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**Alkoholbezogene Störungen und Behandlungspfade von Patienten mit einer
Alkoholkonsumstörung im Bundesland Bremen
- Eine Sekundärdatenanalyse von Routinedaten**

Dissertation
zum Erwerb des Doktorgrades der Humanbiologie
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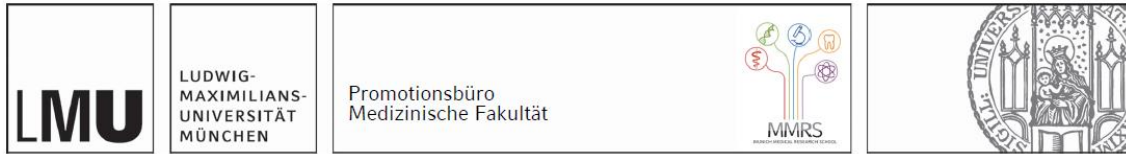
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Abkürzungsverzeichnis

DSM-IV:	Diagnostisches und Statistisches Manual Psychischer Störungen, vierte Version
GeNo:	Gesundheit Nord – Klinikverbund Bremen
GPI:	Deutsche Rentenversicherung (German Pension Insurance)
ICD-10:	Internationale statistische Klassifikation der Krankheiten und verwandter Gesundheitsprobleme, zehnte Revision
QWT:	Qualifizierte Entzugsbehandlung (Qualified withdrawal treatment)
SHI:	Gesetzliche Krankenversicherung (Statutory health insurance)

Publikationsliste

Publikationen als Bestandteil der vorliegenden Dissertation:

Paper I:

Möckl, J., Lindemann, C., Manthey, J., Schulte, B., Reimer, J., Pogarell, O., & Kraus, L. (2023). Estimating the prevalence of alcohol-related disorders and treatment utilization in Bremen 2016/2017 through routine data linkage. *Frontiers in Psychiatry*, 14. <https://doi.org/10.3389/fpsyt.2023.1002526>

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Beitrag zu den Publikationen

1.1 Beitrag zu Paper I

Der Autor der vorliegenden Dissertation (Justin Möckl) hat wesentlich zur Konzeption dieses Papers sowie der Studienfrage beigetragen. Er bereitete den Datensatz für sämtliche Analysen vor, führte die statistischen Analysen durch und interpretierte die Ergebnisse. Er schrieb das Originalmanuskript sowie die endgültige Fassung der veröffentlichten Version und begleitete den Publikationsprozess federführend von der Einreichung des Manuskripts im Journal über den Reviewprozess bis hin zur Bearbeitung der Druckfahnen.

1.2 Beitrag zu Paper II

Der Autor der vorliegenden Dissertation (Justin Möckl) hat wesentlich zur Konzeption dieses Papers sowie der Studienfrage beigetragen. Er bereitete den Datensatz für sämtliche Analysen vor, führte die statistischen Analysen durch und interpretierte die Ergebnisse. Er schrieb das Originalmanuskript sowie die endgültige Fassung der veröffentlichten Version und begleitete den Publikationsprozess federführend von der Einreichung des Manuskripts im Journal über den Reviewprozess bis hin zur Bearbeitung der Druckfahnen.

2. Einleitung

2.1 Epidemiologie des Alkoholkonsums

Alkohol (Ethanol/Ethylalkohol) entsteht durch die Vergärung von Zucker und kann aus verschiedenen zucker- oder stärkehaltigen Stoffen gewonnen werden, wie z.B. Obst, Kartoffeln, Getreide oder Zuckerrohr (1). Aufgrund des natürlichen Vorkommens von Ethanol in überreifen Früchten kann davon ausgegangen werden, dass bereits frühe Vorfahren des modernen Menschen durch das Verspeisen solcher Früchte regelmäßig kleine Mengen Ethanol zu sich nahmen (2). In der Geschichte der Menschheit ist der Konsum alkoholhaltiger Getränke sowie dessen Reglementierung in rituellen Zeremonien bereits in vormodernen Kulturen nachweisbar (3). Alkohol begleitet den Menschen also bereits seit seiner Entstehung und er wird bis heute in verschiedenen Funktionen in Medikamenten und Nahrungsmitteln und auch als Rauschmittel verwendet. Der Umgang mit Alkohol ist dabei stark von historischen, kulturellen, sozio-ökonomischen und religiösen Unterschieden geprägt (4, 5).

Weltweit ist Alkoholkonsum in Europa am verbreitetsten und im Gegensatz zum globalen Trend sind dort in den letzten 20 Jahren rückläufige Zahlen an Konsumierenden und der konsumierten Menge pro Kopf festgestellt worden (6). Im Jahr 2019 war der Pro-Kopf-Konsum reinen Alkohols im globalen Vergleich mit 9,2 Litern in Europa am höchsten (7), besonders Deutschland gilt mit 12,2 Litern im internationalen Vergleich als Hochkonsumland (7, 8). Schätzungen innerhalb der jeweiligen Bevölkerung über 15 Jahre berücksichtigten nicht nur offiziellen Angaben aus Steuern und Verkauf, sondern auch den Konsum von selbst-hergestellten und nicht versteuertem Alkohol, sowie den Konsum durch Touristen.

Im Vergleich mit anderen psychoaktiven Substanzen, ohne Berücksichtigung von Koffein, wird in Deutschland Alkohol mit Abstand am häufigsten konsumiert.

Im Jahr 2021 betrug die Prävalenz des Konsums in den letzten 30 Tagen in der deutschen Bevölkerung zwischen 18 und 64 Jahren für Alkohol 71%, gefolgt von nicht-opioidhaltigen Schmerzmitteln mit 47% und konventionellen Tabakprodukten (Zigaretten, Zigarren, Zigarillos oder Pfeifen) mit 23% (9). Darüber hinaus liegen Schätzungen zu gefährlichen Konsummustern vor, wie Rauschtrinken (mehr als 5 alkoholische Getränke zu einer Gelegenheit) oder ein riskanter Konsum (durchschnittlich mehr als 12 Gramm (Frauen) bzw. mehr als 24 Gramm (Männer) reinen Alkohol pro Tag). Im Jahr 2021 und bezogen auf die letzten 30 Tage hatte unter Alkoholkonsumierenden zwischen 18 und 64 Jahren in Deutschland jeder dritte mindestens eine Episode des Rauschtrinkens und etwas mehr als jeder fünfte konsumierte Alkohol in riskanten Mengen (9). Die Prävalenz für eine Alkoholabhängigkeit oder -missbrauch nach Kriterien der vierten Auflage des diagnostischen und statistischen Manuals psychischer Störungen (DSM-IV) wurde im Jahr 2018 in der deutschen Bevölkerung (18 bis 64 Jahre) auf 3,1% (Abhängigkeit) bzw. 2,8% (Missbrauch) geschätzt (10).

2.2 Schäden des Alkoholkonsums

In Deutschland genießen alkoholhaltige Getränke den Status eines Kulturguts. Beispielsweise wurde Bier von einem bayerischen Ministerpräsidenten gar als „Lebenselixier“ und „Bayerns fünftes Element“ bezeichnet (11). Dass es sich bei alkoholischen Getränken nicht um ein „gewöhnliches Konsumgut“ (4) handelt, zeigen die Auswirkungen, die der Konsum auf individueller und gesellschaftlicher Ebene mit sich bringt. Der Konsum von Alkohol wird ursächlich mit mehr als 200 medizinischen Diagnosen gemäß der 10. Auflage der Internationalen Klassifikation der Krankheiten (ICD-10) in Verbindung gebracht, wovon mehr als 40 spezifisch auf Alkohol zurückzuführen sind (12).

Darunter fallen psychische und Verhaltensstörungen durch Alkohol (ICD-10: F10), Infektionskrankheiten (u.a. Tuberkulose, HIV/AIDS und Lungenkrankheiten), Krebsarten (im Mund-Rachenbereich, Kehlkopf, Speiseröhre, Dick- und Mastdarm, Leber und Brust), Neurologische Erkrankungen (u.a. Epilepsie), Kardiovaskuläre Krankheiten, Krankheiten des Verdauungstraktes (u.a. Leberzirrhose, Pankreatitis) sowie Unfälle und Verletzungen (12). Protektive Effekte des Konsums geringer Mengen von Alkohol wurden für ischämische Herzkrankheiten und ischämische Schlaganfälle sowie Diabetes beobachtet. Studien weisen jedoch auf eine Überschätzung dieser protektiven Effekte hin (12). Die Weltgesundheitsorganisation (WHO), die Deutsche Hauptstelle für Suchtfragen (DHS), sowie die Deutsche Gesellschaft für Ernährung (DGE) kommen in aktuellen Stellungnahmen zu dem Schluss, dass es aufgrund der karzinogenen Effekte von Alkohol keinen gesundheitlich unbedenklichen Alkoholkonsum gibt (13-15).

Laut einer Schätzung zu alkoholbedingter Morbidität und Mortalität in der deutschen Bevölkerung zwischen 15 und 69 Jahren waren im Jahr 2021 bei Männern 9% und bei Frauen 3% von allen Krankenhaus- und Rehabilitationsfällen und von allen Sterbefällen bei Männern 12% und bei Frauen 6% auf den Konsum von Alkohol zurückzuführen (16). Für beide Geschlechter waren der Großteil der alkoholbedingten Krankenhaus- und Rehabilitationsfälle auf Unfälle und psychische und Verhaltensstörungen durch Alkohol (u.a. F10.0 „akute Intoxikation“, F10.1 „schädlicher Gebrauch“, F10.2 „Abhängigkeitssyndrom“ und F10.3-4 „Entzugssyndrom“) zurückzuführen (16). Unter Männern waren F10 Diagnosen im Jahr 2020 laut amtlicher Statistik sogar der dritthäufigste Anlass für eine stationäre Behandlung in deutschen Krankenhäusern, nach den Diagnosen Herzinsuffizienz (I50) und Lebendgeborene nach dem Geburtsort (Z38) (17). Alkoholkonsum und dessen Folgen stellen also eine große Belastung für das deutsche Gesundheitswesen und die Allgemeinheit dar.

Eine Studie schätzte für Deutschland im Jahr 2018 die direkten Kosten (u.a. Kosten der Krankheit, Pflege, Rehabilitationsmaßnahmen, Unfälle) auf 16,6 Milliarden € und die indirekten Kosten (u.a. Ressourcenverlust durch Mortalität, Sozialleistungen durch unfreiwillige Arbeitslosigkeit) auf 40,4 Milliarden € (18). Im selben Zeitraum wurden lediglich 3,2 Milliarden € durch alkoholbezogene Steuern eingenommen (18). Noch nicht in den Zahlen berücksichtigt sind Schäden an betroffenen Dritten, wie Angehörige oder Unfallopfer.

2.3 Suchtspezifische Versorgung in Deutschland

Alkoholkonsum ist mit zahlreichen physischen, psychischen und sozialen Problemfeldern verknüpft. Menschen mit einer Alkoholabhängigkeit haben daher meist in verschiedener Weise Kontakt mit Behörden, Einrichtungen, der medizinischen Versorgung und der Suchthilfe. Das Suchthilfesystem ist in Deutschland sehr ausdifferenziert und lässt sich dabei in verschiedene Bereiche einteilen, die sich sowohl hinsichtlich ihres Versorgungsauftrags als auch ihrer Finanzierung unterscheiden. Die Deutsche Hauptstelle für Suchtfragen (DHS) unterscheidet 12 Segmente: 1. „Beratung und Begleitung“, 2. „Medizinische Behandlung“, 3. „Medizinische Rehabilitation“, 4. „Eingliederungshilfe“, 5. „Beschäftigung, Qualifizierung und Teilhabe am Arbeitsleben“, 6. „Justiz“, 7. „Selbsthilfe“, 8. „Prävention“, 9. „betriebliche Gesundheitsförderung“, 10. „Kinder- und Jugendhilfe“, 11. „Pflege und Altenhilfe“ sowie 12. „Wohnungslosenhilfe“ (19). Die vorliegende Dissertation konzentriert sich dabei auf Anlaufstellen, die eine suchtspezifische medizinische Behandlung und Versorgung gewährleisten, genauer

1. Beratung und Begleitung (z.B. ambulante Suchthilfe)
2. Medizinische Behandlung: ambulant (z.B. Hausarzt-, psychiatrische, psychotherapeutische Praxis) und stationär (z.B. Allgemein-, psychiatrisches Krankenhaus)
3. Medizinische Rehabilitation: ambulant und (teil-)stationär.

Die S3-Leitlinie „Screening, Diagnostik und Behandlung alkoholbezogener Störungen“ sieht für die Behandlung einer Alkoholabhängigkeit unmittelbar nach einer Akutversorgung eine nahtlose Postakutbehandlung vor (20). Die Akutversorgung umfasst mindestens eine körperliche Entgiftung oder eine qualifizierte Entzugsbehandlung, wobei letztere empfohlen wird (21). Im Rahmen einer körperlichen Entgiftung steht die Behandlung der Alkoholintoxikation mit körperlich neurologischen Ausfallerscheinungen und/oder von Alkoholentzugssymptomen im Vordergrund, mit dem Ziel die Vitalfunktion sicherzustellen, Komplikationen (z.B. epileptische Anfälle oder Delirium Tremens) zu vermeiden und Entzugserscheinungen zu reduzieren.

Im Rahmen eines qualifizierten Entzugs werden zusätzlich psychische und somatoforme Begleit- und Folgeerkrankungen berücksichtigt und eine Kontaktvermittlung zum regionalen Hilfesystem (z.B. Psychotherapie, Selbsthilfe) und spezifischen Behandlungsangeboten (Rehabilitation) angestrebt (22). Damit soll neben der körperlichen Entgiftung auch die Behandlung der zugrundeliegenden Abhängigkeitserkrankung sowie eine nahtlos anschließende Postakutmaßnahme initiiert werden. Akutbehandlungen werden in Deutschland von den Krankenkassen finanziert, während eine Rehabilitation bei Erwerbstätigen in der Regel von der Rentenversicherung finanziert wird. Das Ziel eines qualifizierten Entzugs ist die Minimierung administrativer Hürden beim Übergang zwischen Akut- und Postakutbehandlung, die durch die verschiedenen Kostenträger entstehen können (21). Im Jahr 2021 finanzierte die Rentenversicherung etwa 82% der stationären Rehabilitationsmaßnahmen (23). Die Voraussetzungen dafür sind, u.a. Einzahlung in die Rentenversicherung für mindestens sechs Monate in den letzten zwei Jahren, kein Beamtenverhältnis und keine Rente oder Pension. Falls die Voraussetzungen für die Rentenversicherung nicht erfüllt sind, werden Rehabilitationsmaßnahmen von den Krankenkassen finanziert. Darüber hinaus liegen

weitere Postakutbehandlungen, wie z.B. psychotherapeutische Betreuung oder eine medikamentöse Rückfallprophylaxe im Zuständigkeitsbereich der Krankenkassen.

Neben der Inanspruchnahme von Akut- sowie Postakutmaßnahmen gibt es für Menschen mit einer Alkoholabhängigkeit die Möglichkeit im Rahmen der ambulanten Suchthilfe beraten und begleitet zu werden. Dabei sollen vor allem Wissen, Fertigkeiten und Kompetenzen vermittelt werden, um Probleme selbstständig lösen zu können, wie auch eine Vermittlung in zuständige Angebote aus dem Sozial- und Gesundheitswesen sowie der Selbsthilfe stattfinden (24). Als offene Anlaufstelle ist die ambulante Suchthilfe unabhängig vom Versichertenstatus und anderen Voraussetzungen, und soll als erster Kontakt prinzipiell jedem offenstehen. Das Angebot der Suchthilfeeinrichtungen variiert in Deutschland je nach Region. Angebote zur Suchtberatung werden auf Bundeslandebene bzw. kommunal finanziert. Abhängig vom Angebot der Einrichtung gibt es zusätzlich Angebote aus verschiedenen Sozialgesetzbüchern, wie z.B. ambulante Rehabilitation Sucht oder Nachsorge (24).

2.4 Inanspruchnahme suchtspezifischer Versorgung

Im Verhältnis zur Anzahl von Personen mit einer Alkoholabhängigkeit ist die Inanspruchnahme suchtspezifischer Angebote gering. Eine Umfrage in der deutschen Bevölkerung zwischen 18 und 79 Jahren konnte zeigen, dass im Vergleich mit anderen psychischen Störungen Betroffene von Substanzkonsumstörungen am seltensten Behandlungen aufgrund ihrer Störung in Anspruch nehmen (25). In einer Umfrage in Berlin, Brandenburg und Sachsen in der primärärztlichen Versorgung nahmen 17% der Patientinnen und Patienten mit einer Alkoholabhängigkeit eine suchtspezifische Versorgung in Anspruch (26). Eine Schätzung anhand aggregierter Statistiken kam zu dem Ergebnis, dass von den Personen mit Alkoholabhängigkeit nur etwa 16% wegen

ihrer Abhängigkeit im Krankenhaus und/oder in stationären und/oder ambulanten Suchthilfeeinrichtungen behandelt wurden (27).

Diese geringe Inanspruchnahme besteht trotz einer flächendeckenden medizinischen Grundversorgung und existierender evidenzbasierter Verfahren in der Früherkennung, adäquaten Diagnostik und Behandlung von alkoholbezogenen Störungen (28). Laut der Deutschen Hauptstelle für Suchtfragen e.V. bestehen vielfältige suchtspezifische Angebote des erweiterten Gesundheits- und Sozialwesens, trotzdem werden viele Betroffene von Suchterkrankungen häufig nicht bedarfsgerecht versorgt (19). Die starke Segmentierung und Komplexität des Suchthilfesystems kann einerseits Chance für die Erbringung individueller Hilfsangebote sein, und andererseits zu Schnittstellenproblemen führen (19). Um die fehlende Abstimmung beispielsweise zwischen Akutmedizin und Rehabilitation zu verbessern und das Problembewusstsein für alkoholbezogene Störungen zu schärfen, wurde 2016 die S3-Behandlungsleitlinie „Screening, Diagnose und Behandlung alkoholbezogener Störungen“ erstellt und 2021 aktualisiert (28).

Bisherigen Studien zeigten, dass in Deutschland eher ältere Patientinnen und Patienten mit schweren alkoholbezogenen Störungen und vorhandenen somatischen bzw. psychischen Folgeerkrankungen erkannt und behandelt werden (26, 29). Eine Studie aus dem Jahr 2020 im Bundesland Bremen kam jedoch zu dem Ergebnis, dass vor allem schwere Alkoholkonsumstörungen zwar häufig diagnostiziert, meist jedoch nicht leitlinienkonform behandelt werden (30). Bei weniger schweren Alkoholkonsumstörungen wurde mangelndes Problembewusstsein der Patientinnen und Patienten als ein Hauptgrund für eine fehlende suchtspezifische Behandlung berichtet (31).

