Journal of Psychosomatic Research 165 (2023) 111137

Contents lists available at ScienceDirect

Journal of Psychosomatic Research

journal homepage: www.elsevier.com/locate/jpsychores

The burden of somatic diseases among people with alcohol- and drug use disorders are influenced by mental illness and low socioeconomic status. A registry-based cohort study in Norway

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ARTICLE INFO

Keywords:
Alcohol use
Diseases
Drug use
Mental illness
Somatic diseases
Substance use
Socioeconomic status

ABSTRACT

Objectives: Persons with alcohol use disorder (AUD) and drug use disorder (DUD) have a lower life expectancy than the general population. We examined the burden of somatic diseases among persons with AUD or DUD and investigated impact of socioeconomic status (SES) and mental health disorders on the co-occurrence of somatic diseases in these groups.

Methods: We performed a retrospective, register-based cohort study with a 6-year follow-up of persons (aged ≥18 y) with AUD (13,478) or DUD (16,659). Cox regression analyses were used to estimate hazard ratios (HRs) of somatic diseases.

Results: Patients with DUD were, on average, 10 years younger at the point of diagnosis than patients with AUD. Mental illnesses were prominent in both groups (AUD: 40.5%, and DUD: 46.9% vs 3.5% in controls). Adjusting for mental disorders, the risk of all somatic diseases among the AUD and DUD groups was reduced by 30%. Some of the elevated risk of somatic diseases among persons with AUD and DUD is explained by low SES, though less than that explained by the presence of mental disorders. The diseases with highest risk among AUD patients were metabolic disorders (16.9-fold) and hypertension (14.8-fold), and among AUD patients, viral hepatitis (23.3-fold), after adjusting for low SES and mental disorders.

Conclusions: Persons with AUD had a higher risk of most somatic diseases, while those with DUD had specific risks for infections and viral hepatitis. Mental health disorders and SES adjusted the associations regarding most somatic diseases. In general, improvement of socio-economic conditions, preferably in combination with professional support to self-manage mental health problems, will reduce the risk of somatic illness in both groups. For DUD patients, available sterile user equipment will reduce the risk of viral hepatis.

1. Introduction

Substance use disorders (SUD), which include alcohol use disorders (AUD) and drug use disorders (DUD), when comorbid with somatic diseases, are associated with poorer health outcomes, more complex clinical organization and management of health services, and greater consumption of such services and associated costs [11,12]. Such co-occurrence of SUD and somatic disorders is regarded as a potent determinant of quality of life and premature death [57], and thus poses a substantial challenge for individuals, families, health care, and society in general (De Hert et al., 2011).

The lifetime prevalence of AUDs is approximately 8%, and for illicit DUD it is 2%–3% [13,36,51]. Norwegian figures show large variations in estimates for alcohol use disorders in the past year, with 5–16% in men and 2–6% in women [26]. A more recent survey, from 2001, showed that 17% of the sample scored within the WHO-recommended limits for simple advice and/or further monitoring, including 2%, who scored above the limit for the two most serious risk categories. Risky drinking was most prevalent among men, especially those aged 16–50. Among women, most risky drinking occurred in the 16–30 age group. The

Abbreviations: SUD, Substance use disorder; AUD, Alcohol use disorder; DUD, Drug use disorder; SES, Socioeconomic status; NPR, Norwegian Patient Registry; ICD, International Classification of Diseases; HR, Hazard risk ratio; CI, Confidence interval; CVD, Cardiovascular disease.

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https://doi.org/10.1016/j.jpsychores.2022.111137
Received 2 March 2022; Received in revised form 22 December 2022; Accepted 22 December 2022
Available online 23 December 2022

Norwegian Institute of Public health has estimated an incidence of 5–8% of the adult population, that is, approximately 175–350,000 people. The figures on the proportion using illicit drugs in Norway are uncertain, but in 2016 it was estimated that between 78,000 and 120,000 men and between 42,000 and 73,000 women aged 15 to 59 had used illicit drugs in a year, while between 10,000 and 18,000 of them had injected heroin [38].

Both men and women with SUD have significantly higher risks of a comprehensive spectrum of somatic diseases, both as disease events and as causes of death, relative to individuals from the general population [9]. A meta-analysis showed that research has mainly focused on co-morbidity between SUD, severe mental illness, and cardiometabolic diseases, while few studies have focused on SUD and metabolic diseases [55,56]. To date, in Norway there has been little research on somatic diseases in patients with SUD, especially focusing on AUD and DUD separately.

Mental disorders, including substance use disorders (SUD), are often accompanied by co-morbid somatic diseases and a higher risk of mortality [18]. Incidence rates for somatic illness seem to be over twice as high among SUD patients, when comparing to population-based controls [1,16]. According to De Hert [12] around 60% of all-cause mortality among patients with a severe mental illness, is due to somatic diseases. Further, the increased risks for diabetes, cardiovascular diseases, hepatitis, lung disease (including tuberculosis) and stomatognathic disease among patients with serious mental illness, compared to the general population are even higher in the presence of a co-occurring substance use disorder (De Hert. et al., 2011). A population-based study from Finland, showed that excess mortality in patients with severe mental illness was assessed in three common categories: psychotic disorders, SUD, and mood disorders (De Hert. et al., 2011) with the highest excess mortality being found among SUD patients [31]. Patients with SUD also have higher prevalence of infectious and digestive diseases, compared to patients with other mental disorders [18].

The current state of knowledge concerning comorbidities between SUD and somatic diseases in Norway is incomplete. Nevertheless, knowledge about somatic diseases on AUD and DUD patients, including the effects of SES and mental illness, is highly relevant for the management and organization of health services. It is also important for diagnostic and nosological reasons, for treatment, and for etiological research on co-occurring disorders. In this study, we examined the burden of a wide range of somatic disorders among those with AUD or DUD, separately. Further, we investigated the moderating effect of SES and mental disorders on the co-occurrence of somatic disease among these groups.

2. Method

2.1. Study design and population

This was a register-based cohort study combining SES information from Statistics Norway with information, on both somatic diseases and mental disorders, obtained from the Norwegian Patient Registry (NPR). The sampling framework consisted of all individuals aged ≥18 y who were legally resident in Norway from January 1, 2008 (n = 4,652,365).

