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Temporal trends in mortality and associated factors among persons with mental disorders: a register-based cohort study

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Abstract:	Study aims to examine 20-year temporal trends in all-cause mortality among psychiatric patients and investigating impacts of risk factors on the time trends，based on 218703 Finnish adults with mental disorders who were discharged from 87 psychiatric hospitals between 1st Jan 1995 and 31st Dec 2014. The age-period-cohort analysis of Poisson model with random hospital effects estimated temporal trends in death rate and associated factors at individual, healthcare system, and society levels, following the WHO multilevel intervention framework model for six major psychiatric diagnosis. The adjusted annual mortality declined by 2.2% annually (RR: 0.978 [95% CI 0.976-0.980]) for all individuals, and by 2.8% after adjusting for all risk factors, with varied decreasing rate between 2.0% and 3.6% by diagnosis. Individual level factors accounted for the declining rate by 54.5% for all patients, with the highest impact on patients with personality disorders, followed by patients with affeve disorders and patients with schizophrenia.
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Abstract

This study aims to examine 20-year temporal trends in all-cause mortality among psychiatric patients and investigating impacts of risk factors on the time trends， based on 218703 Finnish adults with mental disorders who were discharged from 87 psychiatric hospitals between 1st Jan 1995 and 31st Dec 2014. The age-period-cohort analysis of Poisson model with random hospital effects estimated temporal trends in death rate and associated factors at individual, healthcare system, and society levels, following the WHO multilevel intervention framework model for six major psychiatric diagnosis. The adjusted annual mortality declined by 2.2% annually (RR: 0.978 [95% CI 0.976-0.980]) for all individuals, and by 2.8% after adjusting for all risk factors, with varied decreasing rate between 2.0% and 3.6% by diagnosis. Individual level factors accounted for the declining rate by 54.5% for all patients, with the highest impact on patients with personality disorders, followed by patients with affective disorders and patients with Schizophrenia. Identified declining trends and associated factors which are preventable and modifiable for individuals with specific psychiatric diagnosis may lead to develop targeted service and intervention strategies in bringing down mortality further for the population.