Der erste Kontakt zum Gesundheitssystem für Menschen mit einer alkoholbezogenen Störung findet meist aufgrund psychischer und somatischer Komorbiditäten statt, wobei

Hausärzte als Allgemeinmediziner häufig als erste Ansprechpartner fungieren (32). Für die Betrachtung von Schnittstellenproblemen ist vor allem der Übergang zwischen der allgemeinmedizinischen Behandlung und verschiedenen suchtspezifischen Maßnahmen von Interesse, wie die Zeitspanne zwischen einer Entzugsbehandlung und einer Rehabilitation. Der zeitliche Ablauf zwischen suchtspezifischen Behandlungen kann in individuellen Behandlungspfaden empirisch dargestellt werden. Die genaue Analyse dieser Behandlungspfade ist von Bedeutung, da eine reguläre Beendigung der Entzugsbehandlung sowie eine zeitnahe Anschlussbehandlung das Risiko eines Rückfalls und einer erneuten Entzugsbehandlung senkt (20, 33, 34).

Bisherige Analysen zur Inanspruchnahme suchtspezifischer Versorgung basierten auf aggregierten Daten, wie der Krankenhausstatistik oder dem Diagnoseportal für niedergelassene Vertragsärzte (27), Daten zum Pro-Kopf-Konsum (35), oder auf Umfragedaten (29, 32). Die Darstellung individueller Behandlungspfade ist damit, wenn überhaupt, nur eingeschränkt möglich. Im Rahmen dieser Arbeit kann auf einen umfassenden Datensatz zurückgegriffen werden, der über ein Data-Linkage-Verfahren individuelle Informationen in verschiedenen Routinedaten des Gesundheitssystems im Bundesland Bremen integriert.

2.5 Datengrundlage

Die analysierten Routinedaten wurden im Rahmen des durch das Bundesministerium für Gesundheit geförderten Projekts „Implementierung und Evaluation der S3-Leitlinie zum Screening, zur Diagnostik und zur Behandlung alkoholbezogener Störungen“ (IMPELA) erhoben und auf individueller Ebene miteinander verknüpft.

Die Datensätze umfassen Personen ab 16 Jahren mit Wohnsitz im Bundesland Bremen zwischen 2016 und 2017. Die Gesamtstichprobe enthält alle Personen mit

dokumentierten alkoholspezifischen Diagnosen¹ in mindestens einer der drei verwendeten Datenquellen (36):

1. Ambulante Suchthilfe (Gesundheit Nord – Klinikverbund Bremen)
2. Zwei gesetzliche Krankenkassen (AOK Bremen/Bremerhaven und hkk)
3. Regionale Deutsche Rentenversicherung (DRV Oldenburg-Bremen).

Der Datensatz beinhaltet dabei Besuche in der ambulanten Suchthilfe aufgrund von Alkohol, alle über die gesetzlichen Krankenkassen abgerechneten Behandlungen im stationären und ambulanten Bereich, und alkoholbezogene Rehabilitationsleistungen der regionalen Deutschen Rentenversicherung. Damit kann die Versorgungslage von Menschen mit alkoholbezogenen Störungen in verschiedenen Behandlungssettings in Bremen detailliert analysiert werden. Durch die Verknüpfung mehrerer Datenquellen können auch Überschneidungen der Settings und der suchtspezifischen Versorgung berücksichtigt werden.

2.6 Untersuchte Forschungsfragen

Die vorliegende Dissertation widmet sich der Analyse der Versorgungsrealität von Menschen mit alkoholbezogenen Störungen sowie der suchtspezifischen Behandlung von Menschen mit einer Alkoholabhängigkeit mit dem Ziel Defizite, Schnittstellenprobleme und Verbesserungspotentiale in der suchtspezifischen Versorgung aufzudecken. In die Dissertation gehen zwei Publikationen ein, deren Forschungsfragen im Folgenden genauer vorgestellt werden. Ziel der ersten Publikation ist die Darstellung von alkoholbezogenen Störungen in der medizinischen Versorgung sowie eine Hochrechnung der suchtspezifischen Versorgungssituation von Menschen mit einer

¹ ICD-10-Code: F10, E24.4, E52, G31.2, G62.1, G72.1, I42.6, K29.2, K70, K85.2, K86.0, O35.4, P04.3, Q86.0, R78.0, T51

Alkoholabhängigkeit im Bundesland Bremen. Hierfür wurde zunächst der Anteil von Personen mit einer Alkoholabhängigkeit in der Gesamtbevölkerung Bremens geschätzt. Dafür wurden deutschlandweite Umfragedaten der repräsentativen Stichprobe des Epidemiologischen Suchtsurveys 2018 (10) alters- und geschlechtsspezifisch auf die Bevölkerung des Bundeslands Bremen hochgerechnet. Anschließend wurde die Prävalenz von alkoholbezogenen Störungen in der medizinischen Versorgung im ambulanten und stationären Setting berechnet sowie der Anteil der Patientinnen und Patienten mit Alkoholabhängigkeit und deren suchtspezifische Versorgungsleistungen, wie qualifizierte Entzugsbehandlungen und Rehabilitationsmaßnahmen auf die Gesamtbevölkerung Bremens hochgerechnet.

Das Ziel der zweiten Publikation ist die explorative Analyse suchtspezifischer Behandlungspfade von Menschen mit einer Alkoholabhängigkeit über verschiedene medizinische Versorgungsbereiche hinweg mithilfe einer Sequenzdatenanalyse (37). Diese ursprünglich sozialwissenschaftliche Methode wurde bereits in der Versorgungsforschung anderer Indikationen mit Routinedaten in Frankreich (38, 39), Kanada (40) und Deutschland (41) verwendet. Um eine vergleichbare Stichprobe zu erhalten, wurde ein einheitliches Indexereignis definiert. Anschließend wurden individuelle Sequenzen der stattgefundenen suchtspezifischen Behandlungen für die folgenden 307 Tage inklusive des Indexereignis erstellt. Die Sequenzen wurden dann mithilfe einer Clusteranalyse zu typischen Behandlungspfaden zusammengefasst und hinsichtlich ihrer Konformität mit der S3-Leitlinie überprüft. Schließlich wurden die Cluster der typischen Behandlungspfade visualisiert und ihr Zusammenhang mit soziodemographischen Variablen wie Geschlecht, Alter, Nationalität sowie der allgemeinen Komorbidität und dem Besuch der ambulanten Suchthilfe mithilfe eines Multinomialen Logit Modells analysiert. Die Ergebnisse der beiden Forschungsfragen

wurden jeweils in internationalen Fachzeitschriften publiziert und finden sich abgedruckt in den Kapiteln 5 und 6 dieser Dissertation.

3. Zusammenfassung:

Hintergrund: Alkoholkonsum ist bedingt durch unterschiedliche Wirkmechanismen Ursache für verschiedene Krankheiten, gleichzeitig gilt Deutschland im internationalen Vergleich als Hochkonsumland. Die Prävalenz für eine Alkoholabhängigkeit nach Kriterien der vierten Auflage des diagnostischen und statistischen Manuals psychischer Störungen (DSM-IV) lag in der erwachsenen, deutschen Bevölkerung zwischen 18 und 64 Jahren im Jahr 2018 bei 3,1%. Trotz vorhandener evidenzbasierter Verfahren der Früherkennung, adäquater Diagnostik und Behandlung von alkoholbezogenen Störungen zeigen sich in der Praxis oft Probleme. Bisherige Forschungsarbeiten weisen auf eine geringe Inanspruchnahme suchtspezifischer Behandlungen von Menschen mit einer Alkoholabhängigkeit hin. In dieser Arbeit wird diese Behandlungslücke mithilfe von verknüpften Routinedaten verschiedener Kosten- und Leistungsträger aus dem Bundesland Bremen näher beleuchtet.

Ziele: Das übergeordnete Ziel der Dissertation ist die Analyse der Versorgungssituation von Personen mit alkoholbezogenen Störungen insbesondere einer Alkoholabhängigkeit, um Versorgungslücken und Schnittstellenprobleme identifizieren zu können. Das erste Forschungsziel ist die suchtspezifische Versorgungssituation von Menschen mit alkoholbezogenen Störungen in Bremen in verschiedenen medizinischen Settings darzustellen und die Inanspruchnahme von suchtspezifischen Behandlungen von Menschen mit Alkoholabhängigkeit mithilfe von Umfragedaten auf die Gesamtbevölkerung in Bremen hochzurechnen. Das zweite Forschungsziel besteht in der Analyse der individuellen suchtspezifischen Behandlungspfade von Menschen mit Alkoholabhängigkeit. Diese Pfade wurden in typische Verläufe geclustert und diese Cluster hinsichtlich ihrer Konformität mit den aktuellen S3-Leitlinien überprüft sowie im Hinblick auf soziodemographische Variablen charakterisiert.

Methodik: Datengrundlage sind Routinedaten der Jahre 2016 und 2017 von Personen mit mind. einer alkoholbezogenen Diagnose und Wohnsitz in Bremen (n=11.205). Die Daten beinhalten ambulante und stationären Daten zweier gesetzlicher Krankenkassen (AOK Bremen/Bremerhaven, hkk), alkoholbezogene Rehabilitationsmaßnahmen der regionalen Deutschen Rentenversicherung Oldenburg-Bremen sowie Besuche der ambulanten Suchthilfe des kommunalen Klinikverbunds Bremen Gesundheit-Nord. Die Anzahl der Personen mit in Anspruch genommenen suchtspezifischen Maßnahmen, wie einem stationären qualifizierten Entzug, ambulanter medikamentöser Rückfallprophylaxe, Rehabilitationsmaßnahmen, ambulanter Suchthilfe sowie mit dokumentierten ambulanten und stationären Diagnosen einer Alkoholabhängigkeit wurde auf die Bevölkerung Bremens hochgerechnet. Für die Berechnung der Behandlungsquote wurde darüber hinaus die Anzahl aller Personen mit einer Alkoholabhängigkeit in Bremen mithilfe von Daten des Epidemiologischen Suchtsurveys 2018 alters- und geschlechtsspezifisch auf die Bevölkerung Bremens hochgerechnet. Für das zweite Forschungsvorhaben wurden individuelle suchtspezifische Behandlungspfade von 518 Personen mit Methoden der Sequenzdatenanalyse erstellt, geclustert und analysiert. Die Behandlungspfade beinhalten suchtspezifische Maßnahmen 10 Monate nach einer stationären Indexepisode aufgrund von Alkoholabhängigkeit. Im Anschluss wurden soziodemografische Merkmale und Unterschiede in der Behandlung mithilfe eines Multinomialen Logit Modells für die Clusterzugehörigkeit analysiert.

Ergebnisse: Die erste Studie konnte zeigen, dass im Bundesland Bremen mehr als die Hälfte der Personen mit einer Alkoholabhängigkeit bereits im Gesundheitssystem dokumentiert war, größtenteils im ambulanten Setting. Suchtspezifische Maßnahmen nahmen jedoch nur 11% in Anspruch. Am häufigsten wurde ein qualifizierter Entzug begonnen (4,7%) oder die ambulante Suchthilfe besucht (4,3%). Eine

Postakutbehandlung wurde seltener in Anspruch genommen (0,8% medikamentöse Rückfallprophylaxe und 3,9% Rehabilitation). Unter jüngeren und männlichen Personen war die Behandlungsquote am höchsten. Im Rahmen der zweiten Studie konnten vier Cluster suchtspezifischer Behandlungspfade basierend auf den in Anspruch genommenen Postakutbehandlungen identifiziert werden. Die Mehrheit nahm nach der stationären Episode keine weiteren suchtspezifischen Maßnahmen in Anspruch (n=276) oder keine Postakutbehandlungen (n=205). Nur die wenigsten begannen eine Postakutbehandlung, wie Rehabilitation (n=26) oder medikamentöse Rückfallprophylaxe (n=11).

Schlussfolgerung: Die vorliegenden Analysen der Routinedaten zeigen, dass die Mehrheit der Personen mit Alkoholabhängigkeit zwar, meist im ambulanten Setting, diagnostiziert werden, jedoch nur eine Minderheit die betrachteten suchtspezifischen Maßnahmen in Anspruch nimmt. Eine Stärkung der primärärztlichen Versorgung von Menschen mit alkoholbezogenen Störungen erscheint angebracht, vor allem in Bezug auf die Weitervermittlung in eine suchtspezifische Behandlung. Die Analyse der Behandlungspfade zeigt eine sehr niedrige Inanspruchnahme von Postakutbehandlungen nach einer stationären Episode (Rehabilitation und/oder medikamentöse Rückfallprophylaxe). Zukünftige Forschung sollten alternative Postakutmaßnahmen im ambulanten Setting und der Selbsthilfe berücksichtigen. Eine generelle Verbesserung der Weitervermittlung in Postakutmaßnahmen nach einem Entzug erscheint angebracht.

4. Abstract (English):

Background: Alcohol consumption causes various diseases through different mechanisms of action, with Germany showing high rates of consumption by international comparison. The prevalence of alcohol dependence alone, according to the criteria of the fourth edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV), was 3.1% in the adult German population between the ages of 18 and 64 in 2018. Despite existing evidence-based procedures regarding the early detection, adequate diagnosis and treatment of alcohol-related disorders, problems often arise in practice. Previous research indicates a large discrepancy between the prevalence of people with alcohol dependence and the rates of addiction specific treatment. In this paper, this treatment gap is examined in more detail with the help of linked routine data from various cost and service providers in the German federal state of Bremen.

Objectives: The overall aim of this dissertation is to describe the care situation of people with alcohol-related disorders especially alcohol dependence to identify any gaps in care and networking problems. The first research objective was to describe the addiction-specific care situation of people with alcohol-related disorders in Bremen in various medical settings and to extrapolate the treatment rate of people with alcohol dependence to the overall population in Bremen using survey data. The second research objective comprised the analysis of individual addiction-specific care pathways. These pathways were clustered into typical pathways and then examined regarding their conformity with current guidelines and characterized with socio-demographic variables.

Methods: The data source was routine data from 2016 and 2017 from people with at least one alcohol-related diagnosis and a residence in Bremen (n=11,205). The data included outpatient and inpatient data from two statutory health insurance companies (AOK

Bremen/Bremerhaven, hkk), alcohol-related rehabilitation treatments of the regional German Pension Insurance Oldenburg-Bremen and outpatient addiction care services of the municipal clinic association Bremen Gesundheit-Nord. Persons using addiction-specific treatment and care services, such as inpatient qualified withdrawal, outpatient pharmacotherapy as relapse prevention, rehabilitation, outpatient addiction care, and with documented outpatient and inpatient diagnoses of alcohol addiction were extrapolated to the total population in Bremen. To calculate the treatment rate, also the number of all people with an alcohol addiction in Bremen was extrapolated to the population of Bremen on an age- and gender-specific basis using data from the 2018 Epidemiological Survey of Substance Abuse. For the second research project, individual care pathways of 518 persons were created, clustered, and analyzed using a state sequence analysis. The care pathways consist of addiction-specific treatments 10 months after an inpatient index episode due to alcohol dependence. Subsequently, socio-demographic characteristics and differences in treatment were analyzed using a multinomial logit model for the cluster assignments.

Results: The first study showed that in the federal state of Bremen, more than half of the people with an alcohol addiction are already documented in the healthcare system, mostly in an outpatient setting, but only 11% make use of addiction-specific treatment and care services. The most common services were qualified withdrawal (4.7%) or outpatient addiction care (4.3%). Post-acute treatment was used less frequently (0.8% pharmacotherapy as relapse prevention and 3.9% rehabilitation). The treatment rate is highest among younger and male persons. The second study identified four clusters based on the post-acute treatment utilized after an inpatient episode of alcohol dependence. The majority of persons used no further addiction-specific treatment after the inpatient

episode (n=276) or no post-acute treatment (n=205). The fewest started a post-acute treatment such as rehabilitation (n=26) or pharmacotherapy as relapse prevention (n=11).

Conclusion: The analyses of the routine data show that, although most people with alcohol dependence have been diagnosed, mostly in an outpatient setting, only a minority make use of the addiction-specific treatments under consideration. Therefore, a strengthening of primary medical care for alcohol treatment seems appropriate, especially regarding referral to addiction-specific treatment. The analysis of care pathways also shows a very low utilization of post-acute treatment after an inpatient episode (rehabilitation and/or pharmacotherapy as relapse prevention). Future research should focus more on alternative post-acute treatments in the outpatient setting and self-help. A general improvement in the referral to post-acute treatment after withdrawal seems appropriate.

5. Paper I

Möckl, J., Lindemann, C., Manthey, J., Schulte, B., Reimer, J., Pogarell, O., & Kraus, L. (2023). Estimating the prevalence of alcohol-related disorders and treatment utilization in Bremen 2016/2017 through routine data linkage. *Frontiers in Psychiatry*, 14. <https://doi.org/10.3389/fpsy.2023.1002526>

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<https://www.frontiersin.org/journals/psychiatry/articles/10.3389/fpsy.2023.1002526/full>

Estimating the prevalence of alcohol-related disorders and treatment utilization in Bremen 2016/2017 through routine data linkage

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Abstract

Background: In Germany, most individuals with alcohol dependence are recognized by the health care system and about 16% per year receive addiction-specific care. This paper aimed to analyze the prevalence and treatment utilization rate of people with alcohol dependence by type of addiction-specific care in the federal state of Bremen using routine and survey data.

Methods: The number of individuals with alcohol dependence was estimated using data from the 2018 Epidemiological Survey of Substance Abuse (ESA). Furthermore, linked routine data of two statutory health insurances (SHIs), the German Pension Insurance (GPI) and the communal hospital group Gesundheit Nord (GeNo), from 2016/2017, were analyzed. Based on SHI data, the administrative prevalence of various alcohol-related diagnoses according to the International Classification of Diseases (ICD-10), in various treatment settings, was extrapolated to the total population of Bremen. Based on all routine data sources, treatment and care services for individuals with alcohol dependence were also extrapolated to Bremen's total population. Care services included outpatient addiction care visits and addiction-specific treatments, (i.e., qualified withdrawal treatment (QWT), outpatient pharmacotherapy as relapse prevention, and rehabilitation treatment).

Results: Of the survey-estimated 15,792 individuals with alcohol dependence in Bremen, 72.6% (n=11,467) had a diagnosis documented with an ICD-10 code for alcohol dependence (F10.2) or withdrawal symptoms (F10.3-F10.4). One in ten individuals with alcohol dependence (n=1,689) used one or more addiction-specific care services during the observation period. Specifically, 4.3% (n=675) received outpatient addiction care, 4.7% (n=736) initiated QWT, 0.8% (n=133) received pharmacotherapy, and 3.9% (n=614) underwent rehabilitation treatment. The share of seeking addiction-specific treatment after diagnosis was highest among younger and male patients.

Conclusion: Although more than half of the individuals with alcohol dependence are documented in the health system, utilization rates of addiction-specific treatments are low. These low utilization rates suggest that there are existing barriers to transferring patients with alcohol dependence into addiction-specific care. Strengthening primary

medical care provision in dealing with alcohol-related disorders and improving networking within the addiction support system appear to be particularly appropriate.