We identified 13,478 (0.32%) and 16,559 (0.39%) subjects who had been diagnosed with AUD and DUD, respectively, during the previous two years (2008–2009). They were followed until the registration of somatic diseases from January 1, 2010, through December 31, 2016. We also included the general population (n = 4,255,000) who were not diagnosed with SUD during the same two years (2008–2009) as a control group. Those who were registered as deceased (n = 363,783) during the study period (2008–2016) were excluded from the analyses.

2.2. Event outcomes and explanatory variables

The NPR holds data on all registered diagnoses obtained during initial contact between a patient and specialist health care services. All diagnoses were received during outpatient and inpatient consultations at specialist health care clinics and were in accordance with the International Classification of Diseases (ICD 10th). Table 1 presents the dichotomous variables representing AUD and DUD as explanatory variables and a wide range of specific somatic diseases as event outcomes, including the year of diagnosis.

2.3. Moderators and covariates

Mental disorders were diagnosed based on ICD-10, Chapter V on Mental and Behavioral Disorders. Diagnoses were provided by psychologists or psychiatrists during outpatient and inpatient consultations as part of the specialist mental health care service. We created dummy variables (0 and 1) on whether an individual was diagnosed for any mental disorders (except SUD) between 2010 and 2016. We included being a recipient of social benefits as an index for low SES. Social benefits, refer to economic social assistance which a person receives when they are unable to support themselves. In Norway this financial assistance is due to an imbalance between a person's expenses and income, related to what is deemed necessary for subsistence by the government. Thus, it has been regarded as a satisfactory proxy measure of low SES. Further dummy variables (0 and 1) were constructed to indicate whether participants had received social benefits from 1992 to 2009. Covariates included age (measured continuously) and gender (coded 1 for male and 2 for female).

2.4. Statistical analysis

Cox proportional regression models were applied to estimate the risks of somatic diseases (event outcomes) among persons with AUD or

Table 1
ICD-10 codes and year of diagnosis for explanatory and event outcome variables.

	ICD-10 codes	Year of diagnosis
Explanatory (independent) variables		
AUD	F10	2008–2009
DUD	F11-F19	2008–2009
Event outcome variables		
Cardiovascular diseases		
Hypertensive	I10-I19	2010–2016
Ischemic	I20-I29	2010–2016
Pulmonary	I26-I28	2010–2016
Cerebrovascular	I60-I99	2010–2016
Endocrine, nutritional, and metabolic diseases		
Diabetes melitius	E10-E14	2010–2016
Malnutrition	E40-E46	2010–2016
Obesity	E66	2010–2016
Metabolic	E70-E90	2010–2016
Cancer		
Digestive	C00-C26	2010–2016
Respiratory	C30-C38	2010–2016
Soft tissue	C40-C49	2010–2016
Reproductive organs	C50, C51-C58 & C60-C68	2010–2016
Endocrine and nervous system	C69-C80	2010–2016
Blood	C81-C96	2010–2016
Infectious diseases		
Viral Hepatitis	B15-B19	2010–2016
Influenza and pneumonia	J09-J18	2010–2016
Chronic lower respiratory	J40-J47	2010–2016
Skin diseases		
Infections of the skin and subcutaneous tissue	L00-L08	2010–2016
Dermatitis and eczema	L20-L30	2010–2016
Papulosquamous	L40-L45	2010–2016
Urticaria and Erythema	L50-L54	2010–2016

AUD = alcohol use disorders; DUD = drug use disorders; ICD = The International Classification of Diseases, 10th Revision.

DUD (independent risk factors). Hazard risk ratios (HRs) with 95% confidence intervals (CIs) were reported, with calendar date as the underlying time axis. A stepwise regression was applied: Model 0 presents unadjusted HR estimates; HR estimates in Model 1 were adjusted for age and gender differences, and Models 2 and 3 present HR estimates adjusted to SES and comorbid mental disorders, respectively. Estimates were judged as statistically significant at $p \leq 0.05$. The analyses were performed using Stata SE/16 (https://www.stata.com/install-guide/).

2.5. Ethical approval

All study procedures were approved by the Norwegian Regional Committee for Medical and Health Research Ethics (ref: 17/26919–5). The NPR data is available for research on request from a research institution and at a certain cost.

3. Results

3.1. Description of the study population

The study population is described in Table 2. In the general population, over 56% were male in comparison with 67% in the AUD group and 64% in the DUD group. The prevalence of mental disorders is 3.5% in the general population, while approximately 40% of those with AUD and 47% of those with DUD have such disorders. Compared with the general population, persons with AUD are four times more likely to be a recipient of social welfare, while those with DUD are almost six times as likely. The prevalence of most somatic diseases was at least twice as high in those with AUD or DUD compared with the general population.

3.2. Risk of somatic diseases among persons with AUD or DUD

In Tables 3 and 4, we present the results (HR with 95% CI) from the Cox regression models, where somatic diseases are added as an event outcome. In Table 3, AUD status was added as the explanatory independent variable. In Table 4, DUD was added as the explanatory independent variable. A stepwise regression model was applied, where HR estimates in Model 0 were unadjusted; Model 1 included adjusted estimates for age and gender; and then SES and mental disorders were added in Models 2 and 3, respectively.

Table 3 presents the results for AUD. All age- and gender-adjusted HR outcomes in Model 1 show that persons with AUD had higher risk of all somatic diseases compared with the general population, ranging from two-fold for blood cancer to 23-fold for viral hepatitis. In Models 2 and 3, after adjusting for the SES indictor (being a recipient of social welfare) and mental illness, AUD was still associated with higher risk of somatic diseases, ranging from 1.4-fold for blood cancer to 8-fold for malnutrition. Adjustment for the SES indicator reduced the risk of CVD by about 7% to 13%; 14% to 30% for endocrine, nutritional, and metabolic disorders; 3% to 12% for cancer; 16% to 68% for infectious diseases; and 7% to 14% for skin diseases. In Model 3, adjustment for mental disorders substantially attenuated the risk of all somatic diseases among persons with AUD; thus, the risk of all somatic diseases reduced by at least 30%.

