a selection bias, since relevant patient groups, e.g., undiagnosed patients or patients with osteopenia, are not analyzed. In line with our findings, these three studies confirm high costs in the year after the fracture. Ohsfeldt et al. [13] reported that the costs for pelvic fractures were particularly high in the first month after fracture. Eighty-eight percent of annual costs occurred during this period, which may be due to the approach used, among other reasons. In our study, 30% of the costs of cases and 9% of the costs of controls were incurred within the first month. Pike et al. found high excess costs for Medicare patients within the first year after pelvic fracture/other non-vertebral fractures and therefore examined the economic burden of various fractures over a 2-year period, but only in a privately insured population aged 18–64 years [15]. Comparable to our study, most pelvic fractures were treated in an inpatient care setting, so most costs occurred for inpatient care as well [13, 14]. In our study, 74% of pelvic fracture patients were at some point inpatient treated. Mean inpatient care costs for these patients were €9907, which is approximately 78% of total costs for this patient group. Similar to our results, Ohsfeldt et al. [13] reported that 70% of patients with a pelvic fracture required a hospital stay, causing 86% of fracture-related direct medical costs. Since pelvic fractures come along with high costs, the comparison of major or minor pelvic fracture is of particular interest. It seems possible that the procedures for diagnosis and treatment of major and minor pelvic fractures are rather similar. This argument could explain why we found excess costs for both. To our knowledge, no other study provides findings stratified for major and minor fractures. Our study is therefore an expansion of existing research. However, future research should be conducted.

Implications

As we have already shown, incidence rates of pelvic fracture in Germany are considerably high [9]. The already high health care utilization and excess costs among older people with pelvic fractures—which might further increase due to the demographic change—need to be recognized in the future for planning and allocating health care resources, especially for inpatient treatment. The planning and allocation of resources should not be done in isolation but should take into account all diseases with high excess costs (e.g., chronic diseases like diabetes). The data can also be used for cost effectiveness analysis in the context of prevention.

Limitations and strengths

Several limitations need to be considered: First, we used only specific ICD-10 coding for pelvic fracture and the underlying causes of injury were not recorded. Thus, the level of associated trauma was missing, and we could not distinguish between low-energy and high-energy fractures. However, we assume that the vast majority of pelvic fractures are caused by low-energy trauma resulting from simple falls. Second, clinical parameters could not be described, which could limit the presentation of the study population and interpretation of the results. However, we were able to adjust for comorbidity in a reasonable way, and thus at least consider the coexistence of diseases in terms of cost. Third, we made use of the general consumer price index. However, in many countries, the inflation in health sector outstrips that in general goods. Fourth, due to data limitations, the costs of care services that are covered by the SHI (which also includes payments of the care insurance) could not be included in our analysis, although they are considered a relevant cost component. Fortunately, we were able to perform a descriptive analysis in a subpopulation with complete care costs. It appeared that mean costs of care services, which were higher for cases than for controls, were the second largest component of mean total costs (after costs for inpatient care) 52 weeks after the index date. Initially, the costs of care services for cases did not differ substantially from controls after the index date, but they increased over time to a relatively constant level. This could be explained by the facts that during the frequent inpatient stays at the beginning, fewer costs of care services are incurred and that some persons only need additional care services after the pelvic fracture, so that the costs do not start to count until later in time. Overall, results have to be interpreted with caution, since the subpopulation was selected, the sample size was small—even more limited in subgroups—and large variances were observed. In future research, it would be interesting to examine these findings with more recent and comprehensive data. Fifth, we could only use SHI data up to 2011, which might raise questions regarding the timeliness of the results. However, since no major administrative changes have taken place in Germany in recent years with regard to health care utilization or reimbursement considering pelvic fractures, the study provides relevant insights on health care utilization and costs after pelvic fracture. Sixth, bias from mortality was induced in different directions, which cannot be adjusted by a simple confounding term in the model. There might be further interactions between time and confounders (time specific confounding), as well. We decided not to fit models including interactions between time and confounders, because we expected serious runtime and convergence problems.

Our study has several strengths: First, we were able to analyze longitudinal SHI data from a large population-based sample and take into account a number of possible confounders. Second, since personalized individual data was available 1 year before and 1 year after the event, it was possible to track all insured persons over a long observation period. Finally, we conducted an exact assessment of fracture events, especially regarding treatment setting and fracture severity, and were thus able to gain new insights into the occurrence of health care utilization and costs.

Conclusions

Our study demonstrates a strong increase in utilization of inpatient health care and clear excess costs in older people in the first year after pelvic fracture, the latter even after adjustment for several confounders. Excess costs were particularly high in the first month and again mainly attributable to inpatient treatment. Subgroup analyses regarding treatment setting and severity of fracture reveal substantial differences and provide specific insights for appropriate planning and allocation of health care resources.

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Availability of data and material Data are subject to the legal data protection laws and only available in an aggregated form upon formal request. The contact person is Dr. Burkhard Haastert, responsible Biostatistican of the project group, mediStatistica, 58809 Neuenrade, and associate researcher at the Institute for Health Services Research and Health Economics, Faculty of Medicine, Heinrich-Heine-University Düsseldorf, Germany, who needs to be contacted at haastert@medistatistica.de.

Code availability Not applicable

Declarations

Ethics approval The study was approved by the ethics committee of the Faculty of Medicine, Heinrich-Heine-University Düsseldorf (approval reference 3839). The survey and utilization of secondary health administration data was conducted retrospectively and in compliance with the applicable standards and legal rules on data protection. All procedures performed were in accordance with the Declaration of Helsinki and comparable ethical standards (e.g., Good Epidemiologic Practice (GEP) and Good Practice of Secondary Data Analysis (GPS)). The data were analyzed anonymously; informed patient consent is not required.

Consent to participate Not applicable

Consent for publication Not applicable

Conflicts of interest None.

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Originalarbeit 4

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Methods

Using statutory health insurance data to evaluate non-response in a cross-sectional study on depression among patients with diabetes in Germany

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Abstract

Background: Low response rates do not indicate poor representativeness of study populations if non-response occurs completely at random. A non-response analysis can help to investigate whether non-response is a potential source for bias within a study.

Methods: A cross-sectional survey among a random sample of a health insurance population with diabetes ($n = 3642$, 58.9% male, mean age 65.7 years), assessing depression in diabetes, was conducted in 2013 in Germany. Health insurance data were available for responders and non-responders to assess non-response bias. The response rate was 51.1%. Odds ratios (ORs) for responses to the survey were calculated using logistic regression taking into consideration the depression diagnosis as well as age, sex,

antihyperglycaemic medication, medication utilization, hospital admission and other comorbidities (from health insurance data).

Results: Responders and non-responders did not differ in the depression diagnosis [OR 0.99, confidence interval (CI) 0.82–1.2]. Regardless of age and sex, treatment with insulin only (OR 1.73, CI 1.36–2.21), treatment with oral antihyperglycaemic drugs (OAD) only (OR 1.77, CI 1.49–2.09), treatment with both insulin and OAD (OR 1.91, CI 1.51–2.43) and higher general medication utilization (1.29, 1.10–1.51) were associated with responding to the survey.

Conclusion: We found differences in age, sex, diabetes treatment and medication utilization between responders and non-responders, which might bias the results. However, responders and non-responders did not differ in their depression status, which is the focus of the DiaDec study. Our analysis may serve as an example for conducting non-response analyses using health insurance data.

Key words: Diabetes, non-response, health survey, depression, quality of life

Key Messages

- Unexpectedly, the responders did not differ from the non-responders in having a history of depression diagnosis in a survey among patients with diabetes.
- Responders and non-responders differed in other characteristics, such as age and sex, with older persons being more likely to respond than younger persons and females being less likely to respond than males.
- We could use a comprehensive set of sociodemographic and health-related data for both responders and non-responders to analyse the representativeness of responders with large explanatory power.

Introduction

Traditionally, the representativeness of surveys in social and health-care science is evaluated on the response rates.[1–3] However, within studies using survey data, it is not expected to receive a complete response from every individual invited to participate, even though a complete response is the primary goal.[4] In the past decades, response rates worldwide, especially those in western countries, have declined.[5–8] Recent research suggests that the representativeness of a study is not inevitably dependent on its response rate.[1,9,10] If the non-responses to the survey occurred completely at random, a low response rate does not necessarily indicate poor representativeness of the study population.[1] Unfortunately, the non-responses rarely occur completely at random. With non-responses, we might obtain biased results with regard to prevalence or incidence and with regard to associations between health outcomes and risk factors. Differences between responders and non-responders have been observed with respect to socio-economic and demographic characteristics as well as variations in health status. Non-responders are, for example, more likely to live alone,[5,6] to be less educated, to have a poorer lifestyle and a worse health status than are responders.[6] However, little evidence is available on the difference between responders and non-responders regarding the variables of primary interest in health surveys because key measures are usually not available for non-responders. By using health insurance data, we had the unique opportunity to assess differences between responders and non-responders, focusing on a variable that is the main outcome of our survey: depression status.

This paper focuses on the comparison of responders with non-responders within the project 'Quality of life, disability, health care utilization and costs in patients with diabetes: The role of depression' (DiaDec). The aims of the DiaDec study are to estimate the prevalence of depression symptoms among patients with diabetes and to evaluate the association between comorbid depression status and health-care utilization/costs as well as health-related quality of life (HRQoL). With this paper, we aim to answer the following three questions: (1) Is the depression status different between responders and non-responders? (2) Are sociodemographic characteristics related to non-response in the DiaDec study? (3) Are diabetes treatment, comorbidities and health-care utilization associated with response status?