1. Introduction

Germany has one of the highest alcohol consumption rates worldwide, with a per capita consumption of 10.6 liters of pure alcohol for citizens aged 15 and older in 2019 (1, 2). Survey estimates based on the criteria of the Diagnostical and Statistical Manual (DSM-IV), reported a prevalence of 2.8% (1.4 million individuals aged 18–64 years) for alcohol abuse and 3.1% (1.6 million) for alcohol dependence (3). Furthermore, diagnoses for mental and behavioral disorders due to alcohol (F10.X) according to the International Classification of Diseases (ICD-10) were the third most frequent main diagnosis for inpatient hospitalization in men in 2018 (4).

Multiple treatment options for risky, harmful, and dependent alcohol use are discussed in the current German S3 guideline on "Screening, diagnosis, and treatment of alcohol-related disorders". The goal of the guideline is to give recommendations for professionals as well as people affected by alcohol use and was developed by experts based on the available evidence (5). The recommendations include brief interventions as well as medical rehabilitation and other forms of post-acute treatment. Addiction rehabilitation or other post-acute treatment for alcohol dependence should be preceded by either physical detoxification or qualified withdrawal treatment (QWT). QWT is a German-specific term for an extended withdrawal treatment program, during which psychological and somatic concomitant and secondary diseases are considered, and further treatment for the underlying alcohol dependence is initiated using psychosocial interventions (5). Despite existing evidence-based procedures for early detection, adequate diagnosis, and

the treatment of alcohol-related disorders (6) as well as the integration of different care systems (7, 8), the treatment rates for alcohol use disorders as compared to other mental illnesses are among the lowest globally (9, 10). The main reasons for this gap are, among others, structural barriers (8, 11), insufficient qualifications of doctors in alcohol dependence treatment (12), lack of patient motivation (13), and social stigma (14).

An international meta-analysis based on 12-month and lifetime treatment studies estimated the global treatment rate for alcohol use disorders at 17.3%, when informal support services, such as Alcoholics Anonymous, were also considered (9). A study including six European countries that only accounted for treatments offered by health professionals reported a similar treatment rate of 17.6% (15). In Germany in 2012, about one-third of individuals with alcohol dependence were identified by general practitioners, but in the same period, only about 16% were treated in hospital or outpatient addiction care, with 1.8% receiving rehabilitation treatment (16). A recent study also reported undertreatment of individuals with risky alcohol use and severe alcohol use disorder (17).

Previous estimates of treatment rates in Germany were based on diagnoses from aggregated data, such as hospital diagnosis statistics and the diagnosis portal of the Central Institute of Statutory Health Insurance Physicians [Zentralinstitut für die kassenärztliche

Versorgung (Zi)] (16), were derived from per capita consumption (17) or based on survey data (15). In addition, several studies reported differences in diagnoses depending on the setting and the diagnostic instrument (18, 19). A study among primary care patients showed that general practitioners diagnose alcohol dependence more often in male and older patients compared to a standardized, self-administered closed-ended clinical diagnostic questionnaire (18).

The data linkage was conducted within the project “Implementation and evaluation of the guideline on screening, diagnosis and treatment of alcohol-related disorders” (IMPELA) in the federal state of Bremen (20). The aims of the present analysis were,

- 1) To identify individuals with diagnoses of alcohol-related disorders in various treatment settings (administrative prevalence, i.e., prevalence of a specific disorder in a population based on routine data) as well as addiction-specific treatments and care of individuals with alcohol dependence in the routine data,
- 2) Extrapolation of
 - a. the overall prevalence of individuals with alcohol dependence from survey data to the total population of Bremen
 - b. the number of individuals with alcohol dependence and their addiction-specific treatments and care identified in the routine data to the total population of Bremen, and
- 3) to estimate addiction-specific treatment rates for individuals with alcohol dependence in the total population of Bremen.

2. Methods

The methods section is structured based on the different data sets and estimates. First, the study population of the linked routine data is introduced (section “2.1 Study population”), followed by the definition of identified diagnoses and treatments as well as the total populations for each routine dataset separately (sections “2.1.1. Statutory health insurance: Diagnoses,” “2.1.2. Statutory health insurance: Treatments”, “2.1.3. Hospital group Gesundheit Nord: Outpatient addiction care” and “2.1.4. “German Pension Insurance: Rehabilitation treatment”). In section “2.2. Survey data”, the use of the survey

data and in section “2.3. Overall prevalence of alcohol dependence in Bremen” the estimation of the overall prevalence of alcohol dependence in Bremen is described. Finally, the extrapolation of the administrative prevalence together with the treatments in each data set (section “2.4. Administrative prevalence and extrapolation”) as well as the calculation of treatment rates in the total population of Bremen is explained (section “2.5. Treatment rate”). The notation used for the methods defines N/n as the empirical sample and population sizes, whereas $\hat{N}/\hat{n}$ represent the estimated and extrapolated population sizes.

2.1. Study population

In Germany, health insurance is mandatory and consists of public statutory health insurances (SHIs) and private health insurance. Most people (90%) are insured by one of the SHIs, which cover medical treatments approved by the Joint Federal Committee (21). Depending on the type of treatment, different insurances are responsible for the reimbursement of the treatment costs. For example, withdrawal treatment is covered by health insurance funds, whereas rehabilitation treatment in most cases is financed by the German Pension Insurance (Deutsche Rentenversicherung; hereafter: GPI) (5). Eligibility criteria for the coverage of rehabilitation treatment by the GPI are, among others, having paid for the insurance for at least 6 months over the past two years and not being a civil servant. As the treatment goal is reintegration into the labor market, pensioners are not covered by the GPI. In this study three routine data sources were linked, these included data on diagnoses and treatments in public health care (inpatient and outpatient settings), addiction-specific care (outpatient addiction care) and rehabilitation.

To this end, regional master data and service data from 2016 and 2017 from (1) two SHIs in Bremen (AOK Bremen/Bremerhaven and hkk), (2) on outpatient addiction care services data of the communal hospital group Gesundheit Nord - Bremen Hospital Group (GeNo) in Bremen, and (3) the regional GPI (Deutsche Rentenversicherung Oldenburg-Bremen) were linked on an individual level (20). The individuals included in the study population were 16 years or older in 2016 and 2017, were living in Bremen or Bremerhaven; and had a main or secondary diagnosis of mental as well as behavioral disorders due to alcohol (F10.x) or had another fully alcohol-attributable diagnosis according to documentation of one of the three data sources mentioned above. A detailed list of all relevant diagnoses, as well as a description of the study population and the known total populations, are presented in Table 1 and in the Supplementary Figure 1 and Supplementary Table 1. The routine data was analyzed using R version 4.0.3 (22).

-Table 1-

2.1.1. Statutory health insurance: Diagnoses

The total population of the two SHIs (AOK Bremen/Bremerhaven and hkk) consisted of insured individuals 16 years and older, living in Bremen, with at least one day of insurance coverage in 2016 (N = 302,311) or 2017 (N = 307,245). The population from the year 2017 was used to calculate prevalence rates of diagnoses for both years, 2016 and 2017, combined.

The ICD-10 diagnoses from services in the inpatient and outpatient setting as documented in data from the SHIs were used. All alcohol related diagnoses are presented in the Supplementary Table 1. The diagnoses E24.4, G31.2, G62.1, G72.1, I42.6, K29.2, K70.X, K86.0, O35.4, P04.3, and Q86.0 were considered other alcohol-attributable diagnoses. For a diagnosis to be counted, it had to be present at least once during the observation

period. Only confirmed outpatient diagnoses or inpatient main or secondary diagnoses were used. For the extrapolation and the calculation of treatment rates, alcohol dependence was assumed if either an outpatient or an inpatient diagnosis of a dependence syndrome (F10.2) or a withdrawal state (F10.3 or F10.4) was coded. This approach was chosen to include individuals with only a singular diagnosis of a withdrawal state (F10.3 or F10.4). If both an alcohol dependence was assumed and a diagnosis of ‘harmful use’ (F10.1) was present for an individual, only alcohol dependence was considered for the administrative prevalence.

2.1.2 Statutory health insurance: Treatments

In addition to documented diagnoses in inpatient and outpatient settings, addiction-specific treatments like QWT and drug relapse prevention were also documented. QWT is a German-specific term for an extended withdrawal treatment program (generally 3 weeks) including psychosocial interventions (5). During somatic withdrawal treatment, the main focus is to control and reduce alcohol withdrawal symptoms as well as any neurological or physical symptoms (e.g., epileptic seizures or delirium tremens). In QWT, detoxification is only one component. Additionally, psychological and somatic concomitant and secondary diseases are considered and further treatment for the underlying alcohol dependence is initiated. Motivation to seek further help and more specific treatments (e.g., addiction rehabilitation) should be increased and contact should be established with the regional support system (e.g., psychotherapy, self-help) (23). The following are recommended: motivational discussion techniques; integration of family members; elements from social competence training, relaxation therapy, occupational therapy, and physiotherapy (24).

Inpatient QWT was detected using the diagnosis and the assigned Surgery- and Procedure-Code [“Operationen- und Prozeduren-Schlüssel” (OPS) code]. This official code encompasses all surgeries and medical procedures and is documented, among other reasons, for remuneration by the health insurance funds. Based on the codes, QWTs in both somatic (OPS code 8-985) and psychiatric wards (OPS code 9-647) were considered. However, these codes are not coded for specific substances. To identify a QWT for alcohol dependence, an OPS code in combination with an F10.2, F10.3, or F10.4 main diagnosis for an inpatient episode with a duration not shorter than the QWT had to be present in the observation period 2016/2017. This procedure was necessary due to partially lacking links between the OPS codes and individual inpatient episodes as well as partially missing dates for the OPS codes.

No OPS code is provided for outpatient withdrawal but, based on the pharmaceutical registration numbers [Pharmazentralnummer (PZN)], medicinal drug relapse prevention was detected. The pharmaceutical registration number and the corresponding anatomical-therapeutic-chemical classification (ATC) of the drugs prescribed and invoiced via the SHIs are indicative of drug relapse prevention as pharmacotherapeutic post-acute treatment in the outpatient setting (ATC code: N07BB). The assignment of the pharmaceutical registration numbers to the ATC codes was carried out based on the classification data in the drug master file of the German Drug Index of the Scientific Institute of the AOK [Wissenschaftliches Institut der AOK (WIdO)].

2.1.3. Hospital group Gesundheit Nord: Outpatient addiction care

It was assumed that the data on outpatient addiction care from the GeNo represent a complete data set, as these services are free of charge and not offered based on an individual refunding system for particular services. All individuals with a documented

alcohol dependence receiving outpatient addiction care from the GeNo at least once in 2016 or 2017 were included.

2.1.4. German Pension Insurance: Rehabilitation treatment

The GPI data included individuals that at least initiated full-day outpatient or inpatient alcohol-related rehabilitation in 2016/2017 funded by the regional GPI (Deutsche Rentenversicherung Oldenburg-Bremen). As not all rehabilitation treatment is covered by the regional GPI, the total number of addiction rehabilitation cases is unknown. Besides the regional GPI there are also the federal GPI (Deutsche Rentenversicherung Bund) and GPI Knappschaft-Bahn-See (Deutsche Rentenversicherung Knappschaft-Bahn-See), which can be responsible for funding rehabilitation treatment in Bremen. Which GPI is responsible is decided for each individual by a distribution key when first being ensured in the GPI, so that 45% of insured individuals are ensured federally and 55% in one of the 16 regional GPIs depending on the place of residence. If you are employed in specific work areas, like mining sectors, German railway and maritime shipping the GPI Knappschaft-Bahn-See is responsible. Federal GPI and GPI Knappschaft-Bahn-See together funded around 34% of the approved rehabilitation services in the state of Bremen in 2016/2017 and the regional GPI 66% respectively (Deutsche Rentenversicherung Bund, unpublished data, 2024). Furthermore, according to the documentation of the Fachverband Sucht e.V. for 2017, the GPI (federal, regional and Knappschaft-Bahn-See) funded inpatient rehabilitation treatment in specialized clinics for alcohol and drug dependence for about 84.7% of all individuals receiving it in Germany (25). It was therefore assumed that 55.9% ($84.7\% \times 66.0\%$) of all rehabilitation services were part of the GPI data used for the extrapolation.

2.2. Survey data

For the overall prevalence of alcohol dependence in the population of Bremen the estimate for the whole of Germany from the 2018 Epidemiological Survey of Substance Abuse (ESA) was used. The ESA is a two-stage random sampling of the German-speaking 18- to 64-year-old population living in private households in Germany. The total sample was comprised of 9,287 individuals. The survey was conducted through written or online questionnaires, or telephone interviews. Alcohol dependence was determined using DSM-IV criteria (26). Details on the survey design and the methodology have been published elsewhere (3). The survey data was analyzed using Stata 15.1 (27).

2.3. Overall prevalence of alcohol dependence in Bremen

The ESA estimate of alcohol dependence was stratified by gender (male and female) and age groups (18-34 years and 35-64 years) to account for Bremen's unique age and gender distribution. For the population over 65 years, a logit model was calculated controlling for age (continuous), gender (male/female), education (high/medium/low according to International Standard Classification of Education ISCED (28)), marital status (married vs. single/divorced/widowed), and region (west/east). The probability of alcohol dependence was calculated for the group of individuals aged 65 to 100 years and was used as the mean prevalence for persons over 64 years (16). For the age group of 16- to 17-year-olds, the prevalence of 18- to 34-year-olds was assumed.

2.4. Administrative prevalence and extrapolation

First, the administrative prevalence of alcohol-related diagnoses in the routine data was calculated using the diagnoses and total population as explained in “2.1.1. Statutory health insurance: Diagnoses”. The administrative prevalence describes the prevalence of a specific disorder in a population calculated based on routine data. Since the data sources

do not share the same total population and health insurance funds record all diagnoses in inpatient and outpatient settings, the administrative prevalence was calculated based only on the population of the SHIs.

Second, extrapolations to the total population of Bremen were carried out. The overall prevalence from the ESA survey data was extrapolated to the total population of Bremen, stratified by age and gender. Population figures for Bremen in the year 2017 were taken from the Federal Statistical Office (29). As the three routine data sources cover different populations, the extrapolation of diagnoses and treatments to the federal state of Bremen was carried out for each data source (SHI, GeNo, and GPI) separately. The total population of the SHIs is shown in Table 1. For the extrapolation, the administrative prevalence, stratified by four age groups (16-24, 25-49, 50-64, and 65+ years) and by gender, was multiplied by the total population size of Bremen in 2017. When extrapolating overlapping data (hereafter: overlaps), the age and gender-stratified population not covered by the SHI data was used. This population was established by removing the total population of the SHIs' data from the total population of Bremen. An equal distribution of diagnoses, treatments, and overlaps with the other data sets was assumed for individuals who were not included in the SHIs' total population. These would be individuals with private insurance, another SHI, or no health insurance.

Assuming that 55.9% of all rehabilitation treatments were funded by the GPI, the extrapolated prevalence for Bremen was estimated accordingly at 614 (i.e., $343/0.559$). As the gender and age distribution for the total population of persons who have undergone addiction rehabilitation treatment is unknown, the extrapolation was not stratified. The data on outpatient addiction care from the GeNo represent a complete data set, so no extrapolation had to be made.

To take overlaps into account, it was assumed that the relative shares of the overlaps of persons not included in the study population correspond to those of the study population (see Figure 1). The estimated overlaps in the data sources of the unobserved populations (not in the SHI data and not in the GPI data) were calculated by multiplying the relative shares of overlaps of the observed data sources within their respective total populations by the estimated total population of each unobserved data source. Only overlaps of data from individuals covered by the observed SHIs with individuals not covered by the SHIs were stratified by age and gender in the extrapolations, as the age and gender distributions for the total population of individuals receiving rehabilitation treatment were unknown. To account for multiple counts, the overlaps were then subtracted from the sum of the extrapolations of the individual data sources again, either once (if two data sets overlapped) or twice (if three data sets overlapped).

2.5. Treatment rate

Specific treatment rates were estimated using the overall number of individuals with alcohol dependence in Bremen, the extrapolated administrative prevalence, and addiction-specific treatments carried out. Specific treatment rates were determined for outpatient addiction care, inpatient QWT, outpatient treatments with drug relapse prevention, and rehabilitation. No confidence intervals were calculated for the extrapolation of treatments/care and diagnoses from the routine data. The 95% confidence intervals shown were calculated using the respective confidence interval limits of the overall prevalence in Bremen as the denominator for the rate.

3. Results

3.1. Administrative prevalence

The administrative prevalence of mental and behavioral disorders caused by alcohol (F10) in 2016/2017 among individuals insured by the SHIs is 2.9%, with harmful use (F10.1) at 0.8% and alcohol dependence (including withdrawal syndrome) at 1.9%. Except for ‘acute intoxication’ and ‘withdrawal syndrome’, diagnoses were more often documented in outpatient than inpatient settings. Thus, the administrative prevalence of alcohol dependence (including withdrawal syndrome) in the outpatient setting is 1.6% as compared to 0.6% in the inpatient setting. The administrative prevalence of other alcohol-attributable diagnoses is 0.7% (Table 2).

-Table 2-

3.2. Extrapolation

Figure 1 shows the number of individuals with a documented diagnosis of alcohol dependence in the linked routine data as well as the results of the extrapolation of the overall prevalence from the ESA survey data and of each routine data set for the total population (i.e., the administrative prevalence of the SHI and the rehabilitation data). Based on survey data, the overall number of individuals with alcohol dependence in the Federal State of Bremen in 2016/2017 ($\hat{N}_{\text{Bremen}}$) was estimated at 15,792 [95% confidence interval (CI): 12,163 - 20,120] individuals aged 16 years or older. For details see eTable 2. Based on the individuals with alcohol dependence documented in the SHI data ($n_{\text{SHI}}=5,694$), extrapolated to the total population (Supplementary Table 3), we can assume an additional 5,348 individuals with alcohol dependence are documented with other health insurances or have no insurances ($\hat{n}_{\text{Non-SHI}}$). In addition, 675 individuals with

alcohol dependence used outpatient addiction care services (n_{GeNo}). When extrapolated to the total population, we estimate 614 individuals made use of addiction rehabilitation ($n_{\text{GPI}}=343$; $\hat{n}_{\text{Non-GPI}}=271$). The results of the extrapolation of the overlaps between the data sources to adjust for multiple counts is presented in Supplementary Figure 2 and the extrapolations are shown in Supplementary Tables 4, 5. The number of individuals with alcohol dependence documented in the health system was estimated at 11,467 ($n_{\text{SHI}} + \hat{n}_{\text{Non-SHI}} + n_{\text{GeNo}} + n_{\text{GPI}} + \hat{n}_{\text{Non-GPI}} - \text{Overlaps}$). All extrapolations are shown in detail in the Supplementary Figure 2 and Supplementary Tables 2–5.