Table 4 presents the results for subjects with DUD. All age- and gender-adjusted HR values in Model 1 showed that DUD was associated with higher risks of somatic diseases, from 0.7-fold for soft-tissue cancer to 138-fold for viral hepatitis. In Models 2 and 3, after adjusting for the SES indictor and mental disorders, the risk for viral hepatitis remained high (43.5-fold). Adjustment for the SES indicator reduced the risk of cardiovascular diseases (CVDs) by about 26% to 68%; 35% to 55% for endocrine, nutritional, and metabolic disorders; 15% to 32% for cancers of digestive, respiratory, endocrine, and nervous, and CV systems; 37%

Table 2
Characteristics of the study population.

	General population (N = 4,225,000; 100%)		AUD (*N* = 13,478; 100%)		DUD (*N* = 16,559; 100%)	
Variables	N	%	N	%	N	%
Gender						
Men	2,392,518	56.3	9037	67.1	10,638	64.2
Women	1,862,457	43.7	441	32.9	5921	35.8
Age (years): Mean (SD)	45.4	17.8	45.4	14.2	34.7	11.4
Mental disorders	144,505	3.5	5453	40.5	7768	46.9
Recipient of social welfare: Mean (SD)	0.05	0.3	0.6	1.2	1.6	1.7
Cardiovascular diseases						
Hypertension	339,876	7.9	2004	14.8	867	5.2
Ischemic heart	193,922	4.6	1238	9.2	702	4.2
Pulmonary heart	22,206	0.5	176	1.3	190	1.1
Cerebrovascular	83,776	2.7	855	6.3	395	2.4
Endocrine, nutritional, and metabolic diseases						
Diabetes melitius	173,084	4.1	1116	8.3	704	4.2
Malnutrition	24,328	0.6	440	3.3	334	2.0
Obesity	65,606	1.5	374	2.8	482	2.9
Metabolic	179,600	4.2	2282	16.9	1636	9.8
Cancer						
Digestive	33,532	0.8	226	1.7	70	0.4
Respiratory	9429	0.2	91	0.7	45	0.2
Soft tissue	100,022	2.3	244	1.8	152	0.9
Reproductive organs	108,714	2.5	435	3.2	208	1.3
Endocrine and nervous system	32,599	0.8	167	1.2	75	0.4
Blood	17,328	0.4	52	0.4	42	0.2
Infectious diseases						
Viral Hepatitis	11,035	0.3	297	2.2	3857	23.3
Influenza and pneumonia	97,278	2.3	1175	8.7	1358	8.2
Chronic lower respiratory	164,386	3.8	1749	12.9	1435	8.7
Skin diseases						
Infections of skin and subcutaneous	61,709	1.4	642	4.8	2367	14.3
Dermatitis and eczema	125,942	2.9	653	4.8	673	4.1
Papulosquamous	75,794	1.8	461	3.4	404	2.5
Urticaria and Erythema	17,896	0.4	73	0.5	124	0.7

AUD = alcohol use disorders; DUD = Drug use disorders.

Table 3
Stepwise Cox regression models showing hazard risks of somatic diseases among persons with AUD ($n = 13,478$).

Event outcomes	Model 0 HR (95% CI)	Model 1 HR (95% CI)	Model 2 HR (95% CI)	Model 3 HR (95% CI)
Cardiovascular diseases				
Hypertension	5.7 (4.8–5.3)	5.3 (5.1–5.6)	4.9 (4.5–5.2)	3.3 (3.2–3.5)
Ischemic heart	5.3 (5.0–5.6)	5.4 (5.1–5.7)	4.8 (4.5–5.1)	3.2 (3.0–3.4)
Pulmonary heart	7.2 (6.2–8.3)	7.6 (6.5–8.8)	6.6 (5.7–7.7)	3.9 (3.4–4.6)
Cerebrovascular	8.9 (8.3–9.6)	9.6 (9.1–10.4)	8.5 (7.9–9.2)	4.9 (4.6–5.3)
Endocrine, nutritional, and metabolic diseases				
Diabetes mellitus	4.8 (4.6–5.2)	4.9 (4.6–5.2)	4.0 (3.8–4.3)	2.4 (2.3–2.6)
Malnutrition	19.2 (17.4–21.1)	20.8 (18.9–22.8)	17.0 (15.5–18.8)	8.1 (7.3–8.9)
Obesity	4.7 (4.3–5.3)	5.2 (4.7–5.8)	3.6 (3.3–4.1)	1.6 (1.5–1.8)
Metabolic	11.4 (10.9–11.9)	11.9 (11.4–12.4)	10.2 (9.8–10.6)	5.6 (5.3–5.8)
Cancer				
Digestive	6.2 (5.4–7.1)	6.7 (5.8–7.6)	6.2 (5.5–7.1)	4.5 (3.9–5.1)
Respiratory	9.6 (7.8–11.8)	10.2 (8.3–12.6)	8.9 (7.2–11.0)	6.2 (4.9–7.7)
Soft tissue	2.3 (2.0–2.6)	2.5 (2.2–2.9)	2.7 (2.3–3.0)	1.9 (1.7–2.1)
Reproductive organs	3.1 (2.8–3.3)	3.3 (2.9–3.6)	3.2 (2.9–3.5)	2.3 (2.1–2.5)
Endocrine and nervous system	5.1 (4.4–5.9)	5.4 (4.6–6.3)	5.1 (4.3–5.9)	3.4 (2.8–3.9)
Blood	2.1 (1.6–2.7)	2.2 (1.7–2.8)	2.0 (1.5–2.7)	1.4 (1.1–1.8)
Infectious diseases				
Viral hepatitis	21.8 (19.4–24.5)	22.6 (20.2–25.4)	7.3 (6.4–8.3)	4.8 (4.3–5.5)
Influenza and pneumonia	11.1 (10.5–11.8)	11.6 (10.9–12.3)	9.7 (9.1–10.2)	5.0 (4.7–5.3)
Chronic lower respiratory	8.9 (8.5–9.3)	9.2 (8.7–9.7)	7.7 (7.3–8.1)	4.4 (4.1–4.6)
Skin diseases				
Infections of skin and subcutaneous tissue	5.6 (3.5–9.1)	5.9 (3.6–9.5)	5.5 (3.4–8.9)	3.0 (1.8–4.9)
Dermatitis and eczema	4.7 (4.4–5.1)	4.9 (4.6–5.4)	4.4 (4.0–4.7)	2.4 (2.2–2.6)
Papulosquamous	4.7 (4.3–5.2)	4.8 (4.4–5.3)	4.3 (3.9–4.7)	2.7 (3.5–3.0)
Urticaria and erythema	3.8 (2.9–4.7)	4.1 (3.3–5.2)	3.5 (2.7–4.4)	1.9 (1.5–2.5)

Model 0, unadjusted estimates; Model 1, estimates adjusted for age and gender; Model 2, estimates adjusted for recipient of social welfare (SES indicator); Model 3, estimates adjusted for psychiatric comorbidity. All models are adjusted for covariates in earlier models. AUD, alcohol use disorders; HR, hazard risk; CI, confidence interval; all estimates are significant at $p < 0.001$.

to 56% for infectious diseases; and 20% to 32% for skin diseases. In Model 3, adjustment for comorbid mental disorders substantially reduced the risk of all somatic diseases among persons with DUD by at least 30%. Moreover, the risk of diabetes and obesity, cancers of reproductive organs, the endocrine and nervous system, and blood, and infections of the skin and subcutaneous tissues was fully attenuated after adjusting for comorbid mental disorders.