Methods

Design of the DiaDec study

A detailed description of the study design and methods is available from Kvitkina *et al.*[11] In short, we conducted a

cross-sectional nine-page postal survey in a random sample of a German statutory health insurance (SHI) population with diabetes and later linked the data on an individual level to longitudinal SHI data. The baseline survey was conducted during 2013. All responders who gave consent and the SHI data on health-care utilization patterns and health-care costs that were available for the period between 12 months before and 12 months after the baseline survey were included. The questionnaire assessed sociodemographic variables, depression symptoms, HRQoL and diabetes-specific distress. By linking the survey data with longitudinal SHI data, the association between depression status, HRQoL and health-care utilization/costs in the year before and after the survey were investigated.

Study population and recruitment procedure

Of the 636 451 individuals insured by pronova Betriebskrankenkassen (BKK), a national statutory health insurance company, 46 566 individuals had diabetes and were thus potential study participants in the DiaDec study (Fig. 1). Eligibility was based on a diagnosis of diabetes in the SHI data as defined and validated by the criteria of Hauner *et al.*, that have been used in previous studies.[12,13] From the 46 566 potential study participants, a random sample of 4053 subjects were selected and invited to participate in the study. The postal recruitment procedure was carried out in 3 months: March, May and August 2013. The recruitment materials included a cover letter, which included information on the study, the questionnaire, a data protection and declaration of consent to use the SHI data and a stamped, addressed return envelope. If the individual did not respond within 3–8 weeks, a reminder letter was sent. If the individual did not respond to the reminder letter we attempted to contact the individual by telephone 3–7 weeks later at least twice. People were also contacted if the questionnaire was not filled in completely or if they forgot to return the signed consent form and only sent the questionnaire back.

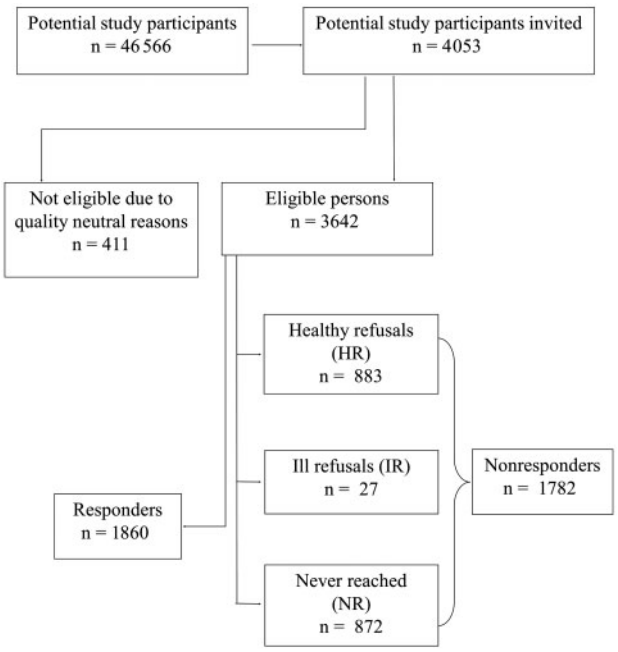

Figure 1. Flow chart for selection of study participants.

Description of the variables included in the non-response analysis

For the non-response analysis, the SHI provided individual-level information for responders and non-responders for the following variables within the year prior to the baseline survey (2012): age (categorized into four groups: <50, 50–59, 60–69, 70–80 years of age), sex, treatment with insulin (yes or no), use of oral antihyperglycaemic drugs (OAD) (yes or no), depression diagnosis (yes or no), number of hospitalization cases, number of medications prescribed (based on the count of pharmaceutical registration numbers in the year prior to the baseline survey) and other comorbidities. Insulin usage was defined as at least one record of an Anatomical Therapeutic Chemical Classification System (ATC) code 'A10A' covering 'insulins and analogues'. The use of OAD was defined as at least one record of an ATC code 'A10B' covering 'blood glucose lowering drugs, excluding insulins', though records of 'A10BX04' (exenatide) and 'A10BX07' (liraglutide) were excluded. The two variables focusing on antihyperglycaemic medication for diabetes were combined into one variable with four characteristics: treatment with insulin only, treatment with OAD only, treatment with a combination of insulin and OAD and no treatment with insulin or OAD. A diagnosis of depression (yes or no) was defined as at least one record of the ICD-10 code 'F32' (major depressive disorder, single episode), 'F33' (major depressive disorder, recurrent) or 'F34.1' (dysthymic disorder). Comorbidities were based on the morbidity-oriented risk compensation scheme.[14] This system covers 80 either 'severe' or 'costly and chronic' diseases that are structured in a system of hierarchical groups. We defined comorbidities as the number of diagnoses the patient had of the 80 included diagnoses. Information on health-care utilization was provided by using the number of hospital admissions and the number of medications prescribed (based on the number of different pharmacy product numbers).

Statistical methods

The available data were used to conduct an analysis of non-response to evaluate whether non-response occurred

completely at random or if the non-responders differed systematically from the responders of the survey.

Of all the potential study participants, except for those not eligible for quality neutral reasons, those who returned the questionnaire and signed consent form were regarded as responders to our survey. All individuals who did not return the questionnaire, the signed consent form or both documents were regarded as non-responders. We further classified the non-responders according to the classification system by Slattery *et al*. and Stang *et al*. as never reached (NR), ill refusals (IR) and healthy refusals (HR).[15,16] The NR are the individuals who never answered the invitation and were not reachable in follow-up telephone calls since they changed their phone number or the telephone was constantly busy. Individuals who refused to participate either due to medical conditions, such as living in an elderly care home, being hospitalized, being in rehabilitation, being dependent on nursing care, or being ill were referred to as IRs. The individuals who refused to participate due to reasons not related to medical conditions were regarded as HRs. The reason for refusal was reported by either the contacted person or a relative of that person either in the questionnaire or during the follow-up telephone call.

The analyses proceeded in three steps. First, we estimated the contact, cooperation and response rates in accordance with the method suggested by Slattery *et al*. and Stang *et al*.[15,16] The contact rate describes the proportion of potential study participants we were able to establish contact with regardless of the participants' eligibility (i.e. the number of responders, HR, IR and persons not eligible for quality neutral reasons divided by the number of potential study participants invited (Supplementary Figure S1, available as Supplementary data at *IJE* online). The cooperation rate indicates the rate of completed and returned surveys among all contacts by eligible persons (i.e. the number of responders divided by the number of responders and refusals). Thus, the cooperation rate expresses the number of individuals willing to participate in relation to the number of eligible persons who could be reached. The response rate provides the proportion of eligible persons who completed and returned the survey (i.e. the number of responders divided by the number of eligible persons). We have listed the exact formulas for calculating the rates in the Supplementary material.

Bivariate comparisons were performed using a Mann–Whitney U test for quantitative variables and a Pearson's chi-square test (alternatively, Fisher's exact test when possible) for categorical variables. The significance level was set to $\alpha = 0.05$. We used logistic regression to determine whether the following variables/terms were associated with response status: age class, sex, interaction between age group and sex, antihyperglycaemic medication, depression diagnosis and comorbidities and health-care utilization (medication and hospital admissions). We dichotomized the following variables based on the median into two categories: comorbidities (≤ 3, >3), number of medication prescriptions (≤ 22, >22) and hospital admissions (0, ≥ 1).

We showed the reliability and reproducibility of our analysis in two ways. First, we compared the original estimated odds ratios (ORs) with the resampled ORs obtained through permutations. In doing so, the group membership becomes arbitrary if we assume that there is no difference in the variables between the responders and non-responders, as any subject from one group could be from the other group. We randomly divided the original sample into two random groups of 1860 and 1782 persons 999 times. We labelled these groups as dummy responders and non-responders and carried out the above-mentioned logistic regression for each of these 999 samples (Supplementary Figure S2, available as Supplementary data at *IJE* online). Resampled ORs mimic the null hypothesis of no difference existing between the responders and non-responders for a given data set. Second, we compared the original ORs with the ORs based on the 999 bootstrap samples (Supplementary Figure S3, available as Supplementary data at *IJE* online). Bootstrap samples were created by selecting 1860 observations for non-responders and 1782 observations for responders from the original groups. One person was selected randomly and returned to the dataset before the selection process was repeated, which suggests that one person could have been chosen multiple times. Bootstrap ORs illustrate how stable the estimated ORs are.

Ethics statement

Ethical approval was obtained from the ethics committee of the Heinrich-Heine University Düsseldorf and is available under the study reference 3762.

Results

We were informed that of the 4053 randomly selected persons identified as potential study participants invited to participate in the DiaDec study, 411 were not suitable to receive a questionnaire due to quality neutral reasons (Fig. 1). In total, 3642 eligible persons insured with the SHI and diagnosed with diabetes received a questionnaire and a consent form. Of these persons, 1860 were responders and 1782 were non-responders. Eight hundred and seventy-two (48.9%) non-responders were classified as NR, 27 persons (1.5%) were considered IR and 883 (49.6%) were considered HR.

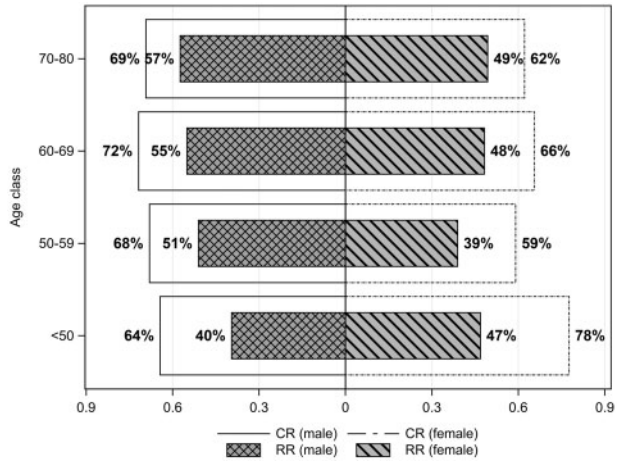

Figure 2. Response rates (RR) and cooperation rates (CR) stratified for age and sex.

Contact, response and cooperation rates

Within the DiaDec study, the overall contact rate was 78.5%, the cooperation rate was 67.1% and the overall response rate was 51.1%.