Keywords: Mortality, Mental illness, Temporal trend, Risk factors

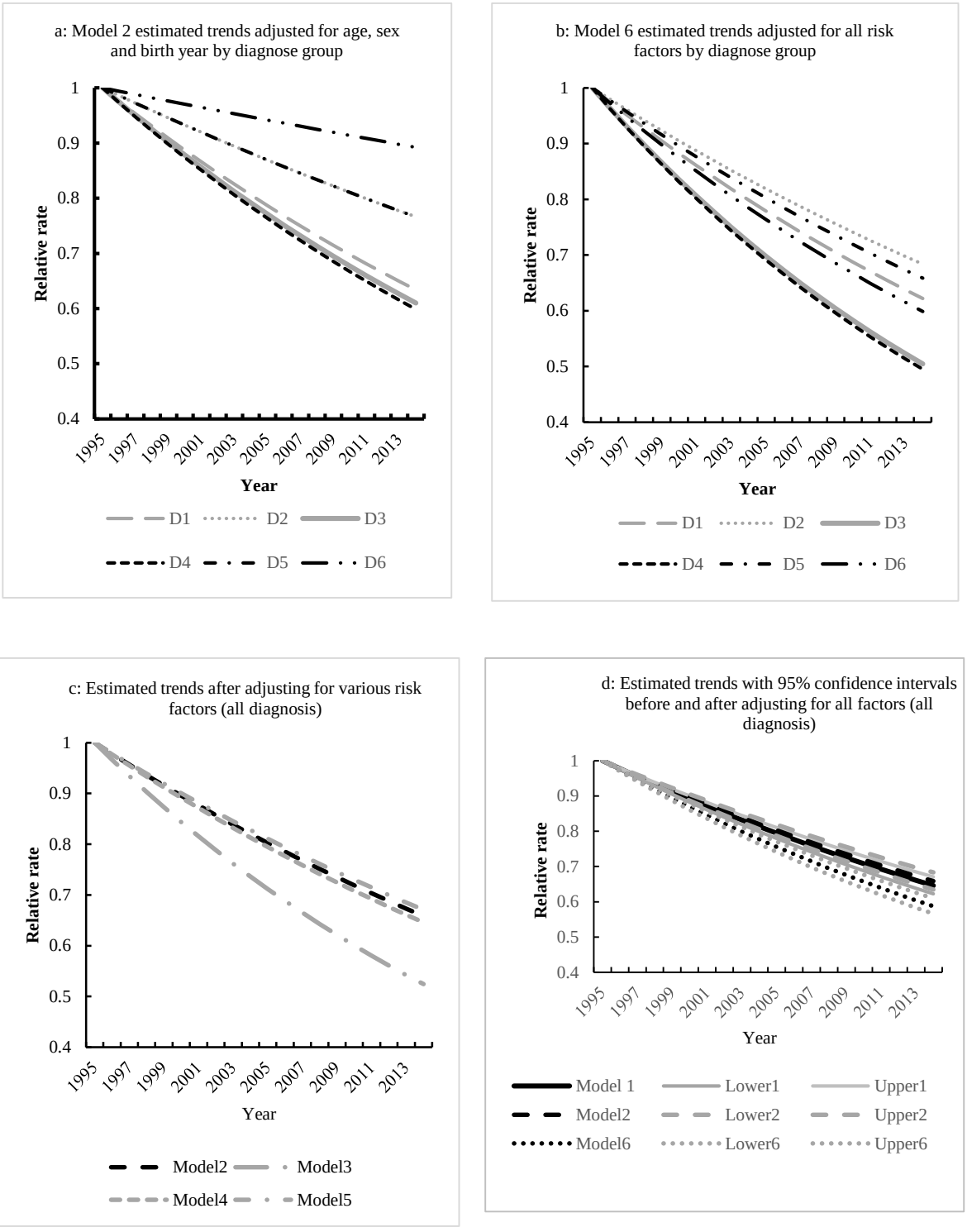

Figure 1 Comparing time trends in estimated RR among models

(Model 1 adjusted for age and sex; Model 2 adjusted for age, sex and birth year; Model 3 adjusted for risk factors at individual level based on Model 2; Model 4 adjusted for health services factors based on Model 2; Model 5 adjusted for societal factors based on Model 2; Model 6 adjusted for all factors based on Model 2)

Table 1 Crude death rate over time by discharge period

	Discharge period											
	1995-1999			2000-2004			2005-2009			2010-2014		
Year	No death/No patients alive	Person years	Death rate/100 person years (SE)	No death/No patients	Person years	Death rate/100 person years (SE)	No death/No patients	Person years	Death rate/100 person years (SE)	No death/No patients	Person years	Death rate/100 person years (SE)
Male	N=24,196			N=26,416			N=29,009			N=34,894		
0-4	4,178/24,196	50,249	8.31 (0.13)									
5-9	3,330/20,018	90,540	3.68 (0.06)	3,970/26,416	56,879	6.98 (0.11)						
10-14	2,013/16,688	78,153	2.58 (0.06)	3,441/22,446	102,458	3.36 (0.06)	3,933/29,009	62,457	6.30 (0.10)			
15-19	1,544/14,675	69,446	2.22 (0.06)	2,133/19,005	89,364	2.39 (0.05)	3,627/25,076	115,211	3.15 (0.05)	3,056/34,894	72,894	4.24 (0.08)
Overall	11,065/24,196	288,388	3.84 (0.04)	9,544/26,416	248,701	3.84 (0.04)	7,560/29,009	177,668	4.26 (0.05)	3,056/34,894	34,894	4.24 (0.08)
Female	N=18,429			N=22,830			N=27,609			N=35,320		
0-4	2,467/18,429	39,328	6.27 (0.13)									
5-9	2,565/15,962	72,665	3.53 (0.07)	2,393/22,830	50,502	4.73 (0.10)						
10-14	1,622/13,397	62,756	2.58 (0.06)	2,538/20,437	95,240	2.66 (0.05)	2,345/27,609	62,475	3.75 (0.08)			
15-19	1,298/11,775	55,475	2.34 (0.06)	1,825/17,899	84,770	2.15 (0.05)	2,688/25,264	119,119	2.26 (0.04)	1,875/35,320	75,113	2.50 (0.06)
Overall	7,952/18,429	230,224	3.45 (0.04)	6,756/22,806	230,512	2.93 (0.04)	5,033/27,609	181,594	2.77 (0.04)	1,875/35,320	75,113	2.50 (0.06)
All	N=42,625			N=49,246			N=56,618			N=70,214		
0-4	6,645/42,625	89,577	7.42 (0.09)									
5-9	5,895/35,980	163,206	3.61 (0.05)	6,363/49,246	107,381	5.93 (0.07)						
10-14	3,635/30,085	140,909	2.58 (0.04)	5,979/42,883	197,699	3.02 (0.04)	6,278/56,618	124,932	5.03 (0.06)			
15-19	2,842/26,450	124,921	2.28 (0.04)	3,958/36,904	174,135	2.27 (0.04)	6,315/50,340	234,330	2.69 (0.03)	4,931/70,214	147,175	3.35 (0.05)
Overall	19,017/42,625	518,613	3.67 (0.03)	16,300/49,246	479,215	3.40 (0.03)	12,593/56,618	359,262	3.51 (0.03)	4,931/70,214	147,175	3.35 (0.05)