4. Discussion

Using data from a nationally representative sample, the present investigation examined the prospective associations of AUD and DUD, mental disorders, and socioeconomic status with transitions to somatic diagnosis during a 6-year period. Mental illness and socioeconomic status greatly increased the participants risk for somatic diseases. The study shows that there are notable differences in the type of somatic diseases that affect patients with AUD and DUD, respectively. The AUD and DUD comorbidity were managed by utilizing the primary diagnosis on the registry data as the primary cause for concern. Nevertheless, from clinical experience, it is reasonable to anticipate heterogeneity in the AUD and DUD groups with regard to misuse; many patients use different types of legal and illegal drugs at different periods.

4.1. Mental illness has a strong impact on somatic health

Importantly, when adjusting for mental disorders, the risk of all somatic diseases among the AUD and DUD groups was reduced by at least 30%. Among persons with DUD, when adjusting for mental disorders, the risk of diabetes, obesity, cancers of reproductive organs, the endocrine and nervous system, and blood, and infections of the skin and subcutaneous tissue was fully attenuated after adjusting for mental disorders.

The consistent and substantial comorbidity between both AUD and DUD groups and a spectrum of mental disorders is well documented ([10]; De Hert et al., 2011; [20,34,39]). And, more than two-thirds of patients admitted to SUD treatment facilities have mental health disorder [3,34].

Mental disorders are a significant risk factor for developing substance abuse disorders [19,51]. The pattern of comorbid SUDs between Norwegian persons with serious mental health problems like; schizophrenia, bipolar disorder, and depressive illness, is highly significant [2,37]. Norwegian studies have shown that 90% of patients in substance abuse treatment centers had one or more mental disorders, and that 70% of patients met the criteria for one or more personality disorders [23,27,28]. There are likely mutual influences between mental health, SES and substance abuse that also increase the common risk for developing somatic disorders [7,8,50].

4.2. Low socioeconomic status is a threat to health

The elevated risk of somatic diseases among persons with AUD and DUD in our study, is also substantially explained by low SES, which has been shown to increase the risk for several somatic diseases in both AUD and DUD groups. This is in line with international studies, showing that the risk of adverse events such as severe morbidity and mortality related to SUD is strongly associated with level of SES deprivation [4,43].

Norwegian social assistance recipients have lower SES, more pain, more prevalent illness, and higher mortality compared with other Norwegians [32]. Serious mental disorders are associated with low employment rates and poor educational outcomes, leading to a substantial loss of total earnings over the life course [22]. The experience of SES disadvantage is also evident from an international perspective [33,49]. Socioeconomic background is also an important correlate and people from more disadvantaged backgrounds are more likely to use illicit drugs [14,33,48]. Further, low social position and educational attainment appear to be the strongest socioeconomic predictors of alcohol consumption, followed closely by housing tenure [4]. In contrast, high educational level and income in adulthood, as well as high neighborhood SES, represent protective factors against SUD [5]. As mentioned, mental health disorders are known to be particularly prominent among marginalized groups, who also struggle with poor SES, experiencing social exclusion, discrimination, and trauma. This might significantly increase the risk for compound vulnerability [23,25,44].

Table 4
Stepwise Cox regression models showing adjusted hazard risks of somatic diseases among persons with DUD ($n = 16,559$).

Event outcomes	Model 0 HR (95% CI)	Model 1 HR (95% CI)	Model 2 HR (95% CI)	Model 3 HR (95% CI)
Cardiovascular diseases				
Hypertension	1.1 (1.1–1.2)	2.6 (2.4–2.7)	1.9 (1.8–2.1)	1.3 (1.2–1.4)
Ischemic heart	1.6 (1.5–1.7)	3.8 (3.5–4.1)	2.7 (2.5–2.9)	1.8 (1.6–1.9)
Pulmonary heart	4.0 (3.4–4.6)	8.5 (7.3–9.8)	5.9 (5.1–6.9)	3.4 (2.9–4.1)
Cerebrovascular	2.1 (1.9–2.4)	5.5 (5.0–6.1)	3.8 (3.5–4.2)	2.1 (1.9–2.3)
Endocrine, nutritional, and metabolic diseases				
Diabetes mellitus	1.6 (1.5–1.8)	2.9 (2.7–3.1)	1.7 (1.6–1.9)	1.1 (0.9–1.1)
Malnutrition	7.3 (6.5–8.1)	15.9 (14.3–17.7)	9.5 (8.4–10.7)	4.3 (3.8–4.8)
Obesity	3.2 (2.9–3.6)	3.3 (3.0–3.6)	1.5 (1.4–1.7)	0.7 (0.6–0.8)
Metabolic	4.2 (4.0–4.4)	7.8 (7.4–8.2)	5.1 (4.8–5.4)	2.8 (2.6–2.9)
Cancer				
Digestive	0.9 (0.8–1.2)	2.3 (1.8–3.1)	1.9 (1.5–2.5)	1.3 (1.1–1.7)
Respiratory	2.4 (1.8–3.2)	5.6 (4.2–7.6)	3.8 (2.8–5.2)	2.6 (1.8–3.5)
Soft tissue	0.7 (0.6–0.9)	1.7 (1.5–2.1)	2.0 (1.7–2.3)	1.4 (1.1–1.6)
Reproductive system	0.8 (0.7–0.9)	1.6 (1.5–1.9)	1.6 (1.4–1.8)	1.1 (0.9–1.3)
Endocrine and nervous system	1.1 (0.9–1.4)	2.0 (1.6–2.6)	1.7 (1.3–2.1)	1.1 (0.8–1.4)
Blood	0.9 (0.7–1.3)	1.8 (1.3–2.5)	1.5 (1.1–2.0)	1.0 (0.7–1.4)
Infectious diseases				
Viral hepatitis	159.8 (154.0–165.9)	138.1 (132.2–143.6)	60.2 (57.1–63.0)	43.5 (41.7–46.4)
Influenza and pneumonia	6.6 (6.2–6.9)	13.6 (12.8–14.3)	8.3 (7.8–8.8)	4.2 (4.0–4.5)
Chronic lower respiratory	3.8 (3.6–4.1)	6.2 (5.9–6.5)	3.9 (3.7–4.1)	2.2 (2.1–2.3)
Skin diseases				
Infections of skin and subcutaneous tissue	2.2 (1.3–3.8)	3.9 (2.3–6.7)	3.1 (1.7–5.6)	1.7 (0.9–3.1)
Dermatitis and eczema	2.5 (2.3–2.7)	2.9 (2.7–3.1)	2.1 (1.9–2.2)	1.2 (1.1–1.3)
Papulosquamous	2.2 (2.1–2.5)	2.8 (2.5–3.1)	2.1 (1.9–2.3)	1.3 (1.2–1.5)
Urticaria and erythema	3.3 (2.7–3.9)	3.4 (2.9–4.0)	2.3 (1.9–2.8)	1.4 (1.1–1.6)

