Chronic Diseases in High-Cost Users of Hospital, Primary Care, and Prescription Medication in the Capital Region of Denmark

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BACKGROUND: A small proportion of patients account for the majority of health care costs. This group is often referred to as high-cost users (HCU). A frequently described characteristic of HCU is chronic disease. Yet, there is a gap in understanding the economic burden of chronic diseases associated with HCU to different types of health care services.

OBJECTIVE: To analyze which frequent chronic diseases have the strongest association with HCU overall, and HCU in hospital, primary care, and prescription medication.

DESIGN: This is a register-based observational study on Danish health service costs for various diseases in different medical settings.

PARTICIPANTS: A total of 1,350,677 individuals aged ≥ 18 years living in the Capital Region of Denmark by 1 January 2012 were included.

MAIN MEASURES: Chronic diseases, costs, and sociodemographic data were extracted from the nationwide registers, including data from hospitals, primary care, and medicine consumption. These information were merged on an individual level.

KEY RESULTS: Cancer, mental disorders except depression, and heart diseases have the strongest association with HCU overall. Mental disorders except depression were in the three diseases most prevalent in HCU in all the three health care services.

CONCLUSIONS: Our results show that the chronic diseases that have the strongest association with HCU differ between different types of health care services. Our findings may be helpful in informing future policies about health care organization and may guide to different prevention, treatment, and rehabilitation strategies that could lessen the burden in the hospital.

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INTRODUCTION

Health care spending has risen significantly in the past decade in the western part of the world and is expected to be even higher in the future.[1, 2] Studies from the USA and Canada have shown that only 5% of the population accounts for half of total health care costs.[1–5] Data from Denmark provide similar results.[6] This group is often referred to as high-cost users (HCU).

The characterization of HCU has received substantial attention.[7–10] Previous studies have found HCU to be older,[8, 9, 11–13] less educated, have low income,[9] and poorer self-perceived health.[8] Another frequently described characteristic of HCU is multimorbidity.[8–13]

Despite increased interest in chronic diseases, HCU, and the conspicuous development in health care costs, knowledge about which chronic diseases are associated with HCU is very sparse. Few studies have examined the most expensive diseases overall but have been limited to the use of self-reports, private insurances, and hospital admissions.[14–17]

Only a few studies have examined spending across different types of health care services, but not with respect to specific chronic diseases.[10, 18] There is still a gap in understanding the economic burden of chronic diseases to different types of health care services to advice future health care policies and create new models of health care delivery.

The aim of this study was to examine which frequent chronic diseases have the strongest association with HCU overall, and HCU in hospital, primary care, and prescription medication, respectively, based on registry data from an unselected general population.

METHODS

Population and Study Design

The present study is an observational study of register data from all individuals aged ≥ 18 years old living in the Capital Region of Denmark by 1 January 2012. In Denmark, health care coverage is universal, predominantly publicly financed by taxes. All individuals registered as residents in Denmark are entitled to health care that is largely free of charge. Prescription medication is however only partially reimbursed.[19] All public health care services as well as costs are registered in Danish central registers on an individual level.[20] In the present study, information from several Danish registers were linked through a unique Danish person identification number (CPR number) to analyze data on an individual level.[21] According to Danish legislation, register-based studies require legislation permission from the Danish Data Protection Agency (j.nr. 2012-58-0004, KPU-2012-09).

Health Care Costs

Information on costs are registered on the date of discharge from hospital, the date of visit to outpatient clinic, the week of visit to primary care, and the day of purchase of medicine in the period 1 January 2012 to 31 December 2012. Costs are presented in USD (exchange rate 1 USD = 5.6438/1 DKK = 0.1772 USD, 31 December 2012).