The response rates were higher for females than for males in the <50 years age group and higher for males than for females in the >50 years age groups (Fig. 2). The cooperation and response rates showed similar patterns, as they were both higher for females than for males in the <50 years age group and higher for males than for females in the >50 years age groups.

Description of the whole sample and comparison of responders and non-responders

The mean age of the sample was 65.7 years, and 41.1% of the individuals were female (Table 1). In the year prior to the survey, 16.3% of the individuals had a diagnosis of depression. Approximately half of the individuals were treated with OAD only, ~14% were treated with a combination of OAD and insulin, ~13% were treated with insulin only and ~24% were not treated with either insulin or OAD. The mean number of comorbidities in the sample in the year prior to the survey was 3.4. The mean number of prescribed medications in the year prior to the survey was 26.3, and the mean number of hospital admissions was 0.4. The responders were slightly older than the non-responders. The responders and non-responders differed in almost all of the characteristics. No difference was found in the diagnosis of depression, which is one of the main variables of interest in the DiaDec study.

Results of the logistic regression

Table 2 presents the results of the logistic regression. All variables included in the model were associated with participation in our study except the depression diagnosis, number of comorbidities and hospital admissions. Higher medication utilization [OR 1.29, confidence interval (CI) 1.10–1.51], treatment with insulin only (OR 1.73, CI 1.36–2.21), treatment with OAD only (OR 1.77, CI 1.49–2.09) and treatment with both insulin and OAD (OR 1.91, CI 1.51–2.43) rates were associated with responses to the mailed survey in our study, whereas being female was associated with a lower likelihood of responding to the survey for those aged 50–59 years (OR 0.60, CI 0.43–0.84), for those aged 60–69 years (OR 0.74, CI 0.58–0.94), and for those aged 70–80 years (OR 0.72, CI 0.58–0.88) (Supplementary Table S1, available as Supplementary data at *IJE* online). The interaction between age group and sex was visible only for the group of individuals <50 years old ($\beta = 0.68$ with P-value 0.01) (Table 2). Although a younger age and being female were associated with non-responses, females <50 years old seemed to participate slightly more often than males of the same age group (Supplementary Table S1, available as Supplementary data at *IJE* online).

Although several of the considered variables were associated with responses, some of the ORs were small to moderate, e.g. those for hospital admission and medical utilization. The (pseudo) R^2 was 0.04, indicating a weak relationship between the considered variables and response status.

The results of the original logistic regression seem to be reliable and reproducible (Supplementary Figures S2 and S3, available as Supplementary data at *IJE* online).

Discussion

The most important result of our analysis was that depression status was not associated with responses to our survey, but the opposite trend could be assumed. Since we assessed the depression diagnoses obtained 1 year prior to the survey, the individuals identified as having depression may not have been experiencing depression symptoms at the time of the survey. Another explanation might be that our study specifically focuses on persons with diabetes and depression, which may be of interest to people who hope to contribute towards the improvement of care of people in a similar situation in the future by participating in the survey.

We found that sociodemographic characteristics were related to non-responses: older age was associated with a higher likelihood of responding to the survey, whereas being female was associated with a lower likelihood of responding to the survey. Nevertheless, young women were more likely to participate in the survey due to a possible interaction between age and sex.

Furthermore, we found antihyperglycaemic medication, health-care utilization and higher medication utilization to be associated with responses to the mailed survey.

Table 1. Description of the whole DiaDec sample

Variable	Whole sample $n = 3642$	Responders $n = 1860$	Non-responders $n = 1782$	*P*-value[a]
Age				
Mean, SD (range)	65.7, 10.6 (17.0 –79.9)	66.5, 9.9 (17.0–79.9)	64.9, 11.2 (17.5–79.9)	0.0002
Median (IQR)	67.9 (59.8 -74.0)	68.7 (60.9–74.2)	67.1 (58.3–73.7)	
Age class, *n* (%)				
<50	321 (8.81%)	135 (7.26%)	186 (10.44%)	0.0001
50–59	618 (16.97%)	288 (15.48%)	330 (18.52%)	
60–69	1130 (31.03%)	591 (31.77%)	539 (30.25%)	
70–80	1573 (43.19%)	846 (45.48%)	727 (40.80%)	
Sex, *n* (%)				
Female	1496 (41.1%)	707 (38.0%)	789 (44.3%)	0.0001
Antihyperglycaemic drugs, *n* (%)				
Insulin only	466 (12.8%)	256 (13.8%)	210 (11.8%)	< 0.0001
Oral antihyperglycaemic drugs only	1785 (49.0%)	959 (51.6%)	826 (46.4%)	
Insulin and oral antihyperglycaemic drugs	525 (14.4%)	310 (16.7%)	215 (12.1%)	
Depression diagnosis, *n* (%)	595 (16.3%)	303 (16.3%)	292 (16.4%)	0.9642
Comorbidities				
Mean, SD (range)	3.4, 2.1 (0.0–17.0)	3.7, 2.2 (0.0–17.0)	3.2, 1.9 (0.0–16.0)	< 0.0001
Median (IQR)	3.0 (2.0 - 4.0)	3.0 (2.0–5.0)	3.0 (2.0–4.0)	
Health care utilization				
Medication utilization				
Mean, SD (range)	26.3, 19.9 (0.0–360.0)	28.7, 20.6 (0.0–360.0)	23.7, 18.9 (0.0–359.0)	< 0.0001
Median (IQR)	22.0 (13.0–35.0)	24.0 (15.0–38.5)	20.0 (11.0–31.0)	
Hospital admissions,				
Mean, SD (range)	0.4, 1.0 (0.0–16.0)	0.5, 1.1 (0.0–16.0)	0.4, 0.9 (0.0–13.0)	0.0009
Median (IQR)	0.0 (0.0–1.0)	0.0 (0.0–1.0)	0.0 (0.0–0.0)	

[a]*P*-values are reported for differences between responders and non-responders.
IQR, inter quartile range; SD, standard deviation.

Response was higher in those taking medications compared with those not taking medications, irrespective of the type of medication. However, comparing the impact of the different types of antihyperglycaemic medications showed that there were no associations with the response status, suggesting that the type of medication was not important. Age and sex as well as medical utilization seem to be of moderate importance with regard to participation in the DiaDec study.

Comparison with other studies

The overall response rate was 51.1% in the DiaDec study, which is within the range reported by a study using a similar methodology (linking questionnaire data with SHI data). The study among patients with coronary heart disease of a German SHI was conducted in 2013 and reported a considerably lower response rate of 32.6%.[17] Lin *et al.* used a comparable population survey for health maintenance organization enrolees with diabetes in the United States in their study conducted in 2003, and they reported a response rate of 62.0%.[18] Pilot surveys of the European Health Examination Survey conducted between 2009 and 2012 in 12 countries (Czech Republic, Finland, Germany, Greece, Italy, Malta, The Netherlands, Norway, Poland, Portugal, Slovakia, The United Kingdom) showed that obtaining participation rates >50% is possible but requires well-planned recruitment strategies and a large amount of effort by the investigators.[19]

Studies on non-response rates differ to a large extent in their design, primary aim, mode of comparison, characteristics compared and various other aspects. Several studies found that sex and age impact the non-response rate [20–24] and that women are less likely to participate in health surveys than men, which is similar to the results of our study. No clear pattern has evolved regarding the sex–age interaction. Education, socio-economic status and marital status also impact non-response rates to health surveys.[5,6,20,21,25,26] However, this relationship could not be investigated within the analysis of non-responders in the DiaDec study due to missing information in our health-care-based data set. Instead, we used, for the first time, other characteristics, such as diabetes treatment, depression status, health-care utilization, number of comorbidities and higher medication utilization, to

Table 2. Results of logistic regression analysis to assess factors associated with participation in the DiaDec study; $n = 3642$. Reference group: age class (70–80), male, no antihyperglycaemic drugs, no depression diagnosis, comorbidities ≤3, medical utilization ≤22, no hospital admission. R^2 of the logistic regression, 0.0401

Variable	β	*P*-value	Odds ratio	95 % Confidence intervals	
				Lower	Upper
Age class[a]					
Age class (<50 vs 70–80)	−0.6285	0.0001	0.53[b]	0.39	0.73
Age class (50–59 vs 70–80)	−0.2123	0.0906	0.81[b]	0.63	1.03
Age class (60–69 vs 70–80)	−0.0678	0.5215	0.93[b]	0.76	1.15
Gender[a]					
Sex (female vs male)	−0.3334	0.0014	0.72[c]	0.58	0.88
Antihyperglycaemic drugs					
Insulin only vs no medication	0.5500	<0.0001	1.73	1.36	2.21
Oral antihyperglycaemic drugs only vs no medication	0.5696	<0.0001	1.77	1.49	2.09
Insulin and oral antihyperglycaemic drugs vs no medication	0.6491	<0.0001	1.91	1.51	2.43
Comorbidities					
Depression diagnosis (yes vs no)	−0.0070	0.9422	0.99	0.82	1.20
Comorbidities (>3 vs ≤3)	0.1588	0.0508	1.17	1.00	1.37
Health-care utilization					
Medication utilization (>22 vs ≤22)	0.2525	0.0017	1.29	1.10	1.51
Hospital admissions (≥1 vs 0)	0.0845	0.3068	1.09	0.93	1.28

[a]Interaction terms for age class and sex were included in the model: sex (female) x age class (<50 years): ß = 0.6800, $P = 0.0093$; Sex (female) x age class (50–59 years): ß = −0.1807, $P = 0.3683$; sex (female) x age class (60–69 years): ß = 0.0276, $P = 0.8639$. The full set of ORs related to gender x age class group comparison is shown in Table 1 Supplementary Table S1.

[b]Age comparison for male participants.

[c]Sex comparison for participants within oldest age class (70–80).

assess the differences between responders and non-responders.