Model 0, unadjusted estimates; Model 1, estimates adjusted for age and gender; Model 2, estimates adjusted for recipient of social welfare (SES indicator); Model 3, estimates adjusted for psychiatric comorbidity.
DUD, drug use disorders; HR, hazard risk; CI, confidence interval; estimates are significant at $p \geq 0.001$.

4.3. Excessive risks of somatic diseases

Our study shows that people with AUD or DUD generally have a significantly excessive risk of somatic diseases compared with the general population. Those with AUD have a higher risk for all the investigated somatic diseases (CVDs, endocrine, nutritional, metabolic, cancer, infectious, and skin diseases), compared with persons with DUD as well as the general population. We also identified heterogeneity in the risk of somatic diseases between AUD and persons with DUD. Those with AUD have a 17-fold elevated risk for metabolic disorders, while those with DUD have a 10-fold risk.

The elevated risk for somatic diseases among people with AUD is well documented, and studies have identified that alcohol-dependent men and women have significantly higher risk of a comprehensive spectrum of somatic diseases, both as disease events and as causes of mortality, relative to individuals from the general population [24,45,53,56,58]. It is also the case that metabolic diseases among persons with AUD, such as diabetes mellitus might cause several somatic diseases, starting with symptoms from kidneys, liver, esophagus, and gastrointestinal tract [59]. People with AUD often exhibit serious illnesses that require treatment specifically for neurological, gastrointestinal, and liver, and dermatological problems [25].

The most striking result among the DUD group was the extremely high risk of viral hepatitis (23.3-fold), which is very different from the AUD group (2.2-fold) and the general population (0.4-fold). Chronic viral hepatitis is a major global public health problem and an important cause of morbidity and mortality in sequelae, which include chronic hepatitis, cirrhosis, and primary liver cancer [29]. In modern societies, most hepatitis C virus (HCV) transmission occurs through injecting drug use or via the transfusion of blood products. Much of the estimated burden of disease attributable to the use of illicit drugs is likely due to blood-borne viral infections through unsafe drug injection [14]. Prevention and detection of hepatitis B virus and HCV infections should be an integrated part of surveillance, diagnosis, and treatment [29]. Sharing of drug preparation equipment is also the main reason for blood borne viral infections among DUD patients [21,41]. Making sterile user equipment available reduces the risk of infection by around three quarters [42].

Persons with AUD had a 3-fold higher risk for hypertension and cerebrovascular diseases and almost double the risk for diabetes mellitus and metabolic diseases compared to those with DUD. Further, the risk for ischemic heart diseases doubled in persons with AUD, compared with those with DUDs. The incidence of cancer was low or nonsignificant in the DUD group. Further, those with DUD had a significantly lower risk for hypertension, ischemic heart diseases, cerebrovascular disease, and cancer compared with persons with AUD and the general population.

There are several possible explanations for the higher morbidity in the AUD group compared with the DUD group. First, the AUD group was 10 years older and consisted of a higher proportion of men. Age-related and gender-specific changes in CVD risk commence at around the mean age of the AUD group [15]. Second, there might be other risk factors that we had not measured, such as smoking behaviors and obesity, that drove these differences. A third explanation is the toxic effects of alcohol, which have been documented in a recent report by the World Heart Federation (2022). The fourth explanation is that AUD seem undertreated. This might be partly due to issues related to stigma, but it might also result from insufficient systematic screening in primary health care though effective and cost-effective psychosocial and pharmacological interventions do exist. It has been suggested that primary health care should be responsible for most treatment, with routine screening for alcohol use, and the provision of a staggered treatment response, from brief advice to pharmacological treatment to ensure a better health service [6].

Both mental illness and low SES resulted in a higher risk of somatic diseases. Dunn [17] showed that it can be a direct causal pathway between low SES and poor health as well as an indirect causal pathway through health behaviors, which reinforce one another over the life course [17]. Traditional individually oriented health behavior education interventions seem not very effective, since those with low SES have

been difficult to reach with such programs [52]. Further, the socioeconomic gradient in both health behaviors and stress responses to environmental stimuli like poverty may be expressions of a person's development early in life.