Annual Hospital Costs. Hospital annual costs included all somatic and psychiatric hospital admissions and visits in outpatient clinics that are based on specialized hospital units. Costs were calculated using the Danish tariff system of the diagnosis-related groups (DRG) and the Danish Ambulatory Grouping (DAG) defined by the Danish National Board of Health.[22] The DRG and DAG charges for 2012 were used as cost estimates. Information about hospital annual costs on an individual level were retrieved from the Danish National Patient Register (DNPR).[23, 24]

Annual Primary Care Costs. The primary care includes general practitioners (GPs), medical specialists in private practice (primarily ophthalmologists, gynecologists, dermatologists, otorhinolaryngologists, psychiatrists), dentists, physiotherapists, occupational therapists, psychologists, podiatrists, and chiropractors.[20] Data from the primary care was retrieved from the Danish National Health Service Register for Primary Care (NHSR) which contains documented information about the activities of health care professionals contracted with the tax-funded public health care system.[20] For some of the services (dentists, physiotherapists, psychologists, podiatrists, and chiropractors), the costs are divided between the public health care system and the patients' self-payment. The patient's self-payment is however not available and therefore not included in this study.

Annual Prescription Medication Costs. Information on filled prescriptions was retrieved from the National Prescription Register (NPR). NPR includes drug information on dispending data, pharmacy retail price, patient copayment, and reimbursement codes.[25] The retail cost at the date of purchase was used to assign annual costs of prescription drugs. Prescription medication costs were calculated as the sum of the tax-financed drug reimbursement and the citizen's own payment. Prescription medication costs in hospitals are included in hospital costs as part of the DRG charges.

Total Annual Costs. Total annual health care costs were calculated as the sum of all costs of all health care services including hospital annual costs, annual primary care costs, and annual prescription medication costs. Further details on costs are found online in Appendix 1.

Definition of High-Cost Users

HCU were defined as those who ranked in the top 5% according to total annual costs in 2012 in hospital, primary care, and prescription medication, and overall. HCU are categorized in $HCU_{hospital}$, $HCU_{primary\ care}$, and $HCU_{prescription\ medication}$, and $HCU_{overall}$.

Measures of Chronic Disease and Multimorbidity

Definition of chronic diseases is primarily based on relevant diagnoses from DNPR, relevant dispensing of medicine from NPR (2 dispensing within 12 months), and relevant procedures from NHSR. To define prevalence of chronic diseases on 1 January 2012, data from the three registers were used from the previous 5 years (2007–2011). Data from 2011 and 2012 were used to define incidence of disease during 2012. Eleven chronic diseases were included due to their frequency and valid register information: diabetes (types 1 and 2), heart disease, stroke, chronic obstructive pulmonary disease (COPD), asthma, cancer, inflammatory joint disease, osteoporosis, long-term depression (treatment with antidepressant medication ≥ 2 years), mental disorders except depression (schizophrenia, schizotypal mental disorder, paranoid psychoses, acute and transient psychoses, and bipolar affective disorder), and dementia. More details of the definition of the diseases including ICD-10 codes and prescription medication are provided online in Appendix 2. Multimorbidity was categorized in one, two, and ≥ 3 chronic diseases.

Sociodemographic Factors

Sociodemographic factors included age, sex, income, highest achieved education, ethnicity, and cohabitation status. Ethnicity was divided into three groups: Danish, other Western countries, and non-Western countries. Education was categorized into four groups: primary school and secondary school, vocational education, short- and medium-cycle higher

education, and long-cycle higher education. Income was categorized into 6 groups, and cohabitant status was categorized as cohabitating or single. Sociodemographic factors are included as covariates in the adjusted models to focus on the diagnoses. Details on the registers are provided online in Appendix 3.

Statistical Analysis

Characteristics of the total study population, $HCU_{overall}$, $HCU_{hospital}$, $HCU_{primary\ care}$, and $HCU_{prescription\ medication}$ are presented as numbers and percentages. By entering all 11 diseases in separate models, the effect (hazard ratio) of having the diseases is compared with not having the disease. One, two, and greater than or equal to three diseases were compared with having no disease. A sensitivity analysis was performed with all diseases in the same model. Data were analyzed by Cox regression models with time since 1 January 2012 as time scale. To define data of event, costs were accumulated on daily basis for each person during 2012 and the date of reaching the cutoff for HCU was identified and used as date of event. Observations were censured at date of death, date of migration from the Capital Region of Denmark, or 31 December 2012, whichever came first. Each of the 11 chronic diseases was entered in separate models as time-dependent variables with change in value at time of disease incidence. Analyses were performed using SAS version 9.4 (TS1M3 SAS/STAT 14.1). All processing and analyses of data were performed through a remote access to Statistics Denmark.