-Figure 1-

3.3. Addiction-specific treatments and care

The extrapolated general and specific treatment rates for individuals with alcohol dependence in the total population are shown in Figure 2. Overall, 72.6% [95% CI: 57.0%-94.3%] of the estimated total number of individuals with alcohol dependence and a corresponding ICD-10 diagnosis were registered in the health care system. For 61.9%, no addiction-specific treatments were identified. The share of individuals with at least one of the treatments or care measures considered here was 10.7% [95% CI: 8.4%-13.9%]. Based on the estimate of the overall prevalence and the extrapolation of the routine data, inpatient QWT was initiated by 4.7% [95% CI: 3.7%-6.1%], whereas 4.3% [95% CI: 3.4%-5.5%] used outpatient addiction care services, 3.9% [95% CI: 3.1%-5.0%] used addiction rehabilitation, and 0.8% [95% CI: 0.7%-1.1%] used outpatient drug-based relapse prevention interventions (i.e. anti-craving medications).

-Figure 2-

Figure 3 shows the proportion of individuals with a diagnosed alcohol dependence in the SHIs' population who used specific treatment/care, stratified by age and gender with a diagnosed alcohol dependence. Overall, the shares of individuals in treatment were higher in younger than older individuals. Gender differences were observed in QWT, outpatient addiction care, and rehabilitation treatment. Compared to young women up to age 24, young men with alcohol dependence more often started QWT (19.6% vs. 8.0%) or attended outpatient addiction care (10.9% vs. 0.0%). For rehabilitation treatment (3.6% vs. 0.0%) and outpatient addiction care (7.2% vs. 1.9%), gender differences were also present in individuals aged 25 to 49 years.

-Figure 3-

Figure 4 shows the prevalence of F10 disorders and the diagnosis setting for individuals in the SHIs' population with a diagnosis but without identified treatment/care. Most of these individuals received an outpatient diagnosis for alcohol dependence (88.8%) and significantly fewer receive an inpatient diagnosis (27.8%) mainly as a secondary diagnosis. Comparable to the general administrative prevalence of F10 disorders only diagnoses of 'acute intoxication' (F10.0) and 'withdrawal state' (F10.3 and F10.4) were documented more often in inpatient than in outpatient settings.

-Figure 4-

4. Discussion

The number of individuals with alcohol dependence in the Federal State of Bremen in 2017 was estimated at 15,792 [95%-CI: 12,163-20,120]. Of these, 11,467 persons (73%

[95% CI: 57%-94%]) received a corresponding ICD diagnosis in medical health care or outpatient addiction care in 2016/2017 and 11% [95%-CI: 8%-14%] made use of addiction-specific care measures according to our estimates. Despite limited comparability due to a longer observation period and different data sources, the treatment rates largely correspond to the Germany-wide estimate from 2012, although a higher diagnosis rate seems to be present in Bremen (16).

Previous routine data analyses showed high prevalence rates of mental disorders in outpatient care, especially in general medicine, but a relatively low proportion in psychiatric or psychotherapeutic care (30). Survey data confirm general practitioners as the most frequently visited contact person and the first point of access to the health care system for alcohol-related problems (31). Consistently, most diagnoses in Bremen were made on an outpatient basis. This emphasizes the importance of primary health care for the identification and further treatment of alcohol dependence, especially as individuals who do not make use of further addiction-specific care very often only receive an outpatient diagnosis. Whether any treatments took place in this setting in addition to the pharmacotherapy shown and, if so, which ones, could not be determined. In general, an increase in addiction-specific treatment rates seems to be indicated due to possible positive effects on per capita alcohol consumption (32), mortality (33, 34), and hospitalization rates (35).

However, the figures reported here do not reflect the actual treatment gap, as not all individuals with alcohol dependence are actually in need of addiction-specific treatment. A study from the Netherlands estimated the treatment gap for individuals with alcohol use disorder according to the DSM-V to be significantly lower if only individuals with persistent alcohol use disorders (over 4 years) were considered (24.5% instead of 90.0%) (36). Treatment gap estimates need to account for remissions without formal help, which

depend on the time interval and the definition of both treatment and remission (37, 38). Previous estimates of natural remissions in individuals with alcohol dependence are about three quarters of cases in Northern America (37, 39) and 66% in Germany (40).

The overall low utilization of addiction-specific treatments and simultaneously high diagnosis rate of alcohol dependence indicate that the care of patients after diagnosis is challenging and tedious. Previous research identified various treatment provision barriers for general practitioners in Germany. For example, referral to the addiction support system is limited among other reasons due to a lack of networking (8). The often uncoordinated access to various care systems sometimes results in a lack of exchange of relevant information (41). A lack of health policy and financial support, as well as a lack of time, are often reported as reasons for the low use of brief interventions and screenings (8, 11, 42, 43). Further barriers to treatment provision include a general lack of private practice physicians that are qualified to adequately treat patients with alcohol dependence as well as physicians' negative expectations of patient adherence (8, 11, 12, 43). On the patient side, a lack of self-awareness, the desire to keep drinking, and the fear of stigmatization or shame were shown to be the most important reasons against seeking further treatment (13, 43). Compared to other mental illnesses, the stigmatization of alcohol use disorders is particularly pronounced (14). Impacts thereof can be seen in the late use of cessation treatments, as, on average, it had been almost 16 years since the onset of symptoms for patients in addiction-specific care (44).

In this study, the proportion of diagnosed individuals with addiction-specific care was lower in older age groups. Although fewer individuals were diagnosed in absolute terms in the younger age groups, the treatment rate was higher among them. An inverted U-shaped relationship with the peak treatment rate occurring in middle age (between 35 and 54 years), as in the USA, is not evident in the already diagnosed population. Rather there

is a linear decrease (45). The higher rate of care among 16 to 24-year-olds may be due to covariates such as comorbidities and risky drinking habits, as well as a presumably lower rate of diagnosis among younger individuals with alcohol dependence. In general, older patients with comorbidities are more likely to be diagnosed (19) and treatment motivation increases with the severity of negative consequences (45, 46).

The lower treatment rates among women found in our study are in line with the current literature (47-49). A literature review identified a lower perceived need for treatment in women compared to men as well as more guilt and shame, less social support, and different socioeconomic characteristics and comorbidities (49). Furthermore, women tend to seek care more often in non-substance abuse-specific settings (47). These important covariables were not controlled for in our study, making a gender specific analysis difficult. In this study, differences in treatment utilization were apparent, but not for all treatments. Differences in QWT were only seen in the youngest age group and could be due to the low absolute number of women in this age group in the study population. The lower utilization rate of outpatient addiction care and rehabilitation treatment for women as compared to men may also indicate that women utilize treatment approaches other than addiction care and rehabilitation.

4.1. Strengths and limitations

The strength of the routine data used here lies in the fact that the utilization of individual addiction-specific measures can be recorded validly without typical survey biases such as memory errors, non-response, or social desirability bias. In contrast to the use of aggregated data, the data linkage procedure made it possible to assign the respective services used to each individual. Generally, the highly fragmented care system for

individuals with alcohol use disorders with many potential payers complicates a complete view of this population in Germany.

The available routine data is limited to medical care and extrapolations are based on the assumption of an equal distribution of certain characteristics across data sets from different payers. The assumption of equal proportions of QWT in individuals with statutory versus private and non-statutory health insurance is only valid to a limited extent. Not all private insurances cover the costs of QWT, and those who are not insured are unlikely to always be able to finance it. In addition, QWT was coded based on the start of treatment, and thus our data represent initiated but not necessarily completed courses of treatment. Likewise, outpatient withdrawal treatment, which is only possible when patients meet certain treatment criteria, was not considered. The implementation of physical detoxification could not be presented as a specific treatment rate, as this is not specifically documented (e.g., by means of an OPS code). However, if inpatient main diagnoses of alcohol dependence were considered in calculating the general treatment rate, not only qualified withdrawal but also inpatient physical detoxification would be included (treatment rate with and without inpatient main diagnosis as a treatment: 16.3% vs 10.7%). Pharmacotherapy was considered independently of previous measures, because it seems reasonable to assume that treatment is carried out after withdrawal or rehabilitation treatment and thus as post-acute treatment.

The routine data analyzed here mainly show the reimbursed services and, to a limited extent, the periods of illness. This should be taken into consideration, especially given that alcohol dependence is a chronic disease. It should be emphasized that the measures reflected by the available data are not exhaustive. Brief interventions, medical consultations, or outpatient psychotherapeutic measures were not documented in the

available routine data. It was also not possible to consider self-help and counseling services outside the GeNo due to a lack of available documentation.

A prevalence estimate from a general population survey was used to estimate the number of individuals with alcohol dependence in Bremen. The influence of non-response and groups not included in the study, such as prison inmates and homeless people with a higher risk of alcohol dependence, indicate this is a conservative estimate (3). In addition, the use of the estimated Germany-wide prevalence of alcohol dependence as a proxy for the federal state of Bremen does not consider regional differences. The state of Bremen is located in Northwest Germany and, compared to the German average, Bremen has a higher share of migrants (19% vs 13%) (50), is younger (mean age 43,7 vs 44,6) (51), has the highest share of people near poverty (52), and a higher rate of alcohol-attributable mortality (53, 54). Thus, the overall prevalence of alcohol dependence in Bremen is likely underestimated. Treatment and diagnosis rates, therefore, tend to be overestimated.

Differences between individuals diagnosed by primary health care, using parts of the routine data, and utilizing clinical diagnostic interviews, which were used for the estimation of the total population of individuals with alcohol dependence in Germany, are irrelevant for an estimation of the total population. In a Europe-wide study, general practitioners were more likely to diagnose alcohol dependence in older, male persons with more somatic comorbidities in comparison to standardized diagnostic interviews, but a similar number of diagnoses were made using either diagnostic method (19).

5. Conclusion

The analyzed secondary data shows a clear picture of the care and treatment that individuals with alcohol dependence receive. The results point to a discrepancy between

outpatient diagnosis and the utilization of addiction-specific treatment services. More than half of the individuals with alcohol dependence in Bremen were identified in the health care system, but only a minority of them received addiction-specific treatment. Despite a broad consensus and an existing guideline in Germany with measures for a stronger networking between care sectors and seamless access to addiction-specific measures, the barriers are still considerable in practice. Ideally, addiction-specific measures should be initiated at an early stage so that treatment is not forced only by existing negative consequences. This also requires a greater self-awareness among this population to increase the patients' motivation for receiving treatment. Improving how primary care providers treat individuals with alcohol-related disorders, as well as increasing networking within the addiction care system, seems particularly appropriate.

List of non-standard abbreviations

SHI	Statutory health insurance
GeNo	Gesundheit Nord - Bremen Hospital Group
GPI	German Pension Insurance
QWT	Qualified withdrawal treatment

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Conflicts of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Supplementary material

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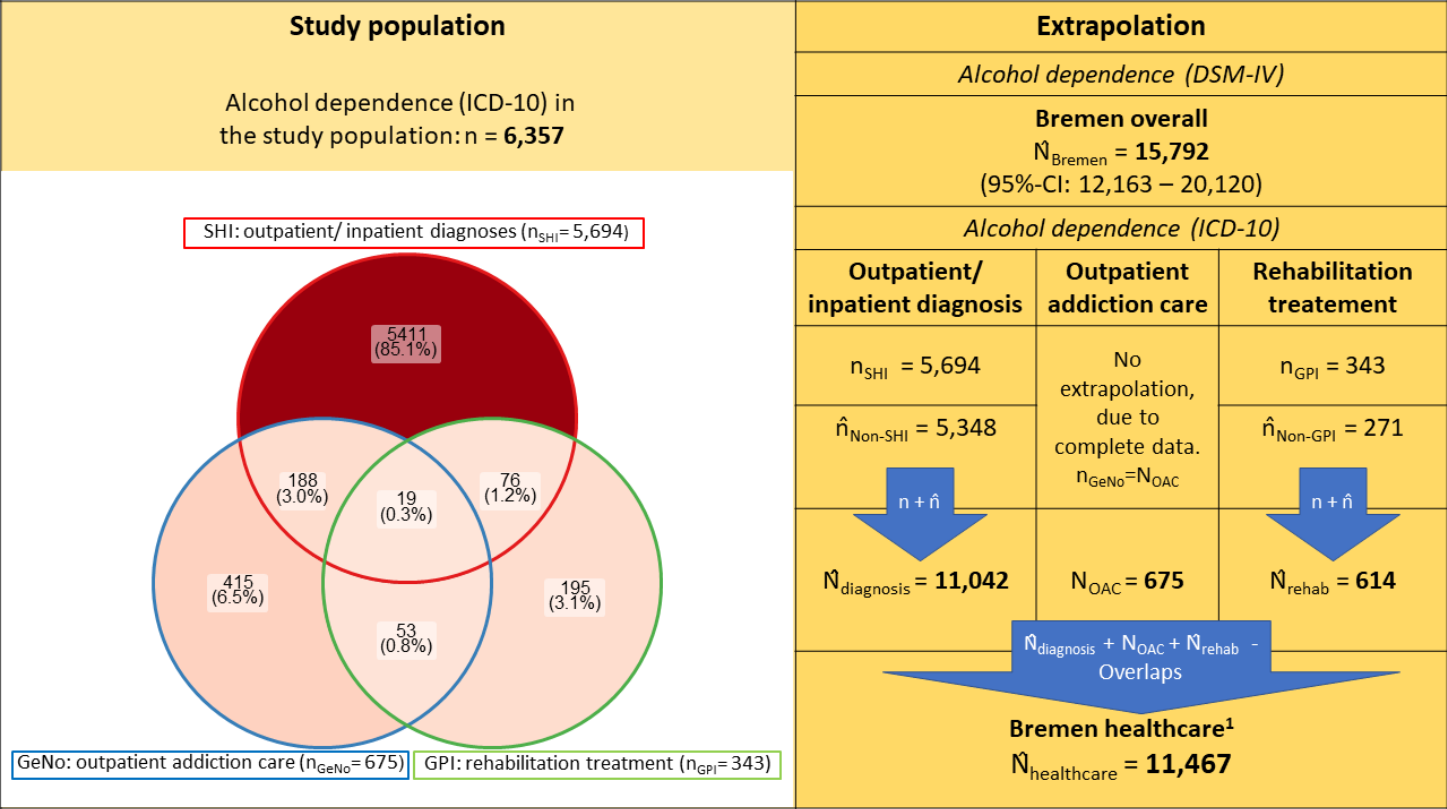
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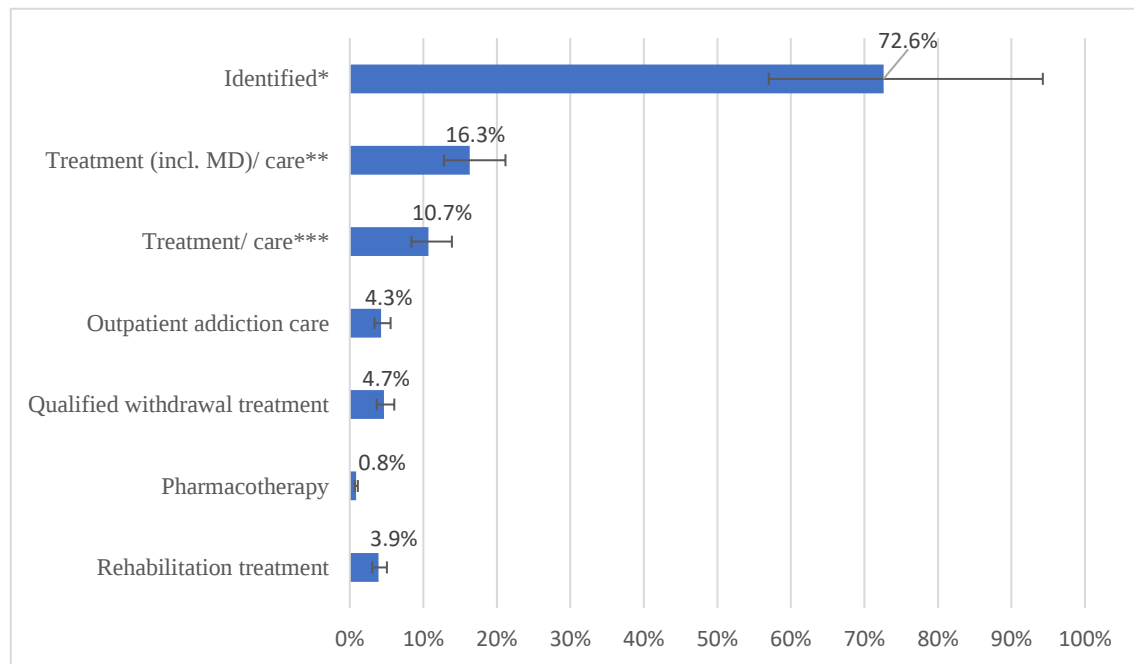
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Figure 1: Prevalence of alcohol dependence in study population and extrapolated to total population of Bremen



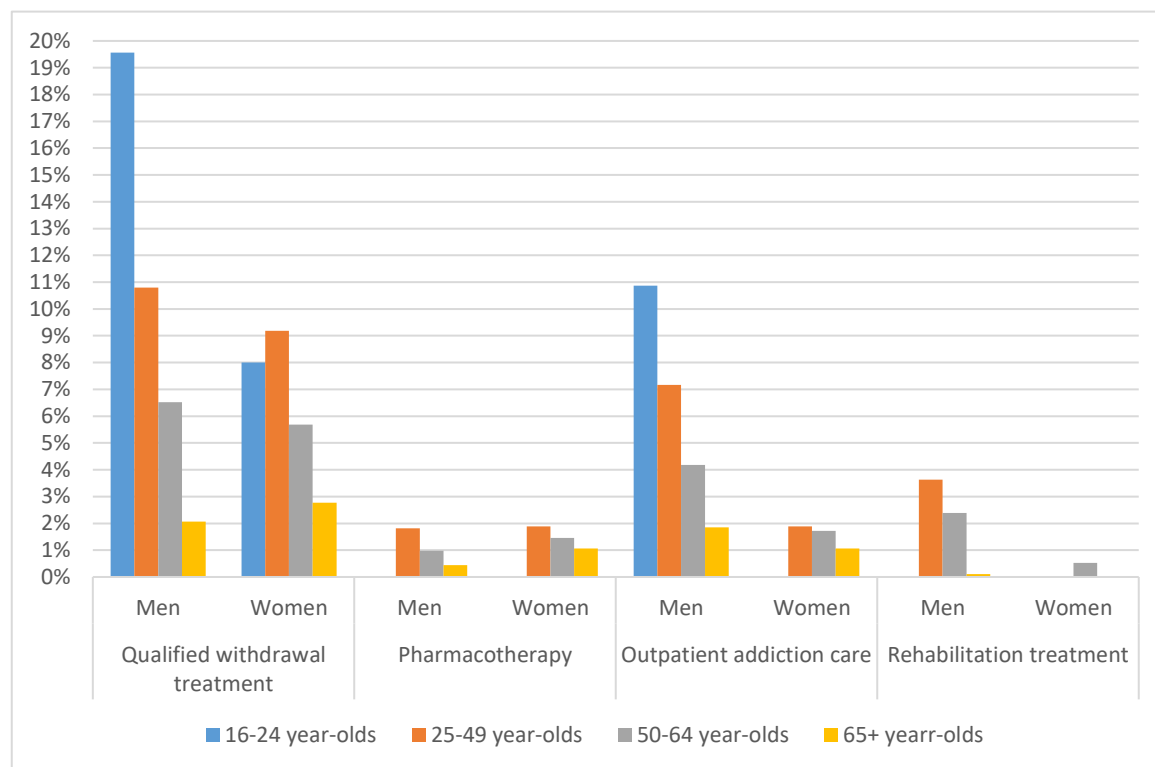
Notes: n/N denote each the empirical sample and population sizes, whereas $\hat{n}/\hat{N}$ represent the estimated and extrapolated population sizes. The study population is represented as a non-proportional Venn diagram using the R package "ggVennDiagram". For detailed extrapolations, see Supplementary Tables 2–5 and Supplementary Figure 2;; SHI: Statutory health insurance; GeNo: Gesundheit Nord - Bremen Hospital Group; GPI: German Pension Insurance ¹ Estimated individuals recognized with a diagnosis of alcohol dependence (ICD-10) or addiction specific treatment/care in the healthcare system of Bremen

Figure 2: Diagnoses and specific treatment/care rates of persons with alcohol dependence in Bremen 2016/2017.