4.4. Strengths and limitations

This study has several methodological advantages in the use of the NPR. First, the coverage of health care services and the quality of health records in Norway are considered to be good [47], which facilitates representativeness and reduces selection bias. Nevertheless, there were also some limitations to this approach; for example, we know that SUD is hugely undertreated in specialist health care and that somatic diseases are in turn undertreated among those with SUD [54]. The first point leads to a possible overestimation of the effect, and the latter to an underestimation. Second, our research is based on clinically set diagnoses from specialist care centers, which might not be fully reliable though we believe it is unlikely that there were systematic differences between the SUD and non-SUD groups, thus making the relative estimates valid. Third, a larger study population would have brought more adequate statistical power to detect differences across age groups and genders. We compared the risk of different types of somatic diseases prospectively between SUD patients and the general population and applied appropriate statistical methods to examine the moderating effects of age and gender. The main limitation of this study, however, was that to ensure statistical power of analysis, we could not differentiate the risk of somatic diseases related to age trends across genders, between problematic alcohol use and alcohol dependency, and among specific types of cancers. Furthermore, SES is dichotomized which might present a considerable loss of information. We also lack information on factors such as smoking habits, nutrition, and physical exercise and the registries do not have information about the onset or duration of problematic alcohol and drug usage. All diagnoses were based on the standard diagnostic manual derived from specialist health care and provides evidence showing heterogeneity in the clinical epidemiology of somatic diseases in the Norwegian population, including those with AUD and DUD. Finally, since we did not have access to data prior to 2008, we were unable to establish whether patients in our samples were newly diagnosed or returning following a previous diagnosis. The percentages given are the number of patients diagnosed with AUD and DUD in relation to the total sample. The data, therefore, reflects either prevalence or incidence figures. In addition, we were unable to establish whether any of those in the control group might have had DUD or AUD before or after the two-year period of data collection.

4.5. Implications

In general, improvement of socio-economic conditions, preferably in combination with professional support to self-manage mental health problems, will reduce the risk of somatic illness in both AUD and DUD patients. Easy access to professional information, counseling, and treatment should be offered. Health professionals should focus clearly on early identification of use of alcohol and drugs. Increasing treatment utilization might be an approach to reduce alcohol and drug usage, as increasing treatment rates have been identified as one important public health strategy on alcohol abuse [46]. Adequate extended treatment has also been proven to alleviate the long-term consequences of AUD [30,35]. Nevertheless, fewer than 20% of people with AUD ever seek help, nor do they receive treatment for their alcohol problems [40].

5. Conclusions

This study provides information about somatic diseases in Norwegians with AUD and DUD. For both the AUD and DUD groups, comorbid mental diseases and having low SES, were associated with higher risk for somatic diseases. There were significant differences between the AUD and DUD groups in terms of their age at SUD diagnosis and the kinds of somatic diseases for which they are at risk. The risk was very high for metabolic diseases among those with AUD, but also CVD, endocrine, nutritional, metabolic, and infectious diseases must be closely observed and treated. Those with DUD had a particularly high risk for viral hepatitis and subcutaneous infections. People with AUD were far older than those with DUD when a SUD diagnosis was given. Mapping and diagnosis provide the basis for treatment. A lack of assessment of SUD may lead to a more serious impact on health. Health professionals and health policies seeking to promote physical and mental health in people with AUD and DUD need to consider not only the direct cross effects, but also the indirect cross effects between somatic diseases, mental health, and SES.

Ethical approval

All study procedures were approved by the Norwegian Regional Committee for Medical and Health Research Ethics (ref: 17/26919–5).

Consent to participate and publication

Not applicable.

Availability of data and materials

The data file was constructed from administrative registers managed by Statistics Norway, the Norwegian Patient Register, and the Norwegian Directorate of Health. The registry data can be made available for research projects approved by the Norwegian Regional Committee for Medical and Health Research Ethics and the Norwegian Data Protection Authority.

Funding statement

This research was funded by the Southern and Eastern Norway Regional Health Authority through a postdoctoral research project awarded to Dr. Dawit Shawel Abebe (DSA): “Patterns and courses of somatic illness and the utilization of health services among persons with substance use disorders and/or mental disorders in Norway” (project number 150901).

Author contributions

DSA designed the study and analyzed the data. DSA and SS interpreted the data and drafted the manuscript. All authors (SS, LL, DSA) contributed substantially to the study concept and design; interpreting the results; drafting and critically revising the manuscript; and approving the final manuscript.

Declaration of Competing Interest

The authors Siv Skarstein (SS), Lars Lien (LL), and DSA, declare they have no conflict of interests.

References

[1] I.D. Alba, J.H. Samet, R. Saitz, Burden of medical illness in drug-and alcohol-dependent persons without primary care, Am. J. Addict. 13 (1) (2004) 33–45.
[2] H.W. Andersson, S.E. Lilleeng, T. Ruud, S.O. Ose, Substance use among patients in specialized mental health services in Norway: prevalence and patient characteristics based on a national census, Nordic J. Psychiatry 75 (3) (2021) 160–169.
[3] K. Bakken, A.S. Landheim, P. Vaglum, Axis I and II disorders as long-term predictors of mental distress: a six-year prospective follow-up of substance-dependent patients, BMC psychiatry 7 (1) (2007) 1–12.
[4] E. Beard, J. Brown, R. West, E. Kaner, P. Meier, S. Michie, Associations between socio-economic factors and alcohol consumption: a population survey of adults in England, PLoS One 14 (2) (2019), e0209442.