Table 1 Characteristics of the Study Population and Overall High-Cost Users

	Total study population (n = 1,350,667)		Overall high-cost users (n = 67,534)	
	n	(%)	*n*	(%)
Sex				
Women	698,301	(51.7)	36,810	(54.5)
Men	652,376	(48.3)	30,724	(45.5)
Age group (years)				
18–29	277,167	(20.5)	4509	(6.7)
30–39	250,940	(18.6)	5674	(8.4)
40–49	250,760	(18.6)	7342	(10.9)
50–59	202,573	(15.0)	9675	(14.3)
60–69	192,839	(14.3)	15,082	(22.3)
70–79	109,598	(8.1)	13,840	(20.5)
≥ 80	66,800	(5.0)	11,412	(16.9)
Ethnicity				
Danish	1,134,518	(84.0)	60,522	(89.6)
Other Western countries	77,119	(5.7)	2598	(3.8)
Non-Western countries	139,040	(10.3)	4414	(6.5)
Cohabitation				
Cohabitant	789,599	(58.5)	32,305	(47.8)
Single	561,078	(41.5)	35,229	(52.2)
Education				
Primary school or secondary education	453,504	(35.6)	26,182	(38.8)
Vocational education	373,698	(29.4)	21,814	(32.3)
Short- and medium-cycle higher education	281,963	(22.1)	11,015	(16.3)
Long-cycle higher education	164,108	(12.9)	5045	(7.5)
Income* (USD)				
0 to < 17,719	118,781	(9.1)	2882	(4.3)
17,719 to < 26,578	185,400	(14.1)	15,978	(23.7)
26,578 to < 44,296	320,924	(24.5)	23,418	(34.7)
44,296 to < 66,445	361,826	(27.6)	15,058	(22.3)
66,445 to < 93,002	215,633	(16.4)	6601	(9.8)
≥ 93,002	109,896	(8.4)	3025	(4.5)

**Missing data. Missing data on income variable is due to citizens with no income or citizens who have not been living in Denmark for the last 5 years*
n number

RESULTS

The study included 1,350,677 individuals ≥ 18 years old living in the Capital Region of Denmark at 1 January 2012. Out of these, a total of 67,534 were ranked in the top 5% ($HCU_{overall}$) according to total annual costs in 2012 with 36,810 women and 30,724 men (Table 1). In 2012, 77% were hospital costs (3,612,887,668 USD as shown in app 4); 13%, primary care costs (585,599,004 USD as shown in app 4); and 10%, prescription medication costs (480,967,464 USD) (online material: Appendix 4). The cutoffs for HCU are also provided online in Appendix 4. Total costs of the top 5% ($HCU_{overall}$) were 2,519,655,536 USD which corresponds to 53.8% of total annual costs.

The $HCU_{overall}$ population tended to be older, of Danish ethnicity, single, having short education, and have an annual income between 17,719 and 26,578 USD (Table 1). Further description of the populations of $HCU_{hospital}$, $HCU_{primary\ care}$, and $HCU_{prescription\ medication}$ is presented online in Appendix 5.

In the unadjusted models, model 1, the hazard ratio (HR) for $HCU_{overall}$ was strongest for cancer, stroke, and heart disease (Table 2). In the fully adjusted model, model 2, HR was attenuated (Table 2): six times as many patients with cancer were HCU (HR 6.23 (95% CI, 6.11, 6.35)), four times as many patients with mental disorders except depression were HCU, and three times as many patients with heart disease were HCU compared with those without these diseases.

The sensitivity analyses, including all diseases (online material: Appendix 6), show that HR was attenuated for all diseases for $HCU_{overall}$ except for long-term depression and mental disorders except depression compared with models 1 and 2 in Table 2.