Limitations and strengths of our study

Our analysis has some limitations. For example, we were not able to gather information on the socio-economic status of non-responders; we did not have information on the migration status of the invited participants, which might also be a determinant of non-responses.[23] Furthermore, we could only analyse the presence of depression in general but could not differentiate between the different types of depression, which might have differed between the responders and non-responders. Last, we did not assess the exact reason for individuals not responding to our survey, which would have helped to obtain a better understanding of the reasons why people did not respond.

As suggested by Kho *et al.*, we collected a minimum dataset of key variables of all the people identified to be eligible to participate in our study by using SHI data.[27] Therefore, we were able to analyse the whole sample of invited persons not only with respect to the demographic characteristics but also with respect to relevant characteristics of primary interest in our health survey. Furthermore, we could directly match the data of the responders and non-responders of our survey with another data set including data that was not self-reported but externally validated and provided the same information for responders as for non-responders.[28]

Since there are considerable differences in the prevalence of chronic diseases in different SHIs in Germany,[29] it cannot be claimed that the results of the DiaDec study are representative of the whole German population, as the sample is only representative of one SHI. However, the SHI is a national SHI.

Conclusion

It is often a concern that responders and non-responders may differ in their health status, introducing a non-response bias to the study results. The aim of the DiaDec study was to analyse how patients with diabetes and depression differ from patients with diabetes but without depression in various aspects, e.g. health-care utilization or health-related quality of life. Since depression is one of the main variables of interest within the DiaDec study, it is of major importance for the interpretation of the results in the DiaDec study that responders and non-responders did not differ with regard to the depression diagnoses. Future research studies should assess the reasons for non-response, at least in a subsample of non-responders, to determine how to minimize the potential bias in this kind of

research study. The thorough assessment of non-response bias in this study is essential for the appropriate interpretation of the possible differences between the DiaDec study participants with and without depression and may serve as an example of how to assess non-response bias by using SHI data.

Supplementary data

Supplementary data are available at *IJE* online.

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Conflicts of interest: None declared.

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Originalarbeit 5

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RESEARCH

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PHQ-9, CES-D, health insurance data—who is identified with depression? A Population-based study in persons with diabetes

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Abstract

Aims Several instruments are used to identify depression among patients with diabetes and have been compared for their test criteria, but, not for the overlaps and differences, for example, in the sociodemographic and clinical characteristics of the individuals identified with different instruments.

Methods We conducted a cross-sectional survey among a random sample of a statutory health insurance (SHI) (n = 1,579) with diabetes and linked it with longitudinal SHI data. Depression symptoms were identified using either the Centre for Epidemiological Studies Depression (CES-D) scale or the Patient Health Questionnaire-9 (PHQ-9), and a depressive disorder was identified with a diagnosis in SHI data, resulting in 8 possible groups. Groups were compared using a multinomial logistic model.

Results In total 33·0% of our analysis sample were identified with depression by at least one method. 5·0% were identified with depression by all methods. Multinomial logistic analysis showed that identification through SHI data only compared to the group with no depression was associated with gender (women). Identification through at least SHI data was associated with taking antidepressants and previous depression. Health related quality of life, especially the mental summary score was associated with depression but not when identified through SHI data only.

Conclusion The methods overlapped less than expected. We did not find a clear pattern between methods used and characteristics of individuals identified. However, we found first indications that the choice of method is related to specific underlying characteristics in the identified population. These findings need to be confirmed by further studies with larger study samples.

Key points

- Patients with diabetes often have comorbid depression. Those patients are struggling to meet their treatment goals. Thus, they have a higher risk of getting diabetes related complications as for example coronary heart diseases.

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- A lot of different tools and instruments are available to diagnose depression, to screen for depression among patients with diabetes or to identify depression symptoms or depressive disorder in clinical or epidemiological studies, including interview, questionnaires or claims data. It would be helpful to know if the tools that are used identify the same people or, if this is not the case, whether people identified by different tools have different characteristics or health outcomes.
- We found that different methods do not identify the same people with depression. There was no clear pattern of differences between the identified groups, however, we found some initial indications that the method chosen is related to particular underlying characteristics in the population identified. Further research with larger data sets is necessary to see if there are differences among the persons that are identified by different tools to give recommendations which screening tool to use for what purpose.

Keywords Depressive disorder diagnosis, Depressive disorder epidemiology, Diabetes Mellitus Type 2 psychology, Diabetes complications

Introduction

Patients with diabetes have an increased prevalence of depression compared to the general population [1]. Although it remains controversial if diabetes leads to depression or vice versa or if there is a bidirectional association, there is sufficient evidence that depression can have a serious impact on a person's wellbeing and their ability to self-manage their diabetes [2–5]. Individuals with diabetes and comorbid depression are found to have unfavorable diabetes related outcomes such as a reduced adherence to their diabetes treatment, higher HbA1c levels, increased diabetes symptoms, or unfavorable micro-, and macrovascular outcomes [2–6]. Beyond unfavorable health outcomes, Brüne et al. (2021) found that people with diabetes and depression had almost two times higher total health care cost compared to people with diabetes without depression [7]. Despite the relevance of comorbid depression in people with diabetes, it is assumed that only 50% are recognized and an even smaller amount is appropriately treated [2].

Several methods are used to identify depression or to estimate the prevalence of it. Prevalence estimates of depression among people with diabetes differ, which is also due to the fact that a range of different methods are used to assess depression [1, 8]. Three systematic reviews found, that in studies where a questionnaire was used to assess depression, the prevalence was about two to three times higher than in those that used a diagnostic interview [8–10].

The method used to assess the presence of depression depends on several factors. For example, it may depend on study design, time constraints, personal preferences of the researchers, availability or the aim of the assessment. Furthermore, there are a variety of questionnaires, each with a different objective and somewhat different background or focus [11–14]. Knowledge of the different methods and instruments to assess depression is therefore important. Up to now, there are a number of studies available that validate these questionnaires in general [15, 16]. Very few studies have compared the different instruments for identifying depression among patients with diabetes. These studies either intended to validate a certain instrument against another in a specific population or wanted to compare psychometric properties or internal reliability [17–20].

A method other than questionnaires is the use of diagnosis in statutory health insurance (SHI) data to identify persons with depressive disorder. Up to now, there is no study, in which SHI data was used for comparison purposes. In our study, we used two of the most common instruments in addition to SHI data to investigate whether the different methods identify - more or less - the same individuals or whether they identify different individuals. In particular - if the identified individuals differ - we were interested in possible patterns of characteristics of the identified groups. Thus, in contrast to existing validation studies, the aim of this study was to assess and describe in detail the overlap and the differences between groups identified by different methods to find persons with depression (symptoms or disorders), as well as potential associations between individual and clinical characteristics and the method used to identify a person.

Specifically, three methods to identify depression were used and compared: the Centre for Epidemiological Studies Depression (CES-D) scale, the Patient Health Questionnaire-9 (PHQ-9) - the two most frequently evaluated questionnaires among people with diabetes [20] - or a diagnosis in SHI data. In this way, we aimed to gain basic insights and better understand the issues associated with the use of different methods.

Methods

Study design

The study design and recruitment of participants have been described elsewhere [21]. In brief, a cross-sectional survey was conducted in a random sample of individuals with diabetes (N=4,053) insured by one SHI covering

673,366 persons in Germany. Individuals with diabetes type 1 or 2 were identified using an algorithm taking into account diagnosis based on the 10th International Classification of Diseases (ICD-10) for 'diabetes' (E10–E14), prescription of antihyperglycemic drugs (Anatomical-Therapeutic-Chemical [ATC] classification A10), and documentation of blood glucose, or a HbA1c measurements. This algorithm has been validated and used in previous studies [22]. We linked data of the survey to longitudinal SHI data on an individual level. The initial aim of the study was to assess differences in people with diabetes and with and without depression regarding costs and health related quality of life. The presented analyses are secondary analyses that were developed in the course of the study.

Data source

The baseline survey was a 9-page postal questionnaire conducted in 2013. It assessed information on sociodemographic characteristics such as age, sex, and years of education, duration of diabetes, and type of diabetes. PHQ-9 and the German version of the CES-D were used to assess depression symptoms.

SHI data on health care utilization patterns and health care costs for all in- and outpatient treatments were available for the period covering four quarters before and after the quarter of the baseline survey.

Study population

Of 46,566 individuals with diabetes in the SHI 3,642 persons were randomly selected and contacted to participate in the study. In total 1,860 persons sent back their questionnaire (response rate: 51%) and gave written informed consent to use their SHI data. Responders did not differ from the non-responders in having a history of depression diagnosis [23]. For 201 of these persons, a lack of data over the complete observation period existed, e.g. because the person switched health insurance during that time. In total 1,659 persons were considered for the analysis. Further 80 persons were excluded as they provided incomplete information in the questionnaire. Thus, a total of 1,579 persons were included in our analysis (Appendix Fig. 1).

Ethical approval was obtained from the ethics committee of the Heinrich Heine University Düsseldorf and is available under the study reference 3762.

Main outcome – assessment of depression

CES-D

The CES-D and the German version of it (Allgemeine Depressionsskala) are brief self-report measures, designed to assess symptoms of depression in the general population in epidemiological studies among nine signs and symptoms of depression defined by the American Psychiatric Association Diagnostic and Statistical Manual, fourth edition [11]. Several studies have assessed the validity of the CES-D in different populations [24, 25]. We used the short form of the German version of the CES-D in our study (allgemeine Depressionsskala Kurzform (ADS-K)) [25]. The instrument comprises 15 statements regarding depression. Based on a four-point scale (ranging from "rarely or never" (0 point) to "frequently, all the time" (3 points)), the frequency of depressive symptoms occurring during the last week can be assessed. A score that can range from 0 to 45 is built by adding up the points from each statement. We used a cut-off value of ≥17 to define clinically meaningful depressive symptoms as suggested by validation studies [25].