Table 2 Associations of time with mortality and attribution by risk factors by primary diagnosis from Poisson random effects models

Primary diagnosis	Time trend in relative rate of death risk (95% confidence interval): exp^{β}					
	Model 1 (M1): adjusted for age and sex	Model 2 (M2): add cohort effects to M1	Model 3 (M3): add individual factors to M2	Model 4 (M4): add health service factors to M2	Model 5 (M5): add societal factors to M2	Model 6 (M6): add all factors to M2
D1 Organic disorders	0.976 (0.972-0.980)	0.976 (0.972-0.981)	0.975 (0.970-0.980)	0.973 (0.969-0.978)	0.978 (0.973-0.982)	0.975 (0.970-0.980)
D2 Psychoactive substance use	0.987 (0.983-0.990)	0.986 (0.982-0.990)	0.974 (0.970-0.979)	0.986 (0.982-0.990)	0.988 (0.984-0.992)	0.980 (0.976-0.985)
D3 Schizophrenia spectrum	0.974 (0.970-0.977)	0.974 (0.971-0.978)	0.959 (0.954-0.963)	0.974 (0.971-0.978)	0.974 (0.971-0.978)	0.965 (0.960-0.969)
D4 Mood affective disorders	0.973 (0.969-0.976)	0.974 (0.970-0.977)	0.960 (0.955-0.964)	0.972 (0.968-0.976)	0.973 (0.970-0.977)	0.964 (0.959-0.968)
D5 Anxiety non-psychotics	0.986 (0.977-0.995)	0.986 (0.977-0.995)	0.974 (0.964-0.984)	0.984 (0.975-0.994)	0.986 (0.977-0.996)	0.979 (0.969-0.989)
D6 Personality disorders	0.995 (0.983-1.007)*	0.994 (0.981-1.006)*	0.967 (0.951-0.982)	0.985 (0.973-0.998)	0.996 (0.984-1.009)*	0.973 (0.957-0.989)
All diagnosis	0.977 (0.975-0.979)	0.978 (0.976-0.980)	0.966 (0.964-0.969)	0.977 (0.975-0.979)	0.979 (0.977-0.982)	0.972 (0.970-0.974)
	Time trend parameter β of death risk (log-scale) and standard error in brackets					
	M1 effect of time β (SE)	M2 effect of time β(SE)	M3 effects of time β (SE)	M4 effects of time β (SE)	Model 5 effects of time β *(SE)*	M6 effects of time β (SE)
D1 Organic disorders	-0.024 (0.002)	-0.024 (0.002)	-0.026 (0.003)	-0.027 (0.002)	-0.022 (0.002)	-0.025 (0.003)
D2 Psychoactive substance use	-0.014 (0.002)	-0.014 (0.002)	-0.026 (0.002)	-0.014 (0.002)	-0.012 (0.002)	-0.020 (0.002)
D3 Schizophrenia spectrum	-0.027 (0.002)	-0.026 (0.002)	-0.042 (0.002)	-0.026 (0.002)	-0.026 (0.002)	-0.036 (0.002)
D4 Mood affective disorders	-0.028 (0.002)	-0.027 (0.002)	-0.041 (0.002)	-0.029 (0.002)	-0.027 (0.002)	-0.037 (0.002)
D5 Anxiety non-psychotics	-0.014 (0.005)	-0.014 (0.005)	-0.027 (0.005)	-0.016 (0.005)	-0.014 (0.005)	-0.022 (0.005)
D6 Personality disorders	-0.005 (0.006)*	-0.006 (0.006)*	-0.034 (0.008)	-0.015 (0.006)	-0.004 (0.006)*	-0.027 (0.008)
All diagnosis	-0.023 (0.001)	-0.022 (0.001)	-0.034 (0.001)	-0.023 (0.001)	-0.021 (0.001)	-0.028 (0.001)
-2log-Pseudo-Likelihood	10,125,955	10,084,850	8,625,077	9,621,483	9,684,219	8,152,055
$\chi^2_{(df)}$		Base of M3-M6	$1,459,773_{(11)}$	$463,367_{(8)}$	$400,631_{(8)}$	$1,932,796_{(27)}$