HR for $HCU_{hospital}$ differed slightly from $HCU_{overall}$ (Table 3). For $HCU_{primary\ care}$, HR was strongest for mental disorders except depression with almost three times (HR 2.84 (95% CI, 2.77, 2.92)) as many patients being HCU compared with those without this disease followed by long-term depression and stroke (Table 3). The strongest HR for $HCU_{prescription\ medication}$ was mental disorders except depression (HR 6.13 (95% CI, 6.00, 6.26)) with six times as many patients being HCU compared with those without this disease followed by COPD and diabetes (Table 3).

The association between number of chronic diseases and HCU is presented in Table 4. For $HCU_{overall}$, more than five times as many patients with one chronic disease were HCU (HR 5.24 (95% CI, 5.11, 5.36)) and almost 17.5 times as many

Table 2 Prevalence of Chronic Diseases in the Total Population and Among Overall HCU, and the Associations Between Chronic Diseases and Overall HCU

	Total population ($n = 1,350,677$)		Overall high-cost users ($n = 67,534$)		Overall high-cost users			
	n	(%)	*n*	(%)	Model 1		Model 2	
					HR	HR (95% CI)	HR	HR (95% CI)
Diabetes	62,891	(4.7)	9708	(14.4)	3.69	(3.62, 3.77)	2.00	(1.96, 2.05)
Heart disease	59,606	(4.4)	12,107	(17.9)	6.54	(6.42, 6.66)	3.12	(3.06, 3.18)
Stroke	27,916	(2.1)	5601	(8.3)	6.69	(6.53, 6.85)	3.08	(3.00, 3.15)
COPD*	38,346	(4.0)	8343	(12.4)	5.07	(4.97, 5.18)	3.04	(2.97, 3.11)
Asthma	68,049	(5.0)	4721	(7.0)	1.41	(1.37, 1.45)	1.38	(1.34, 1.42)
Cancer	44,082	(3.3)	10,903	(16.1)	10.48	(10.30, 10.67)	6.23	(6.11, 6.35)
Inflammatory joint diseases	32,464	(2.4)	6367	(9.4)	4.59	(4.47, 4.71)	2.69	(2.62, 2.76)
Osteoporosis	34,644	(2.6)	6060	(9.0)	4.10	(3.99, 4.20)	1.94	(1.88, 1.99)
Long-term depression	67,277	(5.0)	7759	(11.5)	2.51	(2.45, 2.57)	1.85	(1.81, 1.89)
Mental disorders except depression	38,501	(2.9)	8774	(13.0)	5.83	(5.70, 5.96)	4.28	(4.18, 4.38)
Dementia*	10,191	(3.7)	1778	(2.6)	2.13	(2.04, 2.22)	1.62	(1.54, 1.69)

Individuals may appear in more than one disease group
**COPD variable only includes individuals ≥ 35 years. Dementia variable only includes individuals ≥ 65 years*
Model 1, unadjusted; model 2, adjusted for sex, age, ethnicity, education, income, and cohabitant status
HR hazard ratio, CI confidence interval, n number

patients with three or more chronic diseases were HCU (HR 17.58 (95% CI, 17.00, 18.18)) compared with those with no chronic disease. For $HCU_{prescription\ medication}$, ten times as many patients with one chronic disease were HCU (HR 10.03 (95% CI, 9.77, 10.29) and more than 45 times as many patients with three or more chronic diseases were HCU (44.23 (95% CI, 44.23, 47.23) compared with those with no chronic disease.

DISCUSSION

To our knowledge, this is the first study to examine HCU among patients with chronic diseases across different types of health care services in an unselected general population based on registry data. In this large population-based study of more than 1.3 million individuals, we have examined the association between 11 frequent chronic diseases and their association with HCU. In the fully adjusted analysis, we found that for $HCU_{overall}$, six times as many patients with cancer were HCU, four times as many patients with mental disorders except depression were HCU, and three times as many patients with heart disease were HCU compared with those without these diseases. Several studies have examined the characteristics of HCU, showing that HCU are characterized by the presence of multiple chronic diseases.[8–13] Despite this strong association, studies examining specific chronic diseases associated with HCU are very sparse.[1, 11, 17] One study from 2015, based on The Medical Expenditures Panel Survey which provides a representative estimate of health care use and costs for the US civilian non-institutionalized population, did find the most costly diseases to be cancer, mental disorders, heart diseases, and arthritis, and other non-traumatic disorders[17] which is in line with our results. An explanation for cancer to be highly associated with HCU may be due to very high and rising expenses for cancer drugs.[26] The high costs incurred by patients with cancer may also stem from the increasing number of available and expensive treatments even with disease progression. Specialized palliative care may support a timely cessation of chemotherapy at the end of life as demonstrated in observation and experimental studies.[27, 28]