PHQ-9

The PHQ-9 is a multipurpose instrument used to screen, monitor and measure the severity of depression symptoms. The PHQ-9 can be assessed using different methods: as a diagnostic algorithm to make a probable diagnosis of major depressive disorder using the nine criteria of the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV) or to test for other depressive disorders and a cut-off based on summed-item scores to assess the severity of depression symptoms [12]. The algorithm is the scoring method that was originally proposed to screen for depression. Within this study we focused on the PHQ-9 as a screening instrument. According to Kroenke et al. (2001) we defined depression when two or more of the nine symptoms were present at least "more than half the days" in the past two weeks, and one of the symptoms was depressed mood or anhedonia. If the thought of suicide was present, it is considered to be present, regardless of the reported duration [12]. Several studies have used the PHQ-9 to assess depression among individuals with diabetes and used a similar approach [2, 26].

Depression in SHI data

For a diagnosis in SHI data a ICD-10 code for the diagnosis of unipolar depression during the study period of nine quarters was required. Diagnosis of unipolar depression included the following codes:

F32.0-F32.9 Depressive episode,
F33.0-F33.9 Recurrent depressive disorder,
F34.1 Dysthymia,
F38.1. Other recurrent mood [affective] disorders and.
F41.2 Mixed anxiety and depressive disorder.

Group composition based on depression measurement

We classified the participants into eight groups after linking SHI data with survey data. Group 1 reported depression symptoms in the CES-D and PHQ-9 and had a diagnosis in SHI data. Group 2 reported depression symptoms in the CES-D and PHQ-9 but had no diagnosis in SHI data. Group 3 had symptoms according

to the PHQ-9 but not according to the CES-D and had a diagnosis in SHI data. For group 4 no symptoms were reported with the PHQ-9 but with the CES-D and they had a diagnosis in SHI data. Group 5 was only identified with the CES-D, Group 6 only with the PHQ-9 and group 7 only with a diagnosis in SHI data. Group 8 had no depression symptoms or diagnosis and was considered as a reference group (Appendix Table 1).

Possible associated variables and covariates

All potentially associated variables and covariates considered as potential predictors were recorded during the baseline survey, except information on clinical and disease related measures (based on SHI data). Based on a literature review and clinical expertise, we considered socio-demographic variables, patient-reported measures on health-related quality of life (HRQoL) and diabetes related distress as well as clinical and disease-specific variables.

The following variables were included as sociodemographic factors: age, gender, marital status (married, single, divorced or separated, widowed), relationship status (with/without partner), origin (resident in Germany since birth/not residing in Germany since birth) as well as employment (yes/no), and retirement status (yes/no). The International Standard Classification of Education (ISCED) was used to categorize participants according to the duration of their education (<10 years, 10–14 years, > 14 years) [27]. Furthermore, type and duration of diabetes were also assessed in the baseline survey as well as information on a previous diagnosis of depression by a health professional.

HRQoL was investigated using the 12-item Short Form health survey (SF-12), a multipurpose generic measure of health status [28]. The SF-12 can be used to compose a physical health and a mental health summary score (PCS-12 and MCS-12).

We also assessed diabetes-specific distress using the Problem Areas in Diabetes Scale (PAID), a 20-item scale consisting of emotional problems commonly reported among patients with diabetes [19].

SHI data was used to assess clinical and disease related measures. Comorbidities were measured using diagnostic groupings, which are necessary for the morbidity-oriented risk structure adjustment by SHIs in Germany. We used the number of coded morbidity groups in the year prior to the baseline survey (2012) to assess the number of comorbidities [29].

Healthcare costs were calculated from the perspective of a SHI including all costs imposed to the SHI. We took net costs into consideration without taking discounts into account. Costs were analyzed for every person individually, covering the survey quarter plus the four quarters before and after, a total of nine quarters.

The adapted Diabetes Complications Severity Index (aDCSI) was used to assess diabetes complications thereon to determine diabetes severity [30].

Treatment of diabetes was assessed by looking for prescription of insulin or oral antihyperglycemic drugs (OADs) in the SHI data for each participant during the course of the study. Additional it was checked whether persons took antidepressants during the course of the study. These were defined by the ATC Code N06A.

Statistical analyses

We described the study population by using mean, standard deviation and median for quantitative variables as well as frequency and percentage for categorical variables. We used the Mann–Whitney U test for comparison of quantitative variables in two groups and Kruskal-Wallis test for three and more groups. Pearson's chi-square test was conducted to assess if differences for categorical variables were significant. P-values related to the aforementioned tests show the probability to observe the actual value of the related test statistic or even more extreme values of it assuming the null hypothesis that there are no differences between groups. Smaller p-values indicate against the null hypothesis.

To compare the eight groups, we handled the missing data (cf. description of the study population and Table 1) with the machine learning based R-algorithm missForest to impute. To assess the quality of the imputation we calculated out-of-bag (OOB) imputation errors as the proportion of false classified cases (PFC) for categorical and as normalized root of mean squared error (NRMSE) for quantitative variables. Since the comparison of all eight groups to each other (the so called many-to-many problem) requires 28 pairwise comparisons, each with respect to a variety of characteristics, one should expect a considerable number of false rejections/effects. In order to be able on the one hand to control the type I error (i.e., rejection of at least one true null hypothesis, also known as family-wise error rate) and on the other hand to see any effects after multiple adjustment (done by the Bonferroni correction), we focused on the comparison of seven groups with depressive disorder to the group with no depression or depressive symptoms (i.e., group 8) as the reference group (the so called many-to-one problem). We used a multinomial logistic regression to model the group membership, whereby the log odds of being in one group relative to being in the reference group is modelled as a linear combination of predictor variables. Thus, an indirect comparison of seven groups with depressive disorder to each other may be done by comparing those differences to the reference group.

Gender, age, marital status, employment status, type of diabetes and diabetes duration, insulin and OAD usage, aDCSI score, previous depression and intake of

antidepressant medication, number of comorbidities, HRQoL, PAID score, and total health care costs were used as potential candidates for independent variables in the multinomial model. We selected the finale multinomial model by keeping important variables (age, sex, comorbidities, MCS-12 and PCS-12), removing collinear variables as well as minimizing Akaike information criterion (AIC). The final model includes the independent variables: age, gender, taking insulin, previous depression, taking antidepressant, the number of comorbidities, HRQoL, and the PAID score.

P-values related to the estimates of the multinomial regression odds ratios (OR) for being in a group with depressive disorder compared to the reference group, are the probabilities to observe the actual value of the OR or more extreme values and under the null hypothesis that there is no effect (OR = 1). Smaller p-values are an indication, that null hypothesis may be wrong and there is an effect.

The significance level (also for multiple comparisons) was set to $\alpha = 0{\cdot}05$.

Table 1 Baseline characteristics of the DiaDec sample

	n (%), mean ± SD, median
Sample size, n	1,579
Age, years, n = 1579	67·0 ± 9·9, 69·0
Sex, female, n = 1579	597 (37·8)
Origin, Germany n = 1577	1,397 (88·6)
Family status, in a relationship, n = 1556	1,306 (83·9)
Marital status, n = 1573	
Married	1,188 (75·5)
Divorce/separated	112 (7·1)
Widowed	195 (12·4)
Employment status, employed, n = 1547	402 (26·0)
Retirement status, retired, n = 1564	1,089 (69·6)
Level of education, ISCED ≥ 14 years, n = 1570	337 (21·5)
Diabetes duration in years, n = 1533	11·0 ± 8·3, 9·0
Type of Diabetes, n = 1566	
Type 1 Diabetes	128 (8·2)
Type 2 Diabetes	1,345 (85·9)
Type unknown/other	93 (5·9)
Diabetes severity aDCSI, n = 1579	3·0 ± 2·2, 3·0
Number of comorbidities, n = 1579	3·7 ± 2·1, 3·0
Treatment, n = 1579	
Taking insulin	486 (30·8)
Taking oral antihyperglycemic drugs	1,071 (67·8)
Taking antidepressants	276 (17·5)
Health care costs for 2 years, €, n = 1579	10,123·0 ± 13,188·2, 6,112·7
Health related Quality of Life[$], n = 1544	
physical component summary scale of the SF-12 (PCS-12)	41·7 ± 10·9, 43·5
mental component summary scale of the SF-12 (MCS-12)	50·1 ± 10·5, 53·3
Problem Areas in Diabetes Scale (PAID)[∞], n = 1512	19·4 ± 17·6, 14.0
Previous depression, n (%) (self-reported), n = 1575	
Yes	225 (14·3)
No	1,041 (66·1)
unknown	309 (19·6)

Percentages of categorical variables computed with respect to the total number of subjects within the sample

SD = standard deviation

[$] range from 0 to 100, zero indicates the lowest level of health measured by the scales and 100 indicates the highest level of health

[∞] Possible score can range from 0 to 100, with higher scores indicating greater diabetes-related emotional distress

Results

Description of the study population

Table 1 describes the 1,579 participants and their characteristics. For 271 subjects in the total sample (17·2%) data of at least one variable in the baseline survey were missing while 1,308 persons had complete data.

Participants had a mean age of 67 years and almost 40% were female. About 90% were German and 84% were in a relationship. About one in five had more than 14 years of education. Almost 70% of the participants were retired. More than 75% were married, around 7% were divorced or separated and 12·4% were widowed.

On average participants had diabetes for 11 years, the majority had T2DM (85·9%). About one-third of the participants were treated with insulin, around 67% took OAD. 17·5% took antidepressants. The mean healthcare costs in our sample were 10,123€. Participants had on average 41·7 points on the physical component summary scale (PCS) of the SF-12 and 50·1 on the mental component summary scale (MCS). The average PAID Score in the sample was 19·4. 14% of people in the sample reported that they had previously been diagnosed with depression.

Prevalence of depression according to the different methods

Figure 1 displays overlaps between the different methods and reports the overall prevalence within the sample. In total 33·0% of our analysis sample (521) were identified with some form of depression by at least one method. The prevalence of depression in our sample ranged from 11·6% (PHQ-9) up to 22·4% (SHI data).