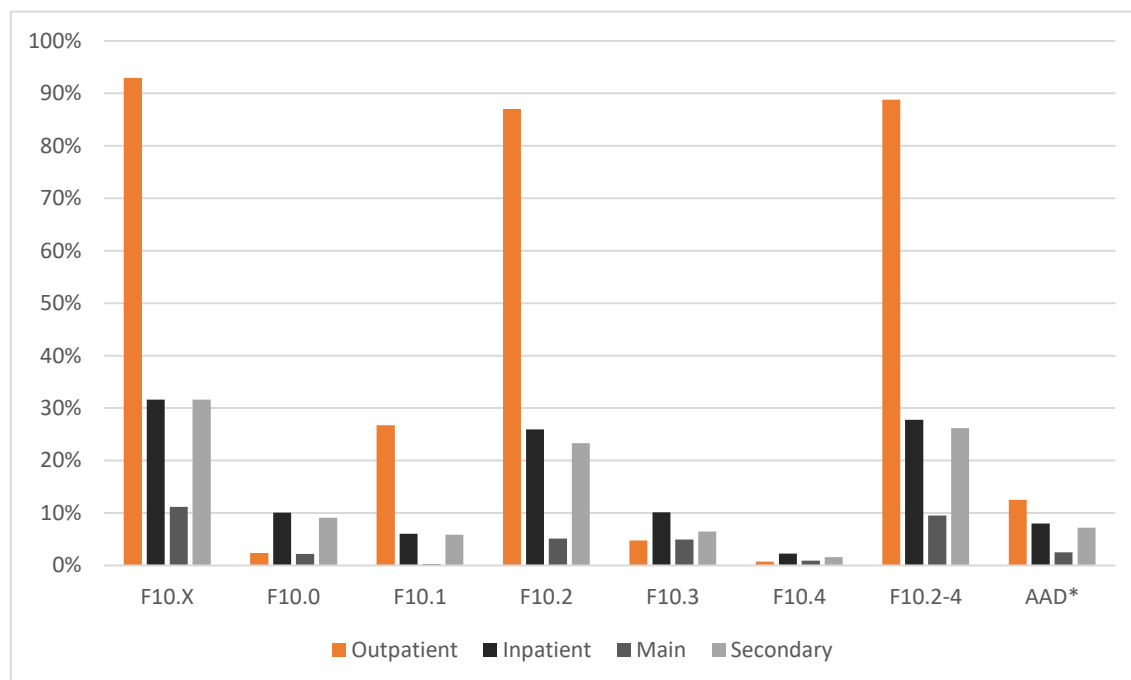
Notes: Proportions of extrapolated treatments in the estimate for persons with alcohol dependence in the total population of Bremen $\hat{N}_{\text{Bremen}}$ 15,792 [12,163 - 20,120]: * Identified* includes individuals with at least one outpatient or inpatient diagnosis, utilization of outpatient addiction care or addiction rehabilitation ** Treatment (incl. MD)/ care include here: Inpatient episode with main diagnosis F10.2-4, qualified withdrawal treatment, pharmacotherapy, outpatient addiction care, and rehabilitation treatment *** Treatment/ care include here: qualified withdrawal treatment, pharmacotherapy, outpatient addiction care, and rehabilitation treatment.

Figure 3: Specific treatment/care rates of the statutory health insurances' (SHIs) population with an alcohol dependence syndrome diagnosis (F10.2-4) in 2016/2017, stratified by age and gender.



Notes: SHIs' population with F10.2-4 diagnosis in 2016/2017: 16-24-year-olds ($n_M = 46$; $n_W = 25$); 25-49-year-olds ($n_M = 1,269$; $n_W = 370$); 50-64-year-olds ($n_M = 1,841$; $n_W = 756$); over 64-year-olds ($n_M = 917$; $n_W = 470$).

Figure 4: Diagnosis and diagnosis setting of persons with an alcohol dependence syndrome diagnosis (F10.2-4) but without addiction-specific care in the statutory health insurances' (SHIs) population in 2016/2017.



Notes: Outpatient (confirmed diagnosis only), inpatient (main or secondary diagnosis); the proportion of individuals in SHIs' population with a diagnosis of F10.2-4 but without addiction-specific care: n=5,097. * AAD: Alcohol-attributable diagnoses include E24.4, G31.2, G62.1, G72.1, I42.6, K29.2, K70.X, K86.0, O35.4, P04.3 and Q86.0

Table 1: Overview of study and total population.

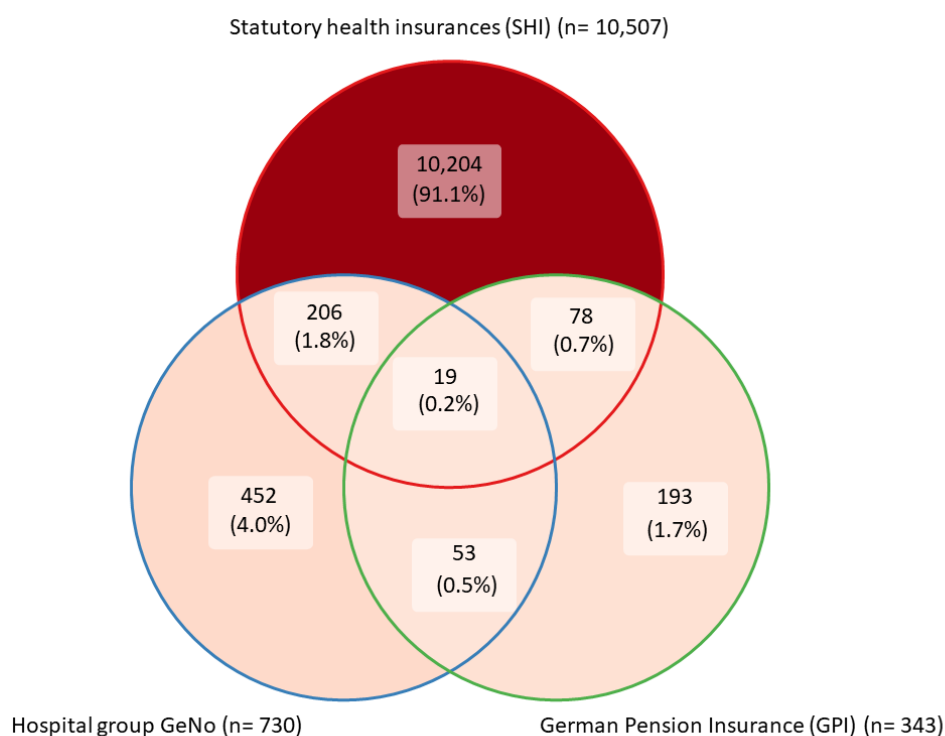
	Total	Gender		Age			
		Men	Women	16 - 24	25 - 49	50 - 64	65+
	N	n (Rows-%)					
Total population	584,516	286,816	297,700	71,815	227,428	141,522	143,751
Bremen 2017		(49.1)	(50.9)	(12.2)	(38.9)	(24.2)	(24.6)
Total population	307,245	147,025	160,219	37,706	117,347	72,263	79,929
SHI ¹ 2017		(47.9)	(52.1)	(12.3)	(38.2)	(23.5)	(26.0)
Study population ²	11,205	7,726	3,479	577	3,272	4,448	2,908
2016/2017		(69.0)	(31.0)	(5.1)	(29.2)	(39.7)	(26.0)
Statutory health	10,507	7,275	3,232	562	2,928	4,151	2,866
insurances (SHI)		(69.2)	(30.8)	(5.3)	(27.9)	(39.5)	(27.3)
Hospital group	730	503	227	19	345	302	64
GeNo		(68.9)	(31.1)	(2.6)	(47.3)	(41.4)	(8.8)
German Pension	343	277	66	< 4	183	157	< 4
Insurance (GPI)		(80.8)	(19.2)		(53.4)	(45.7)	

Notes: ¹ Including people insured in one of two statutory health insurances (SHI) (AOK and hkk) with at least one day of insurance in 2017. ² Study population based on routine data sources (SHI, GeNo, GPI) listed below.

Table 2: Administrative prevalence (%), stratified by diagnosis' setting and type, in the statutory health insurances' population in Bremen in 2016/2017

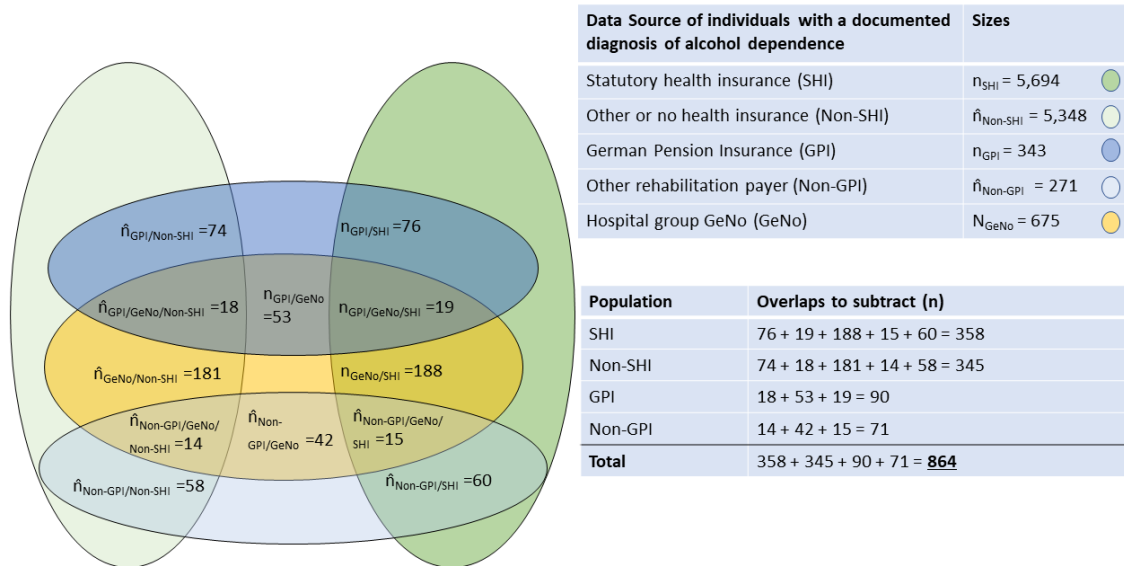
ICD-10-Code	Name of the diagnosis chapter	Setting and type of diagnoses				
		Total	Outpatient confirmed	Inpatient Total	Inpatient Main	Inpatient Secondary
F10.X	Mental and behavioral disorders due to the use of alcohol	2.9	2.6	1.0	0.5	1.0
F10.0	Acute intoxication	0.5	0.1	0.5	0.1	0.4
F10.1	Harmful use	0.8	0.7	0.1	0.0	0.1
F10.2	Dependence syndrome	1.8	1.6	0.6	0.2	0.5
F10.3	Withdrawal state	0.4	0.1	0.3	0.2	0.2
F10.4	Withdrawal state with delirium	0.1	0.0	0.1	0.0	0.0
F10.2-4	Dependence and/or withdrawal syndrome	1.9	1.6	0.6	0.3	0.6
AAD*	Alcohol-attributable diagnoses	0.7	0.5	0.2	0.1	0.2

Notes: Inpatient total includes main or secondary diagnoses. The population includes people insured by two statutory public health insurances (AOK and hkk) with at least one day of insurance in 2017: n= 307,245. * AAD: Alcohol-attributable diagnoses include E24.4, G31.2, G62.1, G72.1, I42.6, K29.2, K70.X, K86.0, O35.4, P04.3 and Q86.0

Supplementary Material**e-Figure 1:** Venn diagram of the study population after data linkage.

Notes: Individuals who received at least one alcohol-related diagnosis (statutory health insurance (SHI) (AOK and hkk)) and/or attended outpatient addiction care at the Gesundheit Nord - Bremen Hospital Group (GeNo) and/or started an addiction rehabilitation treatment financed by the German Pension Insurance (GPI) in the state of Bremen in 2016/2017. Displayed as a non-proportional Venn diagram using the R package 'ggVennDiagram'.

e-Figure 2: Extrapolation to the unobserved populations (not insured in the analyzed statutory health insurances or without health insurance (Non-SHI) and not funded by the German Pension Insurance (Non-GPI)) based on overlaps in the study population with a documented diagnosis of alcohol dependence.



Notes: N/n denotes the empirical sample and population sizes, whereas $\hat{n}$ represents the estimated and extrapolated population sizes. SHI: Statutory health insurance; GeNo: Gesundheit Nord - Bremen Hospital Group; GPI: German Pension Insurance; For detailed extrapolations see eTable3 and eTable4.

eTable 1: Overview of alcohol-related ICD-10 diagnoses

ICD -10 Codes	Meaning according to ICD-10
F10	Mental and behavioral disorders due to use of alcohol (includes F10.1 to F10.9)
F10.0	Acute intoxication
F10.1	Harmful use
F10.2	Dependence syndrome
F10.3	Withdrawal state
F10.4	Withdrawal state with delirium
F10.5	Psychotic disorder
F10.6	Amnesic syndrome
F10.7	Residual and late-onset psychotic disorder
F10.8	Other mental and behavioural disorders
F10.9	Unspecified mental and behavioural disorder
E24.4	Alcohol-induced pseudo-Cushing syndrome
E52	Niacin deficiency [pellagra]
G31.2	Degeneration of nervous system due to alcohol
G62.1	Alcoholic polyneuropathy
G72.1	Alcoholic myopathy
I42.6	Alcoholic cardiomyopathy
K29.2	Alcoholic gastritis
K70.-	Alcoholic liver disease
K85.2	Alcohol-induced acute pancreatitis
K86.0	Alcohol-induced chronic pancreatitis
O35.4	Maternal care for (suspected) damage to fetus from alcohol
P04.3	Fetus and newborn affected by maternal use of alcohol
Q86.0	Fetal alcohol syndrome (dysmorphic)
R78.0	Finding of alcohol in blood
T51.-	Toxic effect of alcohol
T51.0	Ethanol
T51.9	Alcohol, unspecified

eTable 2: Extrapolation of individuals with alcohol dependence according to DSM-IV criteria to the total population of Bremen in 2017 using ESA 2018 survey data

	Age	N ¹	% ²	[95%-CI]	$\hat{N}_{\text{Bremen}}^3$	$\hat{N}_{\text{Bremen}}$ [95%-CI]
Men	16-34	88,723	8.6	[7.3; 10.1]	7,630	[6,476; 8,961]
	35-64	136,420	2.5	[1.7; 3.6]	3,411	[2,319; 4,911]
	65+	61,673	0.6	[0.2; 1.1]	370	[123; 678]
Women	16-34	81,293	3.6	[2.9; 4.3]	2,927	[2,357; 3,496]
	35-64	134,329	0.9	[0.6; 1.3]	1,209	[806; 1,746]
	65+	82,078	0.3	[0.1; 0.4]	246	[82; 328]
Total		584,516			15,792	[12,163; 20,120]

Notes: N denote the empirical population size, whereas $\hat{N}$ represent the estimated population size. The same prevalence of 18–34-year-olds was assumed for 16-17-year-olds. The prevalence of the 65+ age group was estimated from modeling the prevalence of 18-64-year-olds. ¹ Total population in Bremen 2017; ² Weighted prevalence throughout Germany from ESA 2018; ³ Extrapolated total population of individuals with alcohol dependence according to DSM-IV criteria in Bremen; 95% CI = 95% confidence interval.

eTable 3: Extrapolation of the administrative prevalence of alcohol dependence (F10.2-4) and addiction-specific care of the statutory health insurances' (SHI) population 2016/17 to the total population of Bremen

	Age	Bremen ¹	SHI ²	Identified ³			Outpatient diagnosis			Qualified withdrawal treatment			Pharmacotherapy		
		N	N	n	% ⁴	Ň ⁵	n	% ⁴	Ň ⁵	n	% ⁴	Ň ⁵	n	% ⁴	Ň ⁵
Men	16-24	37,666	20,061	46	0.2	86	30	0.1	56	9	0.0	17	0	0.0	0
	25-49	117,355	60,305	1,269	2.1	2,470	1,057	1.8	2,057	137	0.2	267	23	0.0	45
	50-64	70,122	34,968	1,841	5.3	3,692	1,668	4.8	3,345	120	0.3	241	18	0.1	36
	65+	61,673	31,691	917	2.9	1,785	808	2.5	1,572	19	0.1	37	4	0.0	8
Women	16-24	34,149	17,644	25	0.1	48	14	0.1	27	2	0.0	4	0	0.0	0
	25-49	110,073	57,042	370	0.6	714	327	0.6	631	34	0.1	66	7	0.0	14
	50-64	71,400	37,295	756	2.0	1,447	699	1.9	1,338	43	0.1	82	11	0.0	21
	65+	82,078	48,238	470	1.0	800	428	0.9	728	13	0.0	22	5	0.0	9
Total		584,516	307,245	5,694		11,042	5,031		9,754	377		735	68		132

Notes: n/N denote each the empirical sample and population sizes, whereas $\hat{n}/\hat{N}$ represent the estimated and extrapolated population sizes. SHI: Statutory health insurance; GeNo: Gesundheit Nord - Bremen Hospital Group; GPI: German Pension Insurance; ¹ Total population of Bremen 2017; ² Total population with at least one insurance day in the SHIs AOK or hkk in 2017; ³ Diagnosed with an outpatient confirmed or inpatient primary or secondary diagnosis; ⁴ Administrative prevalence of the SHIs' population; ⁵ Extrapolated to the total population of Bremen.

eTable 4: Extrapolation of overlaps from individuals observed in the statutory health insurances' (SHI) population to people with other or no insurance (Non-SHI) between data on rehabilitation from the German Pension Insurance (GPI) data and data on outpatient addiction care from the hospital group Gesundheit Nord (GeNo)