Only two studies have examined spending by types of health care services,[10, 18] but not specified on chronic diseases. Furthermore, none of these studies[10, 18] have results on the primary care. In 2011, Conway and colleagues found that the

Table 3 Associations Between Chronic Diseases and HCU in Hospital, Primary Care, and Prescription Medication

Chronic disease	High-cost users, HR (95% CI)					
	$HCU_{hospital}$		$HCU_{primary\ care}$		$HCU_{prescription\ medication}$	
Diabetes	1.83	(1.79, 1.87)	1.90	(1.85, 1.95)	4.93	(4.84, 5.02)
Heart disease	2.97	(2.91, 3.03)	2.00	(1.95, 2.05)	3.00	(2.93, 3.06)
Stroke	2.97	(2.90, 3.05)	2.20	(2.13, 2.27)	2.04	(1.99, 2.10)
COPD	2.81	(2.75, 2.87)	1.74	(1.69, 1.79)	5.33	(5.23, 5.43)
Asthma	1.30	(1.26, 1.34)	1.80	(1.75, 1.84)	2.94	(2.88, 3.01)
Cancer	6.36	(6.24, 6.48)	1.24	(1.20, 1.28)	1.44	(1.41, 1.49)
Inflammatory joint diseases	2.62	(2.55, 2.69)	2.19	(2.12, 2.25)	1.94	(1.88, 1.99)
Osteoporosis	1.81	(1.76, 1.86)	1.60	(1.55, 1.65)	2.11	(2.05, 2.17)
Long-term depression	1.73	(1.69, 1.77)	2.55	(2.50, 2.61)	2.63	(2.57, 2.68)
Mental disorders except depression	3.91	(3.81, 4.00)	2.84	(2.77, 2.92)	6.13	(6.00, 6.26)
Dementia	1.48	(1.41, 1.55)	1.09	(1.02, 1.16)	4.09	(3.94, 4.23)

Analyses are adjusted for sex, age, ethnicity, education, income, and cohabitant status. Individuals may appear in more than one disease group
HR hazard ratio, CI confidence interval

Table 4 Multimorbidity

High-cost users, HR (95% CI)								
Multimorbidity	**$HCU_{overall}$**		**$HCU_{hospital}$**		**$HCU_{primary\ care}$**		**$HCU_{prescription\ medication}$**	
1 chronic disease	5.24	(5.11, 5.36)	4.61	(4.51, 4.72)	2.43	(2.38, 2.48)	10.03	(9.77, 10.29)
2 chronic diseases	9.76	(9.48, 10.06)	8.01	(7.78, 8.24)	3.81	(3.72, 3.92)	24.74	(24.03, 25.48)
≥ 3 chronic diseases	17.58	(17.00, 18.18)	13.51	(13.06, 13.97)	5.23	(5.06, 5.41)	45.71	(44.23, 47.23)

Analyses are adjusted for sex, age, ethnicity, education, income, and cohabitant status
HR hazard ratio, CI confidence interval

majority (47%) of health care spending was related to chronic diseases of where 29.9% was attributable to inpatient and 34.8% to prescription medicine.[18] We found that chronic diseases having the strongest association with $HCU_{hospital}$ were similar to $HCU_{overall}$. Since most health care costs are hospital costs, this may explain why $HCU_{overall}$ and $HCU_{hospital}$ are similar. Hayes et al. showed that HCU were more than three times more likely to be hospitalized compared with non-HCU,[9] while Joynt et al. found that HCU accounted for 79% of inpatient costs.[11] Our results along with these studies[9, 11] demonstrate that HCU represent a major burden in the hospital. A reason why almost four times as many patients with mental disorders except depression were $HCU_{hospital}$ may be that patients with mental disorders have been reported to be at increased risk of somatic comorbidity[29] and higher risk of hospitalization.[30]