The different groups and their characteristics are described in Table 2. Group 8 – the reference group - was the largest group with 1,058 persons and group 3 identified through the PHQ-9 and a diagnosis in SHI data the smallest with 22 persons. With respect to

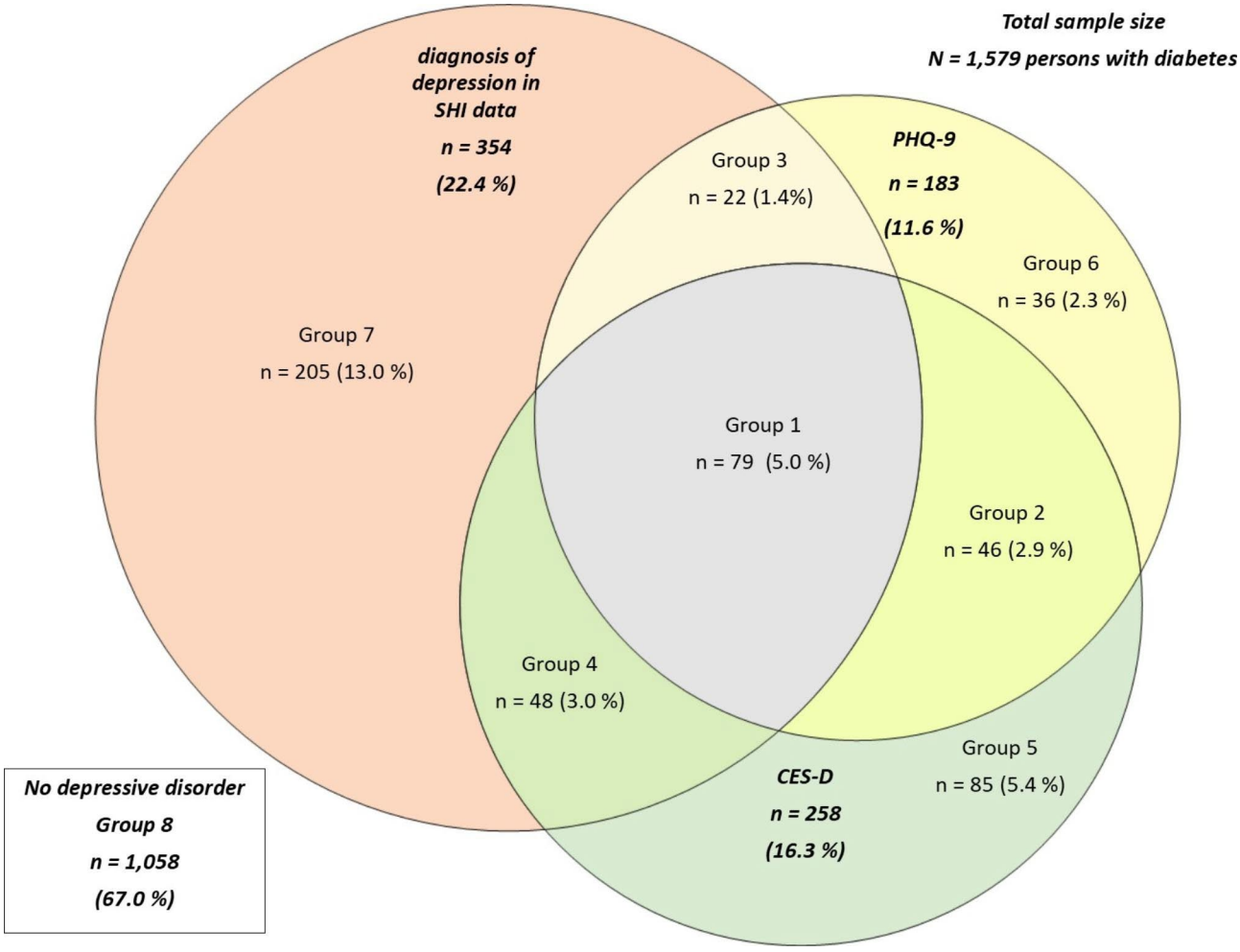

Fig. 1 Venn diagram showing the persons identified by different methods to assess depressive disorder and intersections between the different methods

sociodemographic variables the percentage of females was highest in group 7 (51·7%) while it was lowest in group 6 (33·3%). Group 7 (only identified by a diagnosis in SHI data) was the group with most persons being German of origin (92·7%) and group 2 (identified by both instruments) the one with the smallest number of persons with German origin (76·1%). In group 8 most people were in a relationship (87·7%) and group 1 (identified by all methods) was the group where the smallest number of persons was in a relationship (70·1%). One third of group 6 (identified through PHQ-9 only) were retired but only about 52% of the persons in group 1. A duration of education for more than 14 years was highest in the group 8 (23·2%) and in group 1 (20·3%) and lowest in group 2 (15·2%). Group 1 had also the highest share of persons with type 1 diabetes (12·6%). With regard to diabetes specific and health care related outcomes, the highest number of persons with type 1 diabetes was found in group 1(12·8%) and the lowest amount was found in group 7 (4·9%). Group 2 and 3 had the highest share of persons taking insulin (43·5 and 50%) whereas in all other groups the share was around 30%. For OAD in all groups the share of persons taking them was between 60 and 70%. Average health care costs were highest in group 3 with a median of more than 13,900 € and lowest in group 8 (median 5,283 €).

Looking at HRQoL, the average score on the PCS12 was highest in group 8 (median 47·3) and group 7 (median 42·3) and lowest in group 1 (median 30·6). These findings were similar for the MCS12. The average PAID score was highest in group 1 (median 45·0) and lowest in group 8 (median 10·0) and group 7 (median 15·0). In group 1 was the highest share of persons reporting a previous depression (67·1%) and in group 8 the lowest share (4·9%).

Results of the multinomial model

Table 3 reports the results of the multinomial logistic regression model with imputed data (the OOB imputation errors are reasonably small ranging from 0·086 to 0·71), comparing the seven groups with depressive disorder with the reference group with no depressive disorder

Table 2 Comparison of groups according to depression status

	Group 1 n(%) / mean ± SD, median	Group 2 n(%) / mean ± SD, median	Group 3 n(%) / mean ± SD, median	Group 4 n(%) / mean ± SD, median	Group 5 n(%) / mean ± SD, median	Group 6 n(%) / mean ± SD, median	Group 7 n(%) / mean ± SD, median	Group 8 n(%) / mean ± SD, median	p-value
	P+***C***+***S***+	***P***+***C***+S-	***P***+C-***S***+	P-***C***+***S***+	P-***C***+S-	***P***+C-S-	P-C-***S***+	P-C-S-	
Sample size, n	79	46	22	48	85	36	205	1,058	
Age, years	61·3 ± 10·8, 62·0	64·9 ± 10·9, 65·0	62·4 ± 11·6, 61·0	63·7 ± 10·1, 65·0	66·5 ± 9·3, 68·0	69·7 ± 9·1, 72·5	67·2 ± 9·9, 69·0	67·7 ± 9·7, 70·0	**< 0·001**
Sex, female	38 (48·1)	20 (43·5)	8 (36·4)	24 (50·0)	33 (38·8)	12 (33·3)	106 (51·7)	356 (33·7)	**< 0·001**
Origin, Germany	63 (79·8)	35 (76·1)	19 (86·4)	37 (77·1)	73 (85·9)	28 (77·8)	190 (92·7)	952 (90·2)	**0·001**
Family status, in a relationship	54 (70·1)	35 (79·6)	17 (77·3)	38 (79·2)	62 (73·8)	29 (82·9)	155 (77·1)	916 (87·7)	**< 0·001**
Marital status									
Married	48 (60·8)	28 (60·9)	15 (68·2)	31 (64·6)	58 (69·1)	28 (77·8)	148 (72·6%)	832 (78·9%)	**< 0·001**
Divorce/separated	16 (20·3)	7 (15·2)	3 (13·6)	3 (6·3)	8 (9·5)	1 (2·8)	16 (7·8)	58 (5·5)	
Widowed	10 (12·7)	10 (21·7)	2 (9·1)	9 (18·8)	15 (17·9)	5 (13·9)	32 (15·7)	112 (10·6)	
Employment status, employed	20 (26·0)	16 (35·6)	5 (23·8)	16 (34·8)	25 (30·1)	8 (22·2)	44 (21·8)	268 (25·8)	0·44
Retirement status, retired	41 (51·9)	31 (67·4)	11 (50·0)	26 (54·2)	51 (61·5)	27 (75·0)	142 (69·6)	760 (72·7)	**< 0·001**
Level of education, ISCED ≥ 14 years	16 (20·3)	7 (15·2)	5 (22·7)	11 (22·9)	14 (16·7)	6 (16·7)	34 (16·7)	244 (23·2)	**0·05**
Diabetes duration, years	11·4 ± 8·9 8·5	11·8 ± 7·6 10	14·0 ± 10·4 10	12·7 ± 9·2 10	11·5 ± 8·0 10	11·2 ± 7·1 10	10·7 ± 8·8 8·5	10·9 ± 8·1 9	0·88
Type of Diabetes									
Type 1 Diabetes	10 (12·8)	3 (6·7)	3 (13·6)	6 (12·8)	8 (9·5)	2 (5·7)	10 (4·9)	86 (8·2)	0·07
Type 2 Diabetes	66 (84·6)	39 (86·7)	17 (77·3)	38 (80·9)	70 (83·3)	31 (88·6)	171 (83·8)	913 (86·9)	
Type unknown/other	2 (2·6)	3 (6·7)	2 (9·1)	3 (6·4)	6 (7·1)	2 (5·7)	23 (11·3)	52 (5·0)	
Diabetes severity aDCSI	2·9 ± 2·0, 3·0	3·3 ± 2·3, 3·0	3·2 ± 2·8, 2·5	3·6 ± 2·1, 3·0	3·0 ± 2·3, 2·0	4·1 ± 2·3, 4·0	3·6 ± 2·4, 3·0	2·9 ± 2·1, 3·0	**< 0·001**
Number of comorbidities	4·3 ± 2·0, 4·0	3·6 ± 1·6 3·0	4·6 ± 2·7 4·0	5·6 ± 2·8, 5·0	3·4 ± 1·9, 3·0	4·4 ± 2·5, 4·0	4·6 ± 2·5, 4·0	3·3 ± 1·9, 3·0	**< 0·001**
Treatment									
Taking insulin	27 (34·2)	20 (43·5)	11 (50·0)	17 (35·4)	29 (34·1)	12 (33·3)	57 (27·8)	313 (29·6)	0·17
Taking oral antihyperglycemic drugs	50 (63·3)	31 (67·4)	15 (68·2)	29 (60·4)	53 (62·4)	25 (69·4)	139 (67·8%)	729 (68·9)	0·81
Taking antidepressants	57 (72·2)	16 (34·8)	15 (68·2)	29 (60·4)	9 (10·6%)	4 (11·1)	89 (43·4)	57 (5·4)	**< 0·001**
Health care costs in € for 2 years	12,021·8 ± 9,631·2, 8,941·1	14,755·5 ± 22,196·0, 7,624·6	21,071·6 ± 23,499·2, 13,930·0	16,133·5 ± 16,576·6, 9,418·8	8,841·8 ± 8,848·2, 6,952·5	12,869·1 ± 12,829·9, 7,255·6	13,598·3 ± 15,942·2, 7,414·7	8,617·3 ± 11,730·2, 5,283·5	0·48
Health related Quality of Life									