	Age	Bremen ¹	SHI ²	Non-SHI ³	Overlaps GPI			Overlaps GeNo			Overlaps GPI and GENO		
		N	N	N	n _{GPI/SHI}	% ⁴	$\hat{n}_{GPI/Non-SHI}$	n _{GeNo/SHI}	% ⁴	$\hat{n}_{GeNo/Non-SHI}$	n _{GPI/GeNo/SHI}	% ⁴	$\hat{n}_{GPI/GeNo/Non-SHI}$
Men	16-24	37,666	20,061	17,605	0	-	0	3	0.015	3	0	-	0
	25-49	117,355	60,305	57,050	35	0.058	33	78	0.129	74	11	0.018	10
	50-64	70,122	34,968	35,154	36	0.103	36	66	0.189	66	8	0.023	8
	65+	61,673	31,691	29,982	1	0.003	1	18	0.051	15	0	-	0
Women	16-24	34,149	17,644	16,505	0	-	0	0	-	0	0	-	0
	25-49	110,073	57,042	53,031	0	-	0	7	0.012	7	0	-	0
	50-64	71,400	37,295	34,105	4	0.011	4	13	0.035	12	0	-	0
	65+	82,078	48,238	33,840	0	-	0	5	0.010	4	0	-	0
Total		584,516	307,245	277,272	76		74	188		181	19		18

Notes: n/N denote each the empirical sample and population sizes, whereas $\hat{n}/\hat{N}$ represent the estimated and extrapolated population sizes. SHI: Statutory health insurance; GeNo: Gesundheit Nord - Bremen Hospital Group; GPI: German Pension Insurance; ¹ Total population of Bremen 2017; ² Total population with at least one insurance day in the SHIs AOK or hkk in 2017; ³ Total unobserved population in 2017 ($N_{Bremen} - N_{SHI}$); ⁴ Proportion of observed individuals on total population N_{SHI} .

eTable 5: Extrapolation of overlaps from German Pension Insurance's (GPI) data to individuals not observed in the German Pension Insurance's data (Non-GPI) with observed statutory health insurances' (SHI) data, unobserved health insurances' (Non-SHI) data and data from the Gesundheit Nord hospital group (GeNo)

Total ¹	GPI ²	Non-GPI ³	Overlaps GeNo			Overlaps Non-SHI			Overlaps SHI			Overlaps SHI and GeNo			Overlaps Non-SHI and GeNo		
$\hat{N}$	N	$\hat{N}$	$n_{\text{GPI/GeNo}}$	% ⁴	$\hat{n}_{\text{Non-GPI/GeNo}}$	$\hat{n}_{\text{GPI/Non-SHI}}$	% ⁴	$\hat{n}_{\text{Non-GPI/Non-SHI}}$	$n_{\text{GPI/SHI}}$	% ⁴	$\hat{n}_{\text{Non-GPI/SHI}}$	$n_{\text{GPI/GeNo/SHI}}$	% ⁴	$\hat{n}_{\text{Non-GPI/GeNo/SHI}}$	$\hat{n}_{\text{GPI/GeNo/Non-SHI}}$	% ⁴	$\hat{n}_{\text{Non-GPI/GeNo/Non-SHI}}$
614	343	271	53	15.5	42	74*	21.6	58	76	22.16	60	19	5.54	15	18*	5.25	14

Notes: n/N denote each the empirical sample sizes, whereas $\hat{n}/\hat{N}$ represent the estimated and extrapolated population sizes. ¹ Extrapolated total population of individuals with initiated rehabilitation treatment in 2016/2017; ² Total population with initiated rehabilitation treatment in 2016/2017 financed by the German Pension Insurance (GPI); ³ Total unobserved population with initiated rehabilitation treatment in 2016/2017 ($\hat{N}_{\text{Total}} - N_{\text{GPI}}$); ⁴ Proportion of observed/estimated population on total population N_{GPI} . *Calculation shown in eTable 4.

6. Paper II

Clustering care pathways of people with alcohol dependence using a data linkage of routine data in Bremen, Germany

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Keywords: Alcohol dependence, treatment utilization, data linkage, routine data, state sequence analysis

Abstract

Background: Although many individuals with alcohol dependence (AD) are recognized in the German healthcare system, only a few utilize addiction-specific treatment services. Those who enter treatment are not well characterized regarding their prospective pathways through the highly fragmented German healthcare system. This paper aims to (1) identify typical care pathways of patients with AD and their adherence to treatment guidelines and (2) explore the characteristics of these patients using routine data from different healthcare sectors.

Methods: We linked routinely collected register data of individuals with a documented alcohol-related diagnosis in the federal state of Bremen, Germany, in 2016/2017 and their addiction-specific health care: two statutory health insurance funds (outpatient pharmacotherapy for relapse prevention and inpatient qualified withdrawal treatment (QWT)), the German Pension Insurance (rehabilitation treatment) and a group of communal hospitals (outpatient addiction care). Individual care pathways were analyzed using state sequence analysis. First, daily states of utilized addiction-specific treatment were defined, starting with an index inpatient admission due to AD. Index episodes needed no other inpatient admission due to AD at least 60 days before the index admission. The individual treatments (not outpatient addiction care) within a follow-up time of 307 days (10 months) were combined to state sequences, clustered, and visually presented as typical care pathways. Individuals of the clustered pathways were compared concerning current treatment recommendations (1: QWT followed by post-acute treatment; 2: time between QWT and rehabilitation). Patients' characteristics not considered during the cluster analysis (sex, age, nationality, comorbidity, and outpatient addiction care) were then compared using a multinomial logistic regression.

Results: The analysis of 518 individual sequences resulted in the identification of 4 pathway clusters differing in their utilization of acute and post-acute treatment. Most did not utilize subsequent addiction-specific treatment after their index inpatient episode (n=276) or had several inpatient episodes or QWT without post-acute treatment (n=205). Two small clusters contained pathways either starting rehabilitation (n=26) or pharmacotherapy after the index episode (n=11). Overall, only 9.3% utilized post-acute treatment as recommended.

Conclusion: A concern besides the generally low utilization of addiction-specific treatment is the implementation of post-acute treatments for individuals after QWT.

Background

The consumption of alcohol was responsible for an estimated 5.3% of all global deaths and 5.1% of all disability-adjusted life years in 2016 (1). Germany is considered a high-consumption country, even though per capita consumption of pure alcohol per person aged older than 15 years has decreased over the last 20 years from 12.0 l in 2000 to 10.0 l in 2021 (2). Mental and behavioral disorders due to alcohol (F10. X) according to the International Classification of Diseases (ICD-10) were the fourth most frequent main diagnoses for inpatient hospitalization in 2021 (3). Although an estimated 35% of people with alcohol dependence were diagnosed in medical health care settings in Germany in 2012, only 16% received addiction-specific care services, indicating a significant treatment gap (4).

In general, the treatment of alcohol dependence in Germany occurs in a highly fragmented healthcare system, which is based on mandatory health insurance using either public statutory health insurance or private health insurance. Different actors are responsible for the reimbursement of costs for addiction-specific treatment and care services. While outpatient addiction care services are primarily financed by communes, acute treatments, such as withdrawal management, are covered by health insurance funds. Health insurance funds can also cover the cost of some post-acute treatments, such as outpatient pharmacotherapy. A rehabilitation treatment, either inpatient or outpatient, is nevertheless financed in most cases by the German Pension Insurance [Deutsche Rentenversicherung (DRV)], but only if certain requirements are met (5). These requirements, among others, are not being a pensioner or a civil servant and having paid for the insurance for at least six months over the past two years.

A comprehensive discussion and practical recommendations based on available evidence of multiple treatment options for risky, harmful, and dependent alcohol use were elaborated in the current German S3 guidelines on "Screening, diagnosis, and treatment of alcohol-related disorders" (5). The recommended treatment for people with alcohol dependence consists of acute treatment (e.g., withdrawal treatment including detoxification) followed - ideally seamlessly - by post-acute treatment, either by using pharmacotherapy for relapse prevention, rehabilitation treatment, or other post-acute treatments, such as psychotherapy, and inpatient/outpatient psychiatric care (5). Depending on the severity of withdrawal, the number of prior withdrawal treatments, and the social integration of the patient, withdrawal treatment can take place either in inpatient or outpatient settings. Guidelines recommend providing a so-called Qualified Withdrawal Treatment (QWT), which describes a German-specific term for an extended withdrawal treatment program (generally three weeks) including psychosocial interventions (5). Detoxification, i.e., controlling and reducing alcohol withdrawal symptoms as well as any neurological or physical symptoms (e.g., epileptic seizures or delirium tremens), is but one component during QWT. Additionally, treatment of the underlying dependence is initiated while considering psychological and somatic concomitant and secondary diseases. The goals are to increase motivation to seek further help and more specific treatments (e.g., addiction rehabilitation) and to establish contact with the regional support system (e.g., psychotherapy, self-help) (6). Despite clear recommendations, a recent study indicated that QWT for people with severe alcohol use disorders is considerably underutilized (7).

The aim of this study was the exploratory analysis of empirical addiction-specific care pathways of patients with alcohol dependence using linked data of different payers in addiction-specific care services and treatments. To this end, a state sequence analysis was

performed. State Sequence Analysis was originally developed to analyze educational lifetime trajectories in social sciences but has recently been adapted to epidemiological analyses of care pathways for different conditions (8-10). Here, individual treatment states constitute sequences that represent individual care pathways. By clustering these sequences, typical pathways as well as their adherence to current guideline recommendations were elaborated. Finally, the resulting clusters were compared concerning sociodemographic characteristics and their addiction-specific care utilization.

Methods

Data

Three routine data sources collected within the project "Implementation and Evaluation of the S3 Guideline on Screening, Diagnosis, and Treatment of Alcohol-Related Disorders" (IMPELA) were used. The data sources contained individual information for persons aged 16 years or older living in the northern German federal city-state of Bremen between 2016 and 2017. The overall sample comprised all people with a main or secondary diagnosis of mental and behavioral disorders due to alcohol (F10.x) or another fully alcohol-attributable diagnosis (for a detailed list see Additional file 1: Table S1). The diagnosis was documented in at least one of three used data sources: (a) two statutory health insurance funds (AOK Bremen/Bremerhaven and hkk), (b) the regional German Pension Insurance (DRV Oldenburg/Bremen), and (c) the outpatient addiction care of the municipal clinic association Gesundheit-Nord (11). The three data sources included information on different addiction-specific treatments and care services, i.e., billed treatments in both inpatient and outpatient settings (a: statutory health insurance funds), rehabilitation services in inpatient, outpatient or both settings (b: pension insurance), and visits to outpatient addiction care (c: municipal clinic association). Data from these

sources were linked at the individual level (12). In the state sequence analysis, only sequences of people with information from the statutory health insurance funds were considered.

The population insured with the two statutory health insurance funds represents approximately 50% of the total population in Bremen (307,245 out of 584,516) and shows a similar distribution of age and gender compared to the total population in Bremen (For a more detailed description of the total sample see 13). The overall sample with information from the statutory health insurance funds comprised 10,507 individuals. Individuals who were insured in both funds at the same time ($n=9$), who were not insured in one of these two funds for more than 60 days ($n=338$) or with recorded death ($n=82$) were excluded. An index event was defined to ensure a homogenous and comparable sample. Therefore, only pathways starting with an inpatient episode with a main diagnosis of alcohol dependence (F10.2) or withdrawal syndrome (F10.3-4) ($n=973$) were included if they had no preceding inpatient episode of the same kind for at least 60 days prior and had data available for at least 10 months of follow-up time ($n=518$). The index event could contain QWT. The 60 days served as a kind of wash-out period to ensure a similar baseline for the individual pathways while allowing for a follow-up period of at least 10 months (307 days). As the data were restricted to two calendar years and most first episodes already took place in the first four months of 2016, there was little room for alternative specifications of wash-out and follow-up periods. The distribution of the months in which the first inpatient episode took place is shown for the total sample in the appendix (see Additional file 1: Fig. S1). As the allowed 60 missing insurance days within 2016/2017 could fall into the observation period, a sensitivity analysis was done excluding cases with missing insurance days in the observation period ($n=16$).

Addiction-specific care services and treatments

Several addiction-specific treatments and care services in different settings were identified. For each inpatient hospital episode paid by the statutory insurance fund (a), ICD-10 diagnoses (main, secondary), date of admission and discharge, and administered procedures by assigned Surgery- and Procedure-Codes [Operationen- und Prozeduren-Schlüssel (OPS codes)] were documented. QWT could be identified in both somatic (OPS code 8-985) and psychiatric wards (OPS code 9-647). Since OPS codes are not substance specific, a main diagnosis for alcohol dependence or withdrawal state (F10.2-4) or any F10.X diagnosis with alcohol dependence (F10.2) as secondary diagnosis for the specific inpatient episode had to be present. Detoxification not within a QWT is not specifically coded. The duration of each inpatient episode was calculated by the date of admission and discharge.

For treatments in the outpatient setting paid by the statutory insurance fund (a), diagnoses are billed and documented quarterly. Medication is documented by the pharmaceutical registration numbers [Pharmazentralnummer (PZN)], as well as the date of the prescription. Using this number and the corresponding anatomical-therapeutic-chemical classification (ATC), we identified medications specifically prescribed for drug relapse prevention (ATC code: N07BB). The assignment of registration numbers with ATC codes was based on the drug master file of the German Drug Index of the Scientific Institute of the AOK [Wissenschaftliches Institut der AOK (WIdO)] as of September 2017. For every drug, an exposure window of 90 days after the subscription was defined. Using the data from the regional German Pension Insurance (b), specific dates of rehabilitation treatments in different treatment settings (inpatient, outpatient, both) could be identified. Additionally, the number of visits to outpatient addiction care services of the communal

hospital group Gesundheit-Nord (c) could be identified by visit dates with a documented F10.2 diagnosis.

Concerning treatment guideline adherence, the utilization of QWTs as well as the timing of post-acute treatment after QWT were analyzed. Therefore, the duration in days between the end of a QWT and the onset of a rehabilitation treatment was calculated based on the admission date of the rehabilitation and the discharge date of the nearest QWT.

Pathway construction

First, an alphabet of all possible states must be defined. States were defined as having used one of the explained addiction-specific treatments. Attending outpatient addiction care of the communal hospital group was not counted as a treatment. This resulted in the following alphabet containing five states of addiction-specific treatments:

- A. No addiction-specific treatment
- B. Outpatient pharmacotherapy for relapse prevention
- C. Rehabilitation
- D. Inpatient episode due to alcohol dependence (F10.2-4) incl. QWT
- E. Inpatient episode due to alcohol dependence (F10.2-4)

For each individual, a sequence of 307 days, with each day containing one of the states defined in the alphabet, was created. The number of days in the follow-up period always included the index event to ensure the cluster analysis could take the different lengths of the index event into account. These sequences represent the individual addiction-specific care pathways. If another of the defined treatments, i.e., C, D, or E, which contain clear admission and discharge dates, was present within the exposure window of B, treatment C, D, or E was coded instead of B for this specific time frame. If the discharge date was

still within the 90-day exposure window of B, B was again coded until the end of the 90-day exposure window. Additionally, it was assumed that if B had already started before the index event, it was resumed afterwards.

Cluster analysis of pathways

After defining the state sequences, these individual pathways were clustered. While patients who did not utilize further addiction-specific treatments despite their index episode were set as the reference cluster (Cluster 0), the remaining pathways with at least one further addiction-specific treatment, i.e., states B-E, were clustered to typical care pathways. A dissimilarity matrix was created using a dissimilarity measure called the longest common subsequence (lcs) (14, 15). This measure defines the similarity between sequences (x and y) by using the length of common elements (states) occurring in the same order ($\text{lcs}(x,y)$). The distance d between sequences x and y is then defined as

$$d = l(x) + l(y) - 2(\text{lcs}(x, y))$$

where l denotes the length of the sequence. The distance, therefore, is based on the elements not part of the longest common subsequence.

Based on this dissimilarity measure, clustering techniques were used to group sequences and identify typical addiction-specific care pathways. Hierarchical clustering, as well as partitioning around medoids (PAM), also called k-medoids clustering, were calculated, and then compared. These two methods differ in how clustering is performed. Hierarchical clustering is a bottom-up approach that starts with clustering every sequence as one single cluster and then locally minimizes differences by merging clusters until only one cluster is left. The ward criterion was used, which minimizes the residual variance (16). K-medoids clustering offers an advantage over hierarchical clustering through the optimization of a global parameter instead of a local parameter, as its aim is to identify

the best representatives (medoids) for a given number of groups (16). These medoids are defined as having the smallest weighted sum of distances from other observations in the group. A disadvantage of this method is that the starting points for the optimization and the number of clusters must be defined in advance. To find the optimal solution, the hierarchical cluster solution was used as a starting point for k-medoids clustering using different numbers of clusters (here five).

For both clustering techniques, the best number of clusters must be identified. This was done by calculating the average silhouette width (range: -1-1) and Hubert's C (range: 0-1). The average silhouette width allows for the comparison of different clustering solutions in terms of coherence of assignment by between-group differences and within-group homogeneity (the higher, the better) and Hubert's C, which indicates the gap between the present solution and the best solution theoretically possible (the lower, the better) (16). Finally, the solution with the highest average silhouette width, lowest Hubert's C, and highest interpretability will be presented in the following.

Typical treatment pathways were constructed by selecting the 10 most representative sequences using their neighborhood density (17). Using the distance matrix, a representative score was calculated based on the number of sequences in the neighborhood of each sequence, meaning that their distance was within a selected threshold. This threshold (neighborhood radius) was set at 10% of the maximum theoretical distance between two sequences. The coverage score corresponds to the number of sequences in the neighborhood of a representative sequence, and the total coverage corresponds to the number of sequences with a representative in their neighborhood (18). The data were analyzed using the "TraMineR", "WeightedCluster", "cluster" and "comorbidity" packages in R version 4.2.2 (19). The R script of the analyses is part of the appendix (see Additional file 2).

Patient characteristics

Comorbidities can affect health care utilization and might also influence which addiction-specific care service should be or can be used. To control for different levels of comorbidity at the start of the pathway, the Walraven-Elixhauser comorbidity score was calculated using all inpatient diagnoses, main and secondary, in the index episode and 60 days prior. Another study (20) has previously used this score in a similar manner, and it theoretically ranges from -19 to 89 (21). The score incorporates the association of different comorbidity groups with death in the hospital, in which higher scores signify a more severe level of comorbidity (21).

General and addiction-specific hospitalizations in the follow-up period were compared by the days spent in inpatient episodes and the share of hospitalizations due to alcohol dependence or withdrawal (F10. 2-4) as the main diagnosis. Additionally, visits to outpatient addiction care and the time spent in inpatient episodes, including QWTs, were compared across clusters. Comparisons for categorical variables were performed using χ^2 tests and Fisher's exact tests when cell sizes were smaller than five. Metric variables were compared using ANOVA when assuming normality and the Kruskal–Wallis rank sum test when assuming nonnormality. Additionally, predictors of cluster membership (dependent variable) were calculated by a multinomial regression with the following independent variables: sex (male/female), age (centered), nationality (German/Non-German), Walraven-Elixhauser comorbidity score, inpatient episode before index event (no main diagnosis of alcohol dependence or withdrawal), the use of outpatient addiction care of the communal hospital group both in the 60 days before the index event (yes/no) and in the 10 months following the index event (yes/no).