Chronic diseases associated with $HCU_{primary\ care}$ differed from those associated with $HCU_{hospital}$. The strongest association between chronic diseases and $HCU_{primary\ care}$ was found for mental disorders except depression with almost three times as many patients being HCU compared with those without this disease followed by long-term depression. A reason that both mental disorders except depression and long-term depression have a very strong association with $HCU_{primary\ care}$ may be caused by a political decision of prioritizing psychiatric treatment in the primary care. Our results showed that the association between the studied chronic diseases and $HCU_{primary\ care}$ was similar, likely because all chronic diseases are partially managed in primary care with similar time slots across diagnoses and therefore have a corresponding consumption of resources.

Chronic diseases associated with $HCU_{prescription\ medication}$ also differed from those associated with $HCU_{hospital}$, showing the strongest association between mental disorders except depression and $HCU_{prescription\ medication}$ with six times as many patients being HCU compared with those without this disease. COPD and diabetes did also have a strong association with $HCU_{prescription\ medication}$, while cancer showed to have the weakest association with $HCU_{prescription\ medication}$ which is mainly because antineoplastic treatment is provided by hospitals.

One, two, three, and more chronic diseases were compared with individuals with none of the studied chronic diseases. This is reflected by a strong association between any chronic disease and HCU in all three health care services that gets stronger with the addition of more chronic diseases. For $HCU_{prescription\ medication}$, 46 times as many patients with three or more chronic diseases were HCU. This demonstrates the economic burden associated with long-term pharmaceutical treatment of chronic diseases. This finding is supported by the aforementioned study by Conway et al.[18] In Denmark, patients' annual spending on prescription medication is covered by the state if it exceeds 620 USD.

This study has several strengths. All adults in the Capital Region of Denmark were included in this study. Hence, the study population comprises one-third of the Danish adult population which too has the same life expectancy as the adult population in the rest of the country.[31] Therefore, our population is highly comparable with the Danish population. By using register data, we were able to avoid recall bias on chronic diseases, hospital admissions, disease control in outpatient clinics and GPs, and prescription medication purchases. We have included all costs for each patient and not disease-related costs only. However, except for prescription medication, we did not have any information on the patient's self-payment. By defining diseases primarily through hospital diagnoses and prescription medication purchases, and not on diagnoses in general practice, we may have underestimated the prevalence of diseases primarily controlled by GPs and consequently also their costs in primary care. As such, asthma which is primarily treated by GPs is not strongly associated with $HCU_{primary\ care}$. In the models, in Tables 2 and 3, individuals may appear in more than one disease group. To adjust for this, we made an additional sensitivity analysis (online material: Appendix 6) which showed that the association between chronic diseases and $HCU_{overall}$ attenuated for most diseases compared with the associations in Tables 2 and 3.

In conclusion, we found that cancer, mental disorders except depression, and heart disease had the strongest association with $HCU_{overall}$. Cancer also had the strongest association with $HCU_{hospital}$ while mental disorders except depression were in the three diseases most prevalent in HCU in all three health care services. For $HCU_{prescription\ medication}$, mental disorders except depression had the strongest association with HCU. Our results show that frequent chronic diseases associated with HCU differ between types of health care services. There may be clinical indications for this such as cancer treatment mainly taking place in hospitals, and political priorities may also allocate resources to particular types of health care services for some diseases. Knowledge of this study may be helpful to inform future policies about health care organization and guide to different prevention, treatment, and

rehabilitation strategies that could lessen the burden in the hospital. If more resources in the health care sector are moved from the hospital to the primary care, it might be possible to treat more patients in the primary care where the costs of treatment are lower. However, this does only include diseases that can be handled in the primary care and does not include for instance cancer. The results of this study call for further research into the dynamics of individuals becoming HCU and the relationship with chronic diseases.

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