[5] S. Calling, H. Ohlsson, J. Sundquist, K. Sundquist, K.S. Kendler, Socioeconomic status and alcohol use disorders across the lifespan: a co-relative control study, PLoS One 14 (10) (2019), e0224127.
[6] A.F. Carvalho, M. Heilig, A. Perez, C. Probst, J. Rehm, Alcohol use disorders, Lancet 394 (10200) (2019) 781–792, https://doi.org/10.1016/s0140-6736(19)31775-1.
[7] M. Cerdá, A. Sagdeo, S. Galea, Comorbid forms of psychopathology: key patterns and future research directions, Epidemiol. Rev. 30 (1) (2008) 155–177.
[8] L. Chassin, K.J. Sher, A. Hussong, P. Curran, The developmental psychopathology of alcohol use and alcohol disorders: research achievements and future directions, Dev. Psychopathol. 25 (4pt2) (2013) 1567–1584.
[9] C. Crump, K. Sundquist, M.A. Winkleby, J. Sundquist, Comorbidities and mortality in bipolar disorder: a Swedish national cohort study, JAMA Psychiatry 70 (9) (2013) 931–939.
[10] I. De Alba, J.H. Samet, R. Saitz, Burden of medical illness in drug- and alcohol-dependent persons without primary care, Am. J. Addict. 13 (1) (2004) 33–45, https://doi.org/10.1080/10550490490265307.
[11] M. De Hert, C.U. Correll, J. Bobes, M. Cetkovich-Bakmas, D.A.N. Cohen, I. Asai, S. Leucht, Physical illness in patients with severe mental disorders. I. Prevalence, impact of medications and disparities in health care, World psychiatry 10 (1) (2011) 52.
[12] L. Kohn, Christiaens. W., J. Detraux, J. De Lepeleire, M. De Hert, B. Gillain, V. Jespers, Barriers to somatic health care for persons with severe mental illness in Belgium: a qualitative study of patients' and healthcare professionals' perspectives, Frontiers in Psychiatry 12 (2015) (2022) 798530.
[13] L. Degenhardt, W.T. Chiu, N. Sampson, R.C. Kessler, J.C. Anthony, M. Angermeyer, J.E. Wells, Toward a global view of alcohol, tobacco, cannabis, and cocaine use: findings from the WHO world mental health surveys, PLoS Med. 5 (7) (2008), e141, https://doi.org/10.1371/journal.pmed.0050141.
[14] L. Degenhardt, W. Hall, Extent of illicit drug use and dependence, and their contribution to the global burden of disease, Lancet 379 (9810) (2012) 55–70, https://doi.org/10.1016/s0140-6736(11)61138-0.
[15] C. Delles, G. Currie, Sex differences in hypertension and other cardiovascular diseases, J. Hypertens. 36 (4) (2018) 768.
[16] B. Dickey, S.L. Normand, R.D. Weiss, R.E. Drake, H. Azeni, Medical morbidity, mental illness, and substance use disorders, Psychiatr. Serv. 53 (7) (2002) 861–867, https://doi.org/10.1176/appi.ps.53.7.861.
[17] J.R. Dunn, Health behavior vs the stress of low socioeconomic status and health outcomes, JAMA 303 (12) (2010) 1199–1200, https://doi.org/10.1001/jama.2010.332.
[18] K. Frasch, J.I. Larsen, J. Cordes, B. Jacobsen, S.O. Wallenstein Jensen, C. Lauber, T. Becker, Physical illness in psychiatric inpatients: comparison of patients with and without substance use disorders, Int. J. Soc. Psychiatry 59 (8) (2013) 757–764, https://doi.org/10.1177/0020764012456803.
[19] M.D. Glantz, J.C. Anthony, P.A. Berglund, L. Degenhardt, L. Dierker, A. Kalaydjian, R.C. Kessler, Mental disorders as risk factors for later substance dependence: estimates of optimal prevention and treatment benefits, Psychol. Med. 39 (8) (2009) 1365.
[20] D. Guertler, A. Moehring, K. Krause, A. Batra, S. Eck, J. Freyer-Adam, U. John, Copattern of depression and alcohol use in medical care patients: cross-sectional study in Germany, BMJ Open 10 (5) (2020), e032826.
[21] H. Hagan, H. Thiede, N.S. Weiss, S.G. Hopkins, J.S. Duchin, E.R. Alexander, Sharing of drug preparation equipment as a risk factor for hepatitis C, Am. J. Public Health 91 (1) (2001) 42–46, https://doi.org/10.2105/ajph.91.1.42.
[22] C. Hakulinen, M. Elovainio, M. Arffman, S. Lumme, S. Pirkola, I. Keskimäki, P. Böckerman, Mental disorders and long-term labour market outcomes: nationwide cohort study of 2 055 720 individuals, Acta Psychiatr. Scand. 140 (4) (2019) 371–381, https://doi.org/10.1111/acps.13067.
[23] A.J. Hjemsæter, J.G. Bramness, R. Drake, I. Skeie, B. Monsbakken, J.Š. Benth, A. S. Landheim, Levels of mental distress over 18 years after entering treatment for substance use disorders: a longitudinal cohort study, Nordic Stud. Alcohol Drugs 37 (4) (2020) 352–364.
[24] C. Holst, J.S. Tolstrup, H.J. Sørensen, U. Becker, Alcohol dependence and risk of somatic diseases and mortality: a cohort study in 19 002 men and women attending alcohol treatment, Addiction 112 (8) (2017) 1358–1366.
[25] F. Keaney, M. Gossop, A. Dimech, I. Guerrini, M. Butterworth, H. Al-Hassani, A. Morinan, Physical health problems among patients seeking treatment for substance use disorders: a comparison of drug dependent and alcohol dependent patients, J. Subst. Abus. 16 (1) (2011) 27–37.
[26] E. Kringlen, S. Torgersen, V. Cramer, A Norwegian psychiatric epidemiological study, Am. J. Psychiatr. 158 (7) (2001) 1091–1098, https://doi.org/10.1176/appi.ajp.158.7.1091.
[27] A.S. Landheim, K. Bakken, P. Vaglum, Impact of comorbid psychiatric disorders on the outcome of substance abusers: a six year prospective follow-up in two Norwegian counties, BMC Psychiatry 6 (1) (2006) 1–11.
[28] G. Lauritzen, H. Waal, A. Amundsen, O. Arner, A nationwide study of Norwegian drug abusers in treatment: methods and findings, Nordic Stud. Alcohol Drugs 14 (1_suppl) (1997) 43–63.
[29] D. Lavanchy, Chronic viral hepatitis as a public health issue in the world, Best Pract. Res. Clin. Gastroenterol. 22 (6) (2008) 991–1008.
[30] E. Lenaerts, C. Matheï, F. Matthys, D. Zeeuws, L. Pas, P. Anderson, B. Aertgeerts, Continuing care for patients with alcohol use disorders: a systematic review, Drug Alcohol Depend. 135 (2014) 9–21.
[31] S. Lumme, S. Pirkola, K. Manderbacka, I. Keskimäki, Excess mortality in patients with severe mental disorders in 1996-2010 in Finland, PLoS One 11 (3) (2016), e0152223, https://doi.org/10.1371/journal.pone.0152223 (Accession No. 27010534).