Table 2 (continued)

	Group 1 n(%) / mean ± SD, median	Group 2 n(%) / mean ± SD, median	Group 3 n(%) / mean ± SD, median	Group 4 n(%) / mean ± SD, median	Group 5 n(%) / mean ± SD, median	Group 6 n(%) / mean ± SD, median	Group 7 n(%) / mean ± SD, median	Group 8 n(%) / mean ± SD, median	p-value
	***P*+*C*+*S*+**	***P*+*C*+S-**	***P*+C-*S*+**	**P-*C*+*S*+**	**P-*C*+S-**	***P*+C-S-**	**P-C-*S*+**	**P-C-S-**	
physical component summary scale of the SF-12 (PCS-12)[$]	32·4 ± 9·3, 30·6	28·6 ± 7·6, 26·7	31·8 ± 10·2, 30·3	33·2 ± 9·3, 34·1	35·2 ± 9·6, 35·5	31·1 ± 7·8, 32·3	40·6 ± 10·5, 42·3	44·5 ± 9·8, 47·3	**< 0·001**
mental component summary scale of the SF-12 (MCS-12) [$]	30·6 ± 7·8, 28·5	33·5 ± 6·8, 32·1	37·3 ± 9·1, 37·8	39·1 ± 7·7, 37·9	39·8 ± 7·6, 38·1	42·3 ± 7·3, 43·1	49·8 ± 10·2 52·2	54·1 ± 7·3, 56·0	**< 0·001**
Problem Areas in Diabetes Scale (PAID)[∞]	45·0 ± 22·5, 47·0	48·9 ± 19·8, 51·0	24·7 ± 20·3, 23·0	38·0 ± 19·7, 38·0	36·9 ± 16·7, 39·0	29·5 ± 18·4, 30·0	16·9 ± 13·5, 15·0	14·2 ± 12·7, 10·0	**< 0·001**
Previous depression									
Yes	53 (67·1)	15 (32·6)	11 (50·0)	28 (58·3)	4 (4·7)	2 (5·6)	60 (29·4)	52 (4·9)	**< 0·001**
No	8 (10·1)	13 (28·3)	5 (22·7)	9 (18·8)	42 (49·4)	22 (61·1)	98 (48·0)	844 (80·0)	
unknown	18 (22·8)	18 (39·1)	6 (27·3)	11 (22·9)	39 (45·9)	12 (33·3)	46 (22·6)	159 (15·1)	

SD = standard deviation

[$] range from 0 to 100, zero indicates the lowest level of health measured by the scales and 100 indicates the highest level of health

[∞] Possible score can range from 0 to100, with higher scores indicating greater diabetes-related emotional istress

PHQ-9, Patient Health Questionnaire-9; C = CES-D, Center for Epidemiological Studies Depression Scale; S = SHI data, statutory health insurance data

Group 1 = identified with all 3 instruments, Group 2 = identified by PHQ-9 and CES-D, Group 3 = identified by PHQ-9 and health insurance data, Group 4 = identified by CES-D and health insurance data, Group 5 = identified by CES-D, Group 6 = identified by PHQ-9, Group 7 = identified by health insurance data, Group 8 = no depressive disorder

Table 3 Results of the multinomial model reporting odds ratio (OR) and 95% confidence intervals (95% CI) for belonging to the different groups compared to belonging to the group with no depression (group 8)

	Group 1 (n = 79)	Group 2 (n = 46)	Group 3 (n = 22)	Group 4 (n = 48)	Group 5 (n = 85)	Group 6 (n = 36)	Group 7 (n = 205)
Outcome	***P***+***C***+***S***+	***P***+***C***+S-	***P***+C-***S***+	P-***C***+***S***+	P-***C***+S-	***P***+C-S-	P-C-***S***+
	OR[§] [95% CI] (p-value)	OR[§] [95% CI] (p-value)	OR[§] [95% CI] (p-value)	OR[§] [95% CI] (p-value)	OR[§] [95% CI] (p-value)	OR[§] [95% CI] (p-value)	OR[§] [95% CI] (p-value)
Age (years)	0·94 [0·90, 0·98] **(0.0019)**	0·96 [0·92, 1·00] (0.0559)	0·93 [0·89, 0·98] **(0.0059)**	0·94 [0·91, 0·98] **(0·0024)**	0·97 [0·94, 1·01] (0·1025)	0·99 [0·95, 1·04] (0·7203)	0·98 [0·96, 1·00] **(0·0151)**
Sex (female vs. male[$])	1·80 [0·86, 3·76] (0·1990)	1·09 [0·49, 2·54] (0·8317)	0·77 [0·28, 2·11] (0·6087)	1·91 [0·94, 3·91] (0·0756)	1·01 [0·57, 1·77] (0·9804)	0·67 [0·31, 1·45] (0·3084)	1·86 [1·31, 2·65] **(0·0005*)**
Comorbidities (number)	1·12 [0·94, 1·35] (0·2052)	0·82 [0·65, 1·03] (0·0924)	1·09 [0·87, 1·37] (0·4627)	1·44 [1·23, 1·68] **(< 0·0001*)**	0·91 [0·78, 1·06] (0·2183)	1·08 [0·90, 1·28] (0·4134)	1·31 [1·20, 1·44] **(< 0·001)**
taking insulin (yes vs.no[$])	0·52 [0·24, 1·16] (0·1094)	0·86 [0·37, 1·97] (0·7157)	1·43 [0·52, 3·92] (0·4882)	0·48 [0·22, 1·06] (0·0678)	0·72 [0·40, 1·32] (0·2915)	0·58 [0·26, 1·29] (0·1814)	0·57 [0·37, 0·86] **(0·0075)**
taking antidepressants (yes vs. no[$])	8·94 [3·87, 20·63] **(< 0·0001*)**	2·99 [1·16, 7·74] **(0·0235)**	12·00 [4·16, 34·65] **(< 0·0001*)**	7·25 [3·25, 16·15] **(< 0·0001*)**	1·24 [0·52, 2·93] (0·6244)	1·25 [0·40, 3·92] (0·7019)	8·31 [5·43, 12·73] **(< 0·0001*)**
Health related Quality of Life							
physical component summary scale of the SF-12 (PCS-12 (score)	0·90 [0·86, 0·95] **(< 0·0001*)**	0·84 [0·79, 0·89] **(< 0·0001*)**	0·89 [0·84, 0·94] **(0·0001)**	0·94 [0·90, 0·99] **(0·0106)**	0·94 [0·91, 0·97] **(< 0·0001*)**	0·90 [0·86, 0·94] **(< 0·0001*)**	0.99 [0.97, 1.01] (0·3628)
mental component summary scale of the SF-12 (MCS-12) (score)	0·73 [0·69, 0·78] **(< 0·0001*)**	0·75 [0·71, 0·80] **(< 0·0001*)**	0·86 [0·81, 0·91] **(< 0·0001*)**	0·88 [0·84, 0·92] **(< 0·0001*)**	0·85 [0·82, 0·88] **(< 0·0001*)**	0·88 [0·84, 0·92] **(< 0·0001*)**	0·98 [0·95, 1·00] **(0·0396)**
Problem Areas in Diabetes Scale (PAID) (score)	1·07 [1·05, 1·10] **(< 0·0001*)**	1·08 [1·06, 1·11] **(< 0·0001*)**	1·00 [0·97, 1·03] (0·8948)	1·06 [1·04, 1·08] **(< 0·0001*)**	1·06 [1·04, 1·08] **(< 0·0001*)**	1·03 [1·01, 1·06] **(0·0062)**	1·00 [0·98, 1·01] (0·7238)
Previous depression							
(yes vs. no[$])	8·32 [2·83, 24·48] **(< 0·0001*)**	2·07 [0·66·6·42] (0·2099)	6·86 [1·86, 25·29] **(0·0038)**	9·11 [3·43, 24·20] **(< 0·0001*)**	0·37 [0·11, 1·23] (0·1041)	0·52 [0·11, 2·52] (0·4188)	5·19 [3·10, 8·68] **(< 0·0001*)**
(Do not know vs. no[$])	2·76 [0·97, 7·85] (0·0569)	1·74 [0·68, 4·42] (0·2465)	2·47 [0·68, 8·96] (0·1691)	2·13 [0·80, 5·70] (0·1317)	1·49 [0·84, 2·66] (0·1752)	1·15 [0·52, 2·56] (0·7308)	1·73 [1·11, 2·71] **(0·0158)**

P = PHQ-9, Patient Health Questionnaire-9; C = CES-D, Center for Epidemiological Studies Depression Scale; S = SHI data, statutory health insurance data, MCS-12 = Mental summary score of the SF-12, PCS-12 = Physical summary score of the SF-12, PAID = Problem Areas in Diabetes scale

Group 1 = identified with all 3 methods, Group 2 = identified by PHQ-9 and CES-D, Group 3 = identified by PHQ-9 and health insurance data, Group 4 = identified by CES-D and health insurance data, Group 5 = identified by CES-D, Group 6 = identified by PHQ-9, Group 7 = identified by health insurance data, Group 8 = no depressive disorder

[$]Reference group, OR = odds ratio (corresponding to one unite change in case of age, comorbidities, PCS-12, MCS-12 and PAID)

CI = confidence interval, p-values under 0·05 are bold, *p-values significant at multiple level α/70

Nagelkerke's $R^2 = 0.677$

(i.e., group 8). Overall, several differences in associations with the independent variables and the groups identified by the three methods were identified (even Bonferroni adjusted). We did not find a clear pattern between methods used and characteristics of individuals identified. However, we found some remarkable points.