Results

Cluster analysis

-Table 1-

The analyzed sample comprised 518 patients with individual sequences of addiction-specific care after their index inpatient episode. In the total sample, the most often used addiction-specific care service was QWT (29.9%) and visiting outpatient addiction care within the follow-up period (11.6%). Furthermore, 9.3% utilized a post-acute treatment, i.e., pharmacotherapy for relapse prevention (3.5%) or rehabilitation (6.4%). Just over half were assigned to the predefined Cluster 0 (n=276). Cluster analysis (k-medoids clustering; average silhouette width 0.59, and Hubert's C 0.05) resulted in Cluster 1 (n=205), Cluster 2 (n=26) and Cluster 3 (n=11). The sociodemographic characteristics and utilized care services of the sample in total and by cluster are presented in Table 1. For a graphical representation of all individual sequences, see Additional file 1: Fig. S2.

In Cluster 0 ("No further treatment"), every fifth person (18.8%, see Table 1) utilized a QWT in their index episode, and 4.7% visited outpatient addiction care within the follow-up period. Other than the index episode and outpatient addiction care, no further addiction-specific treatment was used. In the median, the number of days in hospital in the follow-up period was 12 days.

Cluster 1 ("No (seamless) post-acute treatment") shows a more frequent usage of QWT (41.0%) but a low utilization of rehabilitation treatment (4.4%) or pharmacotherapy (1.5%) as post-acute treatment. It shows the second highest number of days spent in hospital (median: 35.0), the highest number of QWTs (third quartile: 2), and the second lowest share of post-acute treatments (5.9%). If QWT was utilized before rehabilitation treatment (1.0%), the median waiting time was 59.5 days.

Pathways in Cluster 2 (“Rehabilitation”) mainly represented rehabilitation as post-acute treatment (92.3%). Some patients also used pharmacotherapy (15.4%) for relapse prevention. This cluster shows the highest number of days spent in the hospital (median: 38.5). If a rehabilitation treatment followed a QWT (57.7%), the median days between the end of QWT and the onset of rehabilitation were less than 23 days (for a plot of the distribution by clusters, see Additional file 1: Fig. S3).

The remaining Cluster 3 (“Pharmacotherapy”) contained the fewest patients ($n=11$). All of them started pharmacotherapy treatment. This cluster has the second lowest median number of hospital days (29 days), and the second lowest share of people using QWT (27.3%).

Typical pathways

-Figure 1-

Figure 1 shows the relative frequency of sorted states on each day of the follow-up period as well as the 10 most typical pathways of each cluster. The representativeness of these typical pathways is shown by the height of the bar width, which is proportional to the represented sequences and the coverage.

In Cluster 0, the most typical pathways only show the index episode, consisting of either an inpatient episode with or without QWT. In Cluster 1, post-acute treatment was typically not utilized during the follow-up period. The most representative sequence is a short index episode followed by a longer inpatient episode within the first month of the follow-up period. Further representative sequences have no clear pattern of timing of subsequent treatment after the index episode. One representative pathway shows up to three QWTs within the follow-up period. In Cluster 2, rehabilitation treatments are mainly within day 40 and day 163 of the follow-up period, which cannot always be explained by a longer or shorter index episode (see Additional file 1: Fig. S2). In Cluster 2, the few

patients additionally using pharmacotherapy for relapse prevention did so some time after finishing their rehabilitation treatment directly following an inpatient episode. Cluster 3 shows several hospital episodes within the follow-up period, but each one is rather short, showing no pattern of timing in the follow-up period. One pathway had already started pharmacotherapy before the index episode.

Patient characteristics by cluster

-Table 2-

Table 2 shows the results of the multinomial logistic regression based on a sample of 514 patients. Four patients from Cluster 1 (n=2) and Cluster 2 (n=2) were excluded from this analysis due to missing data on nationality. The multivariate regression showed no significant differences concerning sex, which were significant in the univariate analysis (p value=.044, see Table 1).

In total, Cluster 0 had the highest share of females of all clusters (26.4%, see Table 1). The smallest share of females was seen in Cluster 2, with 3.8%. Cluster 2 had the lowest mean age (47.5 years), but the differences between all clusters were neither significant overall (p=.546, see Table 1) nor in the regression model. The other clusters had a similar mean age of approximately 50 years. No differences concerning nationality could be identified. Differences in the comorbidity score were neither significant in univariate analysis (p=.593, see Table 1) nor in the regression model. However, Cluster 2 had the highest interquartile range (0.0 to 10.3, see Table 2). There were no statistically significant differences concerning hospital episodes not due to alcohol dependence 60 days before the index event or the share of inpatient episodes due to alcohol dependence in the observation period. Both Cluster 1 and Cluster 2 showed a higher usage of outpatient addiction care services than Cluster 0 (see Table 1). In the regression model,

this difference was only statistically significant when looking at the follow-up period (see Table 2).

The sensitivity analysis excluding individuals with missing insurance days in the observation period yielded similar results (see Additional file 1: Table S2 and Fig. S4).

Discussion

The exploratory state sequence analysis presented here shows that after an inpatient episode due to alcohol dependence or withdrawal symptoms, generally few patients utilized further post-acute treatment. The cluster analysis resulted in four clusters. The two largest clusters are best represented by either no further addiction-specific treatment besides the index event or no (seamless) post-acute treatments. The two very small clusters are best represented by using rehabilitation or pharmacotherapy as post-acute treatment. These clusters of addiction-specific care pathways showed statistically significant differences in the utilization of outpatient addiction care services. However, there were no statistically significant differences in terms of sociodemographic characteristics or general comorbidities. Furthermore, differences in the utilization of treatment and care services could be visualized and described. The most typical care pathway consisted of not using any of the addiction-specific treatment/care services included in this study. The most used addiction-specific treatment was QWT with no further post-acute treatment. To a lesser extent, there seemed to be some patients best characterized by multiple inpatient episodes and QWTs without post-acute treatment. There also seemed to be a small subgroup of people showing a revolving door phenomenon of QWTs. Studies among people with psychiatric disorders have most consistently identified previous admissions to be connected to higher readmission rates (22, 23). A Swiss study could additionally identify symptom load at discharge as an

important predictor for higher readmission rates for patients with substance use disorder (24). Other studies showed a high readmission risk for patients with alcohol use disorder, especially if an alcohol-induced psychiatric disorder was present (25, 26).

Current guidelines recommend withdrawal treatment to be followed seamlessly by post-acute treatment, i.e., either rehabilitation treatment, pharmacotherapy for relapse prevention, or other types of post-acute treatments (5). Only two very small clusters of pathways utilize post-acute treatments. If a QWT was utilized before a rehabilitation treatment, patients had a waiting period of under 23 days in the median. This indicates quite quick transfers in most cases, nevertheless, leaves room for further reductions of waiting periods. In a nationwide survey of hospital personnel in 81 clinics that provided QWT in 2013, long waiting times for rehabilitation and psychiatric post-acute treatments were significant obstacles for seamless referrals. Additionally, clarification of cost coverage and insufficient specific treatment options for patients with severe comorbidities as well as parents of school-age children were reported major challenges (27). The follow-up period theoretically encompasses the introduction of new recommendations for action by healthcare providers and payers set in effect in August 2017, with the goal of improving seamless access to medical rehabilitation after QWT (28). They are specifically set up to improve and increase seamless transfers directly from the hospital to rehabilitation treatment. In our data, however, sequences started in most cases well before August 2017, and the effects were likely not yet visible. In the total sample, only 30% of patients utilized QWT, and overall, the usage of post-acute treatments was rather low, with only 9.3% using either pharmacotherapy for relapse prevention (3.5%) or rehabilitation (6.4%).

These results cannot be generalized to all of Germany but rather represent the city of Bremen in northern Germany. However, rates of addiction-specific treatment utilization

in the general population in Bremen based on the total sample of the used data set were found to be comparable to German-wide estimates (13). In the present study, the proportion of patients utilizing pharmacotherapy, i.e., acamprosate, disulfiram, or naltrexone, was 3.5%. These results are in line with another analysis of routine data in northern Germany concluding an underutilization of pharmacotherapy as post-acute treatment, i.e., acamprosate and naltrexone (29). Only 2.2% of patients in the six months following an inpatient treatment due to alcohol dependence (F10.2) or withdrawal state (F10.3-4) received this kind of anti-craving medication (29). An increase in pharmacotherapy for relapse prevention may have desirable effects on hospitalization rates among people with alcohol use disorders (30). A study from the UK evaluated nalmefene, in combination with psychosocial support, as a cost-efficient treatment option for a population with high drinking risk levels but without the need for immediate detoxification (31). This shows that pharmacotherapy for relapse prevention may not be suitable for every individual with alcohol dependence but poses an option in specific cases. Therefore, increasing the utilization may be beneficial. However, more comparable studies are needed to formulate generally effective strategies to achieve this, as a review concluded (32).

The utilization of other types of post-acute treatments was not documented in the analyzed data sets. It can be assumed that not everyone with a diagnosis of alcohol dependence needs the kind of post-acute treatments analyzed here, i.e., pharmacotherapy for relapse prevention or a rehabilitation treatment. However, there is robust evidence that post-acute treatments are beneficial for those who need it. Timely access of patients to addiction-specific care/treatment after withdrawal reduces readmissions and can be seen as a “teachable moment” for patients to increase their motivation to engage in further treatment (5). Studies from the US and Canada indicate higher initial engagement and

reduced readmissions when withdrawal treatment is followed by seamless post-acute care (33, 34). In particular, early rehabilitation (within three months of detoxification) appears to be beneficial in reducing the likelihood of relapse (35). One possible way to improve referrals to post-acute treatment may be patient-centered placement matching approaches using a standardized assessment of the level of care needed for patients after a QWT (36). In a randomized control trial in four German psychiatric clinics analyzing patients following an inpatient QWT due to alcohol dependence without organized aftercare, reductions in days of heavy drinking and lowering of costs were identified as benefits, whereas the actual referral to aftercare remained unchanged (37). This indicates the need for more research on how to increase the number of people who utilize the recommended post-acute treatment.

Since 2010, there has been a negative trend in the utilization of rehabilitation treatments overall, particularly for addiction treatment (38). Reasons were structural barriers like the high bureaucratic effort required for applications, low expectations of successful outcomes, and insufficient information about available rehabilitations (38). Beside these structural barriers a general improvement in outpatient offers of addiction specific post-acute care and outpatient psychotherapeutic measures (38), as well as a decline in alcohol use, alcohol dependence and alcohol related morbidity and mortality indicate an overall lower demand for rehabilitation treatments (39, 40). Future analyses should therefore include more outpatient post-acute treatments. However, alcohol dependence is highly stigmatized, and research has shown that higher levels of stigma are associated with reduced help-seeking behavior in general (41). Also, patient related barriers are relevant, such as a lack of problem awareness, a desire to continue drinking, and a preference to handle the issue independently. Interestingly, problem awareness appears to be negatively correlated with the severity of dependence (42).

This study focused on people in a more severe stage of their dependence as only patients with at least one inpatient episode were analyzed. Hospital episodes appear to help facilitate motivation for further addiction-specific treatment. Patients with alcohol dependence who were admitted to a hospital show a higher motivation to change than people with alcohol dependence in the general population (43). In our study, people with a higher number of hospital days utilized more addiction-specific care services. However, pharmacotherapy for relapse prevention was the only addiction-specific treatment that could be identified in the outpatient setting, in which more than half of the individuals with alcohol dependence are estimated to already be recognized (13). Additionally, only inpatient QWTs could be identified, which under specific circumstances can also take place in outpatient settings. Hence, the number of total QWTs is underestimated.

The data set also only contains rehabilitation data from one of three German Pension Insurances (DRV), namely the regional DRV Bremen/Oldenburg and is missing rehabilitation treatments financed by health insurances (Germany-wide around 15% of all inpatient rehabilitation treatments in specialized clinics for alcohol and drug dependence (44)) and the other German Pension Insurances, i.e., federal DRV Bund and DRV Knappschaft-Bahn-See. Of all approved rehabilitation services financed by the German Pension Insurance in Bremen in 2016/2017 66% were financed by the regional DRV Bremen/Oldenburg, 29% by the federal DRV Bund and 5% by the DRV Knappschaft-Bahn-See (Deutsche Rentenversicherung Bund, unpublished data, 2024). Hence, the total number of utilized post-acute treatment is underestimated. In a randomized control trial study of patients with alcohol-use disorder in eight clinics in southern Germany, post-acute care was used by almost half of the sample following inpatient withdrawal management (with and without QWT) without organized after care (35). Outpatient addiction care (22-37%) and self-help groups (7-15%) were the

predominant post-acute care services utilized, alongside rehabilitation, while psychiatric treatment was not reported (35).

Strengths and limitations

The primary strength of this paper is the data linkage of routine data of several addiction-specific care providers for inpatient and outpatient services as well as rehabilitation treatment services. This approach mitigates potential biases typically associated with surveys, such as response or memory bias. Additionally, the insurance data covers all services utilized by people living in Bremen and is therefore except for the outpatient addiction care data of the communal hospital group not reduced on services taking place in Bremen. Additionally, since data from the pension funds was used, rehabilitation treatments were also independent of location and setting of the treatment. Furthermore, the present data set represents a large part of the highly fragmented care system for people with alcohol dependence in Germany.

Nevertheless, there are some drawbacks. Specific areas of addiction-specific help are not part of the data set, for example, self-help therapy groups. Furthermore, the analysis is missing additional addiction-specific care services and treatments in the outpatient setting, e.g., brief interventions and psychotherapy. These services could not be identified since necessary codes, like uniform assessment standard [Einheitlicher Bewertungsmaßstab (EBM)], were not part of the data set. Also, outpatient addiction care outside of the communal hospital group is not part of the data. Utilization of addiction-specific treatments and care services, in general, relies on different variables, such as drinking patterns or severity of dependence, which could not be measured in the present data.

The analyzed population of the statutory health insurances show similar age and gender distribution compared to the total population (13). Still, systematic differences regarding addiction specific care pathways cannot be ruled out, since important variables associated with health care utilization can differ between health insurance funds. Earlier studies using AOK data for Lower Saxony, which is the state surrounding Bremen, showed an overrepresentation of people with a lower socio-economic status and migration background compared to the total population (45). At the same time there is a higher share of people with a high socio-economic status in private health insurance funds (requirements: earning more than the compulsory insurance threshold, being a public servant or self-employed), and other funds than AOK (46). To mitigate biases in this study also data from the hkk was integrated. If possible, data from all insurance funds should ideally be used in future studies. A higher utilization of addiction-specific treatments seems unlikely, as e.g., private health insurance companies, in which only approx. 10% are insured in Germany (47), do not always cover addiction specific treatments like QWT. The cluster sizes in the present analysis are very small, however, the cluster solution presented shows an average silhouette width above 0.5, which can be described as a reasonable structure (48). When analyzing the clusters graphically, several differences in the usage of care services and patterns of utilization were visible. The small cluster sizes are mostly due to the low number of sequences that used addiction-specific treatment and the rather heterogeneous sample. Additionally, the cluster solution was not robust. When setting the effect window of the pharmacotherapy to 60 days, all cluster solutions had an average silhouette width under 0.5 and therefore could be described as weak and potentially artificial (data not shown).

The index event and the pre-index period were selected to obtain a homogenous sample with a comparable severity of addiction and a comparable stage of treatment.

Nevertheless, some pathways already showed post-acute treatment in the earliest quarters following an inpatient episode, or pharmacotherapy after rehabilitation treatment. This suggests that patients could have been in different stages of their addiction. The data are both right- and left-censored, which makes it difficult to define a follow-up time that is long enough and still having a comparable sample. In particular, alcohol dependence is characterized by a long time gap between the onset of symptoms and treatment seeking (44) and a high readmission risk. Future studies should consider a longer observation period to be able to analyze long-term care pathways and have a large enough sample to be able to define more homogenous groups.

Conclusions

The state sequence analysis showed that even when addiction-specific care services are utilized, only a minority use post-acute treatments after QWT, i.e., rehabilitation treatment or pharmacotherapy for relapse prevention. Even though the cluster solution was not very robust and cluster sizes were small, different patterns of utilizing addiction-specific treatment and care services, specifically concerning post-acute treatments, could be presented. The different patterns of utilization could not be explained by differences in sociodemographic characteristics or general comorbidity. Although using QWT and therefore being in contact with addiction-specific care networks, many people either seek treatment after withdrawal outside the healthcare system or do not utilize further addiction-specific care services at all. Therefore, not only is the generally low utilization of addiction-specific care services of concern but also the low utilization of post-acute treatments in the care pathway of individuals after withdrawal treatment despite being recommended by the current treatment guidelines.

List of non-standard abbreviations

QWT	Qualified withdrawal treatment
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Supplementary Information

The online version contains supplementary material available at <https://doi.org/10.1186/s12916-024-03438-4>

Declarations**Ethics, consent and permissions**

The type and scope of the analyses of the used routine data are regulated in the data protection concept following the European Data Protection Regulation (GDPR). A separate ethics approval was not needed.

Consent for publication

Not applicable.

Availability of data and materials

The IMPELA dataset used and/or analysed during the current study is available on reasonable request. Requests to access these datasets should be directed to <https://www.impela.de/kontakt/>

Competing interests

The authors declare that they have no competing interests. Unrelated to the present work, JMa has worked as a consultant for public health agencies and has received honoraria for presentations/workshops/manuscripts funded by various public health agencies.

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Authors' contributions

LK, CL, JMa, BS, and JR designed the study. JMö analyzed the data and wrote the initial draft of the manuscript. JMa and MM gave important feedback on the analysis and the interpretation of the results. All authors commented on various versions of the manuscript and approved the final version.