[32] B. Løyland, Å. Hermansen, E. Dahl, A.K. Wahl, Differences in income trajectories according to psychological distress and pain: A longitudinal study among Norwegian social assistance recipients,Scandinavian, Journal of Public Health 49 (8) (2021) 865–874.
[33] A. Macintyre, D. Ferris, B. Gonçalves, N. Quinn, What has economics got to do with it? The impact of socioeconomic factors on mental health and the case for collective action, Palgrave Communicat. 4 (1) (2018) 1–5.
[34] R.K. McHugh, R.D. Weiss, Alcohol use disorder and depressive disorders, Alcohol Res. Curr. Rev. 40 (1) (2019).
[35] J.R. McKay, Is there a case for extended interventions for alcohol and drug use disorders? Addiction 100 (11) (2005) 1594–1610.
[36] K.R. Merikangas, V.L. McClair, Epidemiology of substance use disorders, Hum. Genet. 131 (6) (2012) 779–789.
[37] R. Nesvåg, G.P. Knudsen, I.J. Bakken, A. Høye, E. Ystrom, P. Surén, T. Reichborn-Kjennerud, Substance use disorders in schizophrenia, bipolar disorder, and depressive illness: a registry-based study, Soc. Psychiatry Psychiatr. Epidemiol. 50 (8) (2015) 1267–1276.
[38] Norwegian Institute of Public Health, Norwegian Institute of Public Health, Norwegian Institute of Public Health - NIPH (fhi.no), 2022. Retrieved 10th October 2022.
[39] B. Odlaug, A. Gual, J. DeCourcy, R. Perry, J. Pike, L. Heron, J. Rehm, Alcohol dependence, co-occurring conditions and attributable burden, Alcohol Alcohol. 51 (2) (2016) 201–209.
[40] J. Oleski, N. Mota, B.J. Cox, J. Sareen, Perceived need for care, help seeking, and perceived barriers to care for alcohol use disorders in a national sample, Psychiatr. Serv. 61 (12) (2010) 1223–1231.
[41] N. Palmateer, J. Kimber, M. Hickman, S. Hutchinson, T. Rhodes, D. Goldberg, Evidence for the effectiveness of sterile injecting equipment provision in preventing hepatitis C and human immunodeficiency virus transmission among injecting drug users: a review of reviews, Addiction 105 (5) (2010) 844–859, https://doi.org/10.1111/j.1360-0443.2009.02888.x.
[42] L. Platt, S. Minozzi, J. Reed, P. Vickerman, H. Hagan, C. French, M. Hickman, Needle syringe programmes and opioid substitution therapy for preventing hepatitis C transmission in people who inject drugs, Cochrane Database Syst. Rev. 9 (9) (2017) Cd012021, https://doi.org/10.1002/14651858.CD012021.pub2.
[43] C. Probst, S. Lange, C. Kilian, C. Saul, J. Rehm, The dose-response relationship between socioeconomic deprivation and alcohol-attributable mortality risk—a systematic review and meta-analysis, BMC Med. 19 (1) (2021) 1–13.
[44] A. Rafferty, Skill underutilization and under-skilling in Europe: the role of workplace discrimination, Work Employ. Soc. 34 (2) (2020) 317–335.
[45] J. Rehm, The risks associated with alcohol use and alcoholism, Alcohol Res. Health 34 (2) (2011) 135.
[46] J. Rehm, K. Shield, G. Gmel, M. Rehm, U. Frick, Modeling the impact of alcohol dependence on mortality burden and the effect of available treatment interventions in the European Union, Eur. Neuropsychopharmacol. 23 (2) (2013) 89–97.
[47] Å. Ringard, A. Sagan, I. Sperre Saunes, A.K. Lindahl, Organization, W. H, Norway: Health System Review, 2013.
[48] M. Roerecke, J. Rehm, Cause-specific mortality risk in alcohol use disorder treatment patients: a systematic review and meta-analysis, Int. J. Epidemiol. 43 (3) (2014) 906–919, https://doi.org/10.1093/ije/dyu018.
[49] A. Rogers, D. Pilgrim, Mental Health and Inequality, Macmillan International Higher Education, 2002.
[50] J.E. Schulenberg, J.L. Maggs, A developmental perspective on alcohol use and heavy drinking during adolescence and the transition to young adulthood, J. Stud. Alcohol Supplement(14) (2002) 54–70.
[51] J. Swendsen, K.P. Conway, L. Degenhardt, M. Glantz, R. Jin, K.R. Merikangas, R. C. Kessler, Mental disorders as risk factors for substance use, abuse and dependence: results from the 10-year follow-up of the National Comorbidity Survey, Addiction 105 (6) (2010) 1117–1128.
[52] L. Syme, Preventing disease and promoting health: the need for some new thinking, Sozial- und Präventivmedizin/Soc. Prevent. Med. 51 (5) (2006) 247, https://doi.org/10.1007/s00038-006-6062-x.
[53] L.C. Thygesen, P. Mikkelsen, T.V. Andersen, H. Tønnesen, K. Juel, U. Becker, M. Grønbæk, Cancer incidence among patients with alcohol use disorders—long-term follow-up, Alcohol Alcohol. 44 (4) (2009) 387–391.
[54] F.A. Torvik, E. Ystrom, K. Gustavson, T.H. Rosenström, J.G. Bramness, N. Gillespie, T. Reichborn-Kjennerud, Diagnostic and genetic overlap of three common mental disorders in structured interviews and health registries, Acta Psychiatr. Scand. 137 (1) (2018) 54–64.
[55] D. Vancampfort, C.U. Correll, B. Galling, M. Probst, M. De Hert, P.B. Ward, B. Stubbs, Diabetes mellitus in people with schizophrenia, bipolar disorder and major depressive disorder: a systematic review and large scale meta-analysis, World Psychiatry 15 (2) (2016) 166–174.
[56] D. Vancampfort, M. Hallgren, J. Mugisha, M. De Hert, M. Probst, D. Monsieur, B. Stubbs, The prevalence of metabolic syndrome in alcohol use disorders: a systematic review and meta-analysis, Alcohol Alcohol. 51 (5) (2016) 515–521.
[57] H.A. Whiteford, L. Degenhardt, J. Rehm, A.J. Baxter, A.J. Ferrari, H.E. Erskine, N. Johns, Global burden of disease attributable to mental and substance use disorders: findings from the global burden of disease study 2010, Lancet 382 (9904) (2013) 1575–1586.
[58] E.C. Williams, J.A. Hahn, R. Saitz, K. Bryant, M.C. Lira, J.H. Samet, Alcohol use and human immunodeficiency virus (HIV) infection: current knowledge, implications, and future directions, Alcohol. Clin. Exp. Res. 40 (10) (2016) 2056–2072.
[59] A.A. Howard, J.H. Arnsten, M.N. Gourevitch, Effect of alcohol consumption on diabetes mellitus: a systematic review, Ann. Intern. Med. 140 (3) (2004) 211–219.