First, we observed that a person who took antidepressants compared to a person who did not take antidepressants was 12 times (or for that matter about 9, 8 and 7 times) more likely to be in group 3 (group 1, 7 or 4, respectively) than in the reference group, i.e., OR = 12·00 (8·94, 8·31 and 7·25, respectively). These four groups are characterized by a diagnosis in SHI data. Contrastingly, in groups not identified through a diagnosis in SHI data, i.e., groups 2, 5 and 6, the estimated effects of taking antidepressants were considerably smaller and even not significant for groups 5 and 6 (depression symptoms according to CES-D and PHQ-9 only). A quite similar pattern was noticed for reporting previous depression and comorbidities: Persons reporting a previous depression where

significantly more likely to be in one of the groups identified through a diagnosis in SHI data (group 1, 3, 4 and 7) compared to the reference group and people with more comorbidities were more likely to be groups 4 and 7 (both identified through SHI diagnosis).

Second, women were almost twice more likely to be in the group with an SHI data-based diagnosis only (group 7) than in the reference group (OR=1.86). But there were no further significant associations related to other groups.

Third, age was a significant factor for group membership probability. With each year of life, it is less likely to be in any group with depressive disorder than in the reference group (all OR's are less than one), however, not significant for groups without SHI-based depression diagnosis. Low HRQoL values and especially low MCS-12 values were associated with belonging to any group but not the one identified by SHI data only, each in comparison to the reference group. We observed that a person with low MCS-12 is significantly more likely to be in a group with both symptoms according to PHQ-9- and CES-D (i.e., group 1 and group 2) than in any other group. Furthermore, the results regarding the PAID Score point in the same direction, values were associated with belonging to any group (except the smallest group) but not the one identified by SHI data only.

Discussion

National and international guidelines recommend screening people with diabetes for depression to identify patients in need of psychological treatment [31, 32]. However, neither of these guidelines give detailed instructions on which screening instrument to use or describe the differences for the identified groups. A recent meta-analysis of diagnostic accuracy of depression questionnaires in adult patients with diabetes by de Joode et al. (2019) showed, that the CES-D and the PHQ-9 are the most frequently evaluated depression questionnaires among patients with diabetes [20]. They differed in terms of sensitivity and specificity, however none of the two instruments was found to be superior over the other. The results of our study show that between 14·6% and 22·4% of individuals with diabetes had depression depending on the method used to assess it. High prevalence estimates can be expected, since on the one hand, there is evidence that depression is a risk factor for diabetes and, on the other hand, studies show that the distress caused by diabetes contributes to the development of depression [1, 8, 33–36]. The results of our study are within the range of findings from the two most recent meta-analyses on depression among persons with diabetes where prevalence ranged from 1·8% up to 88·0% [1, 8]. One could assume, that both instruments used would identify more or less the same persons since they both measure depression symptoms within the last or the last two weeks. One could also assume an overlap between the two instruments and the persons identified through SHI data, however this overlap would be expected to be a little less pronounced as SHI data covers diagnosis from two years. We indeed found some overlap between the methods; however, surprisingly the majority of persons was identified by one instrument only (20·7% of the total sample), 7·3% of the whole sample were identified using two methods and 5·6% were identified with all three methods. The largest number of persons was identified through SHI data only (group 7). In total 68·0% of those identified with depression in our sample were identified through SHI data of which 42·1% were also identified through one of the two instruments. The characteristics of individuals identified by either of the two instruments were quite similar. Within our sample women were more likely to belong to the group identified through SHI data only (group 7). This is in line with results of an analysis of routine German SHI data that found women are diagnosed more frequently than men in all age groups [37].

It seems that persons who have a diagnosis of depression in SHI data but do not show symptoms in either of the questionnaires (group 7) do not noticeably differ in their HRQoL when compared with the group with no depression. Neither were the reported scores for diabetes related distress high in this group.

Screening for depression among individuals with diabetes seems to be necessary since all groups identified through at least one questionnaire (groups 1–7) had more unfavorable outcomes compared to the group with no depression.

Our findings show that, even though the same disease should be measured, the degree of variability in persons identified across the methods is substantial. If we would have used the PHQ-9 only we would have missed 133 patients who have depressive symptoms according to the CES-D but not according to the PHQ-9. Similarly, if we would have used only the CES-D we would have missed 58 persons who had symptoms according to the PHQ-9 but not according to the CES-D. Unfortunately, the differences between the groups were not pronounced enough to draw conclusions on which method is to be preferred.

To keep in mind: We found some indication that the method chosen to identify persons with a depressive disorder might be related to particular underlying characteristics in the population identified. To our knowledge, there is no study, which has used a similar many-to-one approach. It will be interesting to compare findings of future studies with larger samples.

Strength and limitations

To our knowledge, this is the first study which analyses groups identified by different instruments to assess depression, and includes also SHI data. The linkage of survey data with SHI data allows a more detailed description of the identified persons which would not be possible with using only one of the two data sources. The analyzed data set is rather large allowing for robust estimates. Moreover, the response rate was with 51·0% reasonably high for a survey-based study. An nonresponse analysis did not reveal any major differences between responders and nonresponders especially with respect to depression [23]. Thus, nonresponse bias should be small. However only persons of one SHI could participate in the study which might influence the results since, for example, the prevalence of diabetes varies among the different SHIs in Germany [38]. Survey data was only assessed at one point during the study period whereas the SHI data covers the whole study period thus the prevalence observed in SHI data might be, among other reasons, higher as the time frame during which it is assessed is longer. Moreover, it has to be kept in mind that a diagnosis in SHI data is not valid as a screening measure for depression since people with a diagnosis have most likely received some form of therapy. Furthermore, within SHI data we find clinical diagnosis whereas the results of the CES-D and the PHQ-9 are not clinical diagnosis but results of screening measures for depression. Additionally, it might be the case that once a person has received a depression diagnosis it will not be removed from the track record even though the person does not have depression anymore. Likewise, we could not get a full history of diagnosed depression but only data on depression diagnosis 12 month before and after the baseline assessment. Our focus is on acute depression, in line with the two instruments used during the baseline survey, which is not covered by a lifetime history of depression. Since we include a considerable time frame before and after the baseline assessment misclassification is assumed to be low.

Conclusion

Our study is the first study that describes the overlap and differences between individuals identified with different methods to detect depression. Although several characteristics were found to be associated with belonging to the different groups; we did not find a clear pattern among those characteristics. However, we have found some initial indications that the method chosen is related to particular underlying characteristics in the population identified. The methods have a relatively low overlap. The majority of persons were identified using a diagnosis in SHI data. Those identified through SHI data only did not differ in their HRQoL when compared to those with no depression. This could be either due to a successful therapy or due to a spontaneous relapse. Our study shows, that there might be similarities but also differences in characteristics of identified persons depending on the method used. By using either of the three methods, one should be aware that certain persons are missed. Therefore, further research with a comprehensive data set, that is sufficiently large in terms of case numbers, is needed to address the implications of using either of the methods.Especially prospective studies investigating clinical outcomes would be important. This knowledge is crucial to enable clinicians to make an informed decision about the usage of either of the two instruments in every day practice, taking into account setting, time constraints and other relevant circumstances.

Supplementary Information

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Supplementary Material 1

Supplementary Material 2

Supplementary Material 3

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Author contribution

Linnenkamp and Andrich wrote the paper. Chernyak, Icks, Brüne and Kruse conceived and designed the experiments. Brüne, Kvitkina and Arend performed the experiments, Linnenkamp, Andrich, Gontscharuk, Ogurtsova, Icks, Hoffmann, Hermanns, Kulzer, Evers and Hilligsmann analyzed and interpreted the data, Schmitz-Losem contributed data. All authors carefully read and approved the final manuscript.

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Data availability

Due to ethical concerns, supporting data on the results of the questionnaire cannot be made openly available. Additionally, data of the statutory health insurance was already existing and was obtained upon request and subject to licence restrictions from a number of different sources. Full details how these data were obtained are available in the documentation available at: https://doi.org/10.14312/2398-0281.2016-3.

Declarations

Conflict of interest

The authors declare that they have no conflict of interest.

Role of the funder/sponsor

The funder had no role in the design and conduct of the study; collection, management, analysis, and interpretation of the data; preparation, review, or approval of the manuscript; and decision to submit the manuscript for publication.

Ethics approval
Ethical approval was obtained from the ethics committee of the Heinrich-Heine University Düsseldorf and is available under the study reference 3762.

Statement to confirm that all methods were carried out in accordance with relevant guidelines and regulations
We have adhered to best practice guidelines for Strengthening the Reporting of Observational Studies in Epidemiology (STROBE).

Precis
Different instruments to screen for depression do not identify the same persons, however no systematic differences exist between the different groups of persons.

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