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Table 1: Summary statistics of patients with an index episode by clusters

		Total	Addiction-specific care after the index episode				P value
			Cluster 0	Cluster 1	Cluster 2	Cluster 3	
	n	518	276	205	26	11	
Female	%	23.7	26.4	22.9	3.8	18.2	.044
German Nationality	%	90.3	91.2	89.2	88.5	90.9	.806
Age	mean (SD)	50.1 (11.7)	50.4 (12.2)	50.2 (11.3)	47.0 (9.9)	49.5 (8.9)	.546
Comorbidity Score	median	0.0	0.0	0.0	0.0	0.0	.593
	[IQR]	[-2.8, 5.0]	[-3.0, 5.0]	[-1.0, 5.0]	[0.0, 10.3]	[-2.5, 5.0]	
Hospital days within follow-up period	median	21.0	12.0	35.0	38.5	29.0	<.001
	[IQR]	[10.0, 39.0]	[7.0, 21.0]	[21.0, 56.0]	[28.0, 62.0]	[16.5, 42.0]	
% Hospital days due to Alcohol Dependence ¹	median	100.0	100.0	97.0	95.3	100.0	.088
	[IQR]	[72.6, 100.0]	[67.6, 100.0]	[73.7, 100.0]	[88.0, 100.0]	[93.7, 100.0]	
Alcohol specific care/treatment services							
OAC ² prior to Index Episode	%	5.8	2.9	9.8	7.7	0.0	.012
OAC ² follow-up period	%	11.6	4.7	18.5	30.8	9.1	<.001
Total visits	median	2.0	1.0	2.5	4.5	2.0	.091
	[IQR]	[1.0, 5.0]	[1.0, 2.0]	[1.0, 4.8]	[2.8, 5.8]	[2.0, 2.0]	
Pharmacotherapy	%	3.5	0.0	1.5	15.4	100.0	<.001
Qualified Withdrawal Treatment (QWT)	%	29.9	18.8	41.0	61.5	27.3	<.001
Number of started QWT	median	1.0	1.0	1.0	1.0	1.0	<.001
	[IQR]	[1.0, 1.0]	[1.0, 1.0]	[1.0, 2.0]	[1.0, 1.0]	[1.0, 1.0]	
Post-Acute Treatment	%	9.3	0.0	5.9	96.2	100.0	<.001
QWT before Post-Acute Treatment	%	3.9	0.0	1.0	57.7	27.3	<.001
Started rehabilitation	%	6.4	0.0	4.4	92.3	0.0	<.001
QWT before rehab	%	3.1	0.0	1.0	53.8	0.0	<.001
Days between QWT and rehab	median	22.5		59.5	22.5		.427
	[IQR]	[13.5, 38.5]	-	[40.3, 78.8]	[10.5, 29.8]	-	

Notes: SD: Standard Deviation; IQR: Inter Quartiles Range; When nonnormality was assumed, the median instead of the mean is presented, and the p value of the Kruskal–Wallis rank sum test instead of a t test. Variables, where percentages are presented, were compared with a χ^2 -test and Fisher's-exact test for the comparison of the clusters when cell sizes were small.

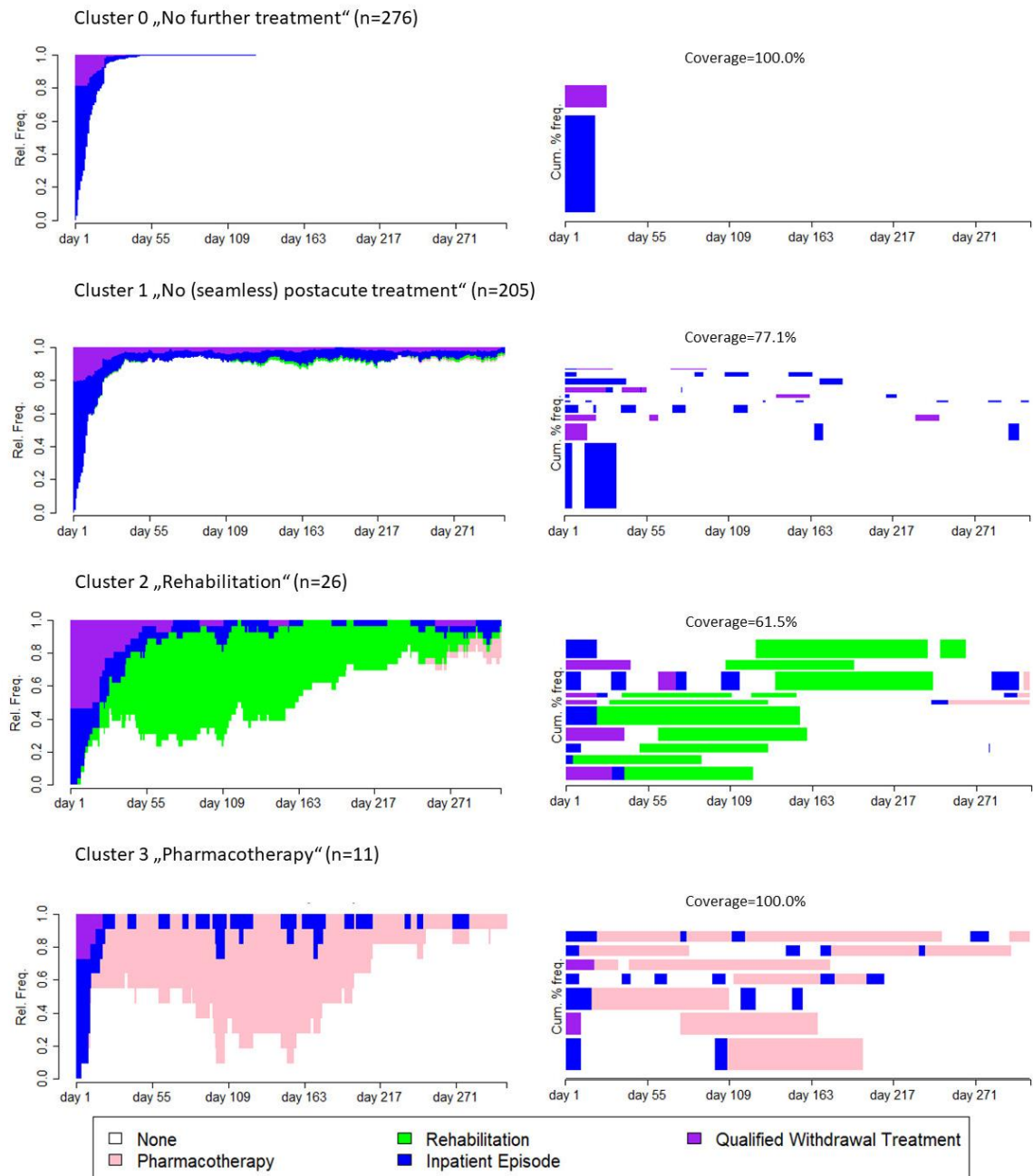
¹⁾ Main diagnosis of Dependence F10.2 or Withdrawal F10.3-4 ²⁾ OAC: Outpatient Addiction Care

Table 2: Multinomial logistic regression for cluster membership

	Cluster 1 ¹		Cluster 2 ¹		Cluster 3 ¹	
	OR	95%-CI	OR	95%-CI	OR	95%-CI
Female (ref.: Male)	0.99	0.64 – 1.54	0.15	0.02 – 1.12	0.61	0.12 – 3.02
Age (centered)	1.00	0.98 – 1.01	0.97	0.94 – 1.01	0.99	0.93 – 1.05
Nationality (ref: Not German)	1.10	0.58 – 2.10	0.83	0.21 – 3.25	0.87	0.10 – 7.42
Comorbidity Score	1.00	0.97 – 1.03	1.03	0.98 – 1.10	1.03	0.94 – 1.14
Inpatient Episode (not F10.2-4) before Index-Episode	1.15	0.67 – 1.98	1.77	0.62 – 5.02	0.00	0.00 – 0.00
% Hospital days due to Alcohol Dependence (F10.2-4) in follow-up period	1.00	1.00 – 1.01	1.01	0.99 – 1.03	1.04	0.99 – 1.10
Outpatient addiction care 60 days before Index Episode	1.39	0.50 – 3.88	0.42	0.07 – 2.59	0.00	0.00 – 0.00
Outpatient addiction care within follow-up period	3.82	1.75 – 8.35	9.35	2.95 – 29.62	3.15	0.34 – 29.03

Notes: Regression parameters in bold signify p value<0.001; OR: Odds-Ratio; CI: 95%-Confidence Interval; ¹ Cluster 0 served as the reference cluster. Based on a sample of 514 patients. Four patients from Cluster 1 (n=2) and Cluster 2 (n=2) were excluded from this analysis due to missing data on nationality

Figure 1: Relative frequency of addiction-specific care services after the index episode and typical pathways by cluster



Notes: Plotted on the left are the relative frequencies of states sorted per day for each cluster. Plotted on the right are the 10 most typical pathways for each cluster by highest neighborhood density bottom up according to their representative score and a bar width proportional to the number of assigned sequences. The neighborhood radius (i.e., the percentage of the maximum theoretical distance between two sequences) was set to 10%. Coverage describes how many sequences are represented by the 10 most typical pathways.

Supplement:**Table S1: Overview of alcohol-related ICD-10 diagnoses**

ICD -10 Codes	Meaning according to ICD-10
F10	Mental and behavioral disorders due to use of alcohol (includes F10.1 -
F10.0	Acute intoxication
F10.1	Harmful use
F10.2	Dependence syndrome
F10.3	Withdrawal state
F10.4	Withdrawal state with delirium
F10.5	Psychotic disorder
F10.6	Amnesic syndrome
F10.7	Residual and late-onset psychotic disorder
F10.8	Other mental and behavioral disorders
F10.9	Unspecified mental and behavioral disorder
E24.4	Alcohol-induced pseudo-Cushing syndrome
E52	Niacin deficiency [pellagra]
G31.2	Degeneration of nervous system due to alcohol
G62.1	Alcoholic polyneuropathy
G72.1	Alcoholic myopathy
I42.6	Alcoholic cardiomyopathy
K29.2	Alcoholic gastritis
K70.-	Alcoholic liver disease
K85.2	Alcohol-induced acute pancreatitis
K86.0	Alcohol-induced chronic pancreatitis
O35.4	Maternal care for (suspected) damage to fetus from alcohol
P04.3	Fetus and newborn affected by maternal use of alcohol
Q86.0	Fetal alcohol syndrome (dysmorphic)
R78.0	Finding of alcohol in blood
T51.-	Toxic effect of alcohol
T51.0	Ethanol
T51.9	Alcohol, unspecified

Figure S1: Month of first inpatient episode due to alcohol dependence (F10.2) or withdrawal (F10.3-4) in the total sample

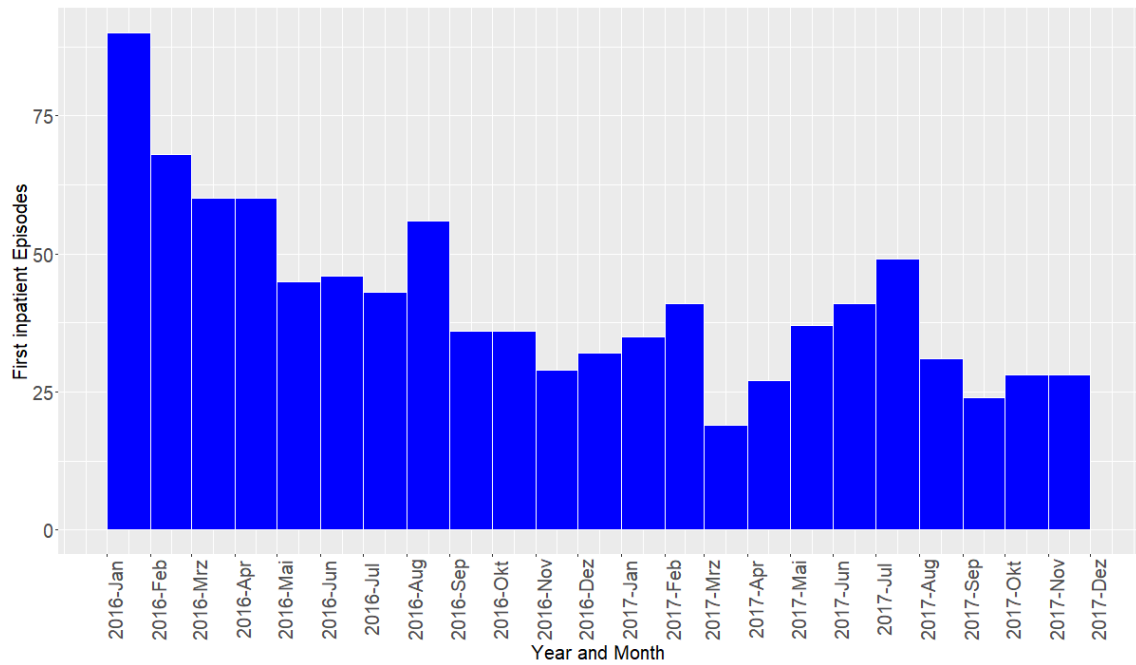


Figure S2: Sequences of addiction-specific care services after an inpatient episode with main diagnosis alcohol dependence (F10.2-4) total and by clusters

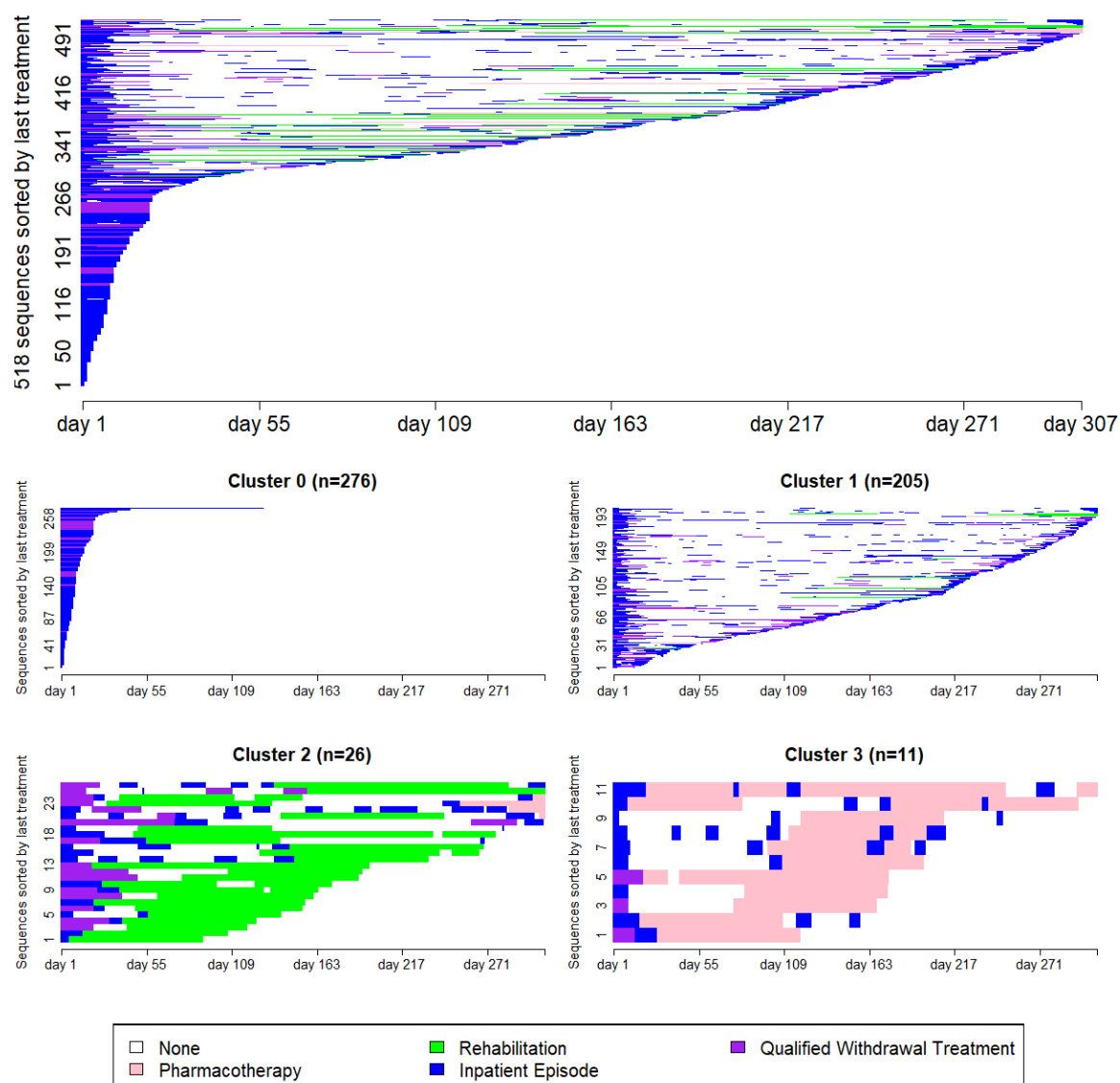
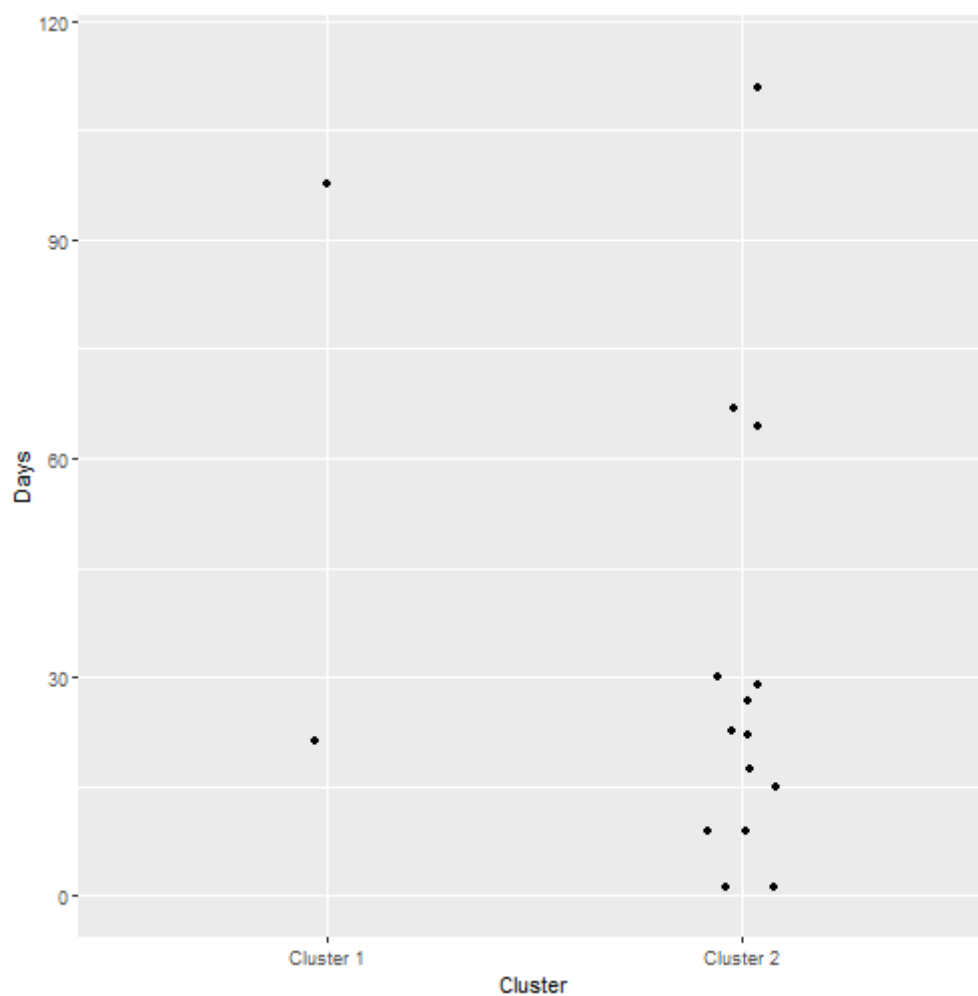


Figure S3: Days between the end of qualified withdrawal treatment and the onset of rehabilitation by cluster



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