* The time trend was by chance

Table 3 Estimated associations of factors with relative rate (RR) of mortality from Model 6

Factor category	Factors	D1 (N=13,828) RR: 95% CI	D2 (N=36,923) RR: 95% CI	D3 (N=61,946) RR: 95% CI	D4 (N=73,620) RR: 95% CI	D5 (N=21,388) RR: 95% CI	D6 (N=6,598) RR: 95% CI	All (N=218,703) RR: 95% CI
Demographics	Gender Female (Ref)							
	Male	1.625:1.553-1.700	1.473:1.401-1.548	1.699:1.639-1.762	1.838:1.772-1.908	1.729:1.577-1.896	1.657:1.462-1.879	1.771:1.738-1.806
	Age at most recent discharge (year)	1.060:1.044-1.077	1.043:1.032-1.054	1.039:1.030-1.047	1.025:1.016-1.035	1.038:1.021-1.054	0.985:0.962-1.008	1.030:1.025-1.035
	Age*age	0.9999:0.9998-1.0000	0.99987:0.99976-0.99998	1.00018:1.00011-1.00025	1.00029:1.00021-1.00037	1.0002:1.00005-1.00035	1.00065:1.00042-1.00089	1.00023:1.00019-1.0003
Time effect	Year of most recent discharge	0.975:0.970-0.980	0.980:0.976-0.985	0.965:0.960-0.969	0.964:0.959-0.968	0.979:0.911-1.006	0.973:0.957-0.989	0.972:0.970-0.974
Individual factors				Severity of disorder				
	Log (Hospital days)	0.955:0.934-0.976	0.971:0.949-0.994	0.950:0.934-0.966	0.912:0.893-0.932	0.957:0.911-1.006	0.960:0.901-1.024	0.896:0.888-0.905
	Total number of hospital admission							
	Once (Ref)							
	Twice	1.102:1.037-1.171	1.229:1.163-1.300	1.163:1.104-1.225	1.291:1.225-1.361	1.199:1.053-1.365	1.216:1.001-1.477	1.249:1.212-1.283
	3-5 times	1.217:1.117-1.327	1.511:1.409-1.620	1.435:1.353-1.522	1.679:1.580-1.785	1.683:1.434-1.975	1.865:1.528-2.276	1.615:1.564-1.667
	6-10 times	1.378:1.167-1.626	2.120:1.908-2.354	1.869:1.724-2.025	2.299:2.100-2.517	2.435:1.893-3.133	2.568:1.986-3.320	2.230:2.128-2.337
	More than 10 times	1.295:0.980-1.712	2.607:2.241-3.032	2.345:2.131-2.580	3.012:2.671-3.396	2.641:1.886-3.698	3.657:2.643-5.061	2.865:2.699-3.042
	Symptoms/Pathophysiology							
	At discharge GAS score ≥75 (Ref)							
	At discharge GAS score 1-23	2.435:2.060-2.878	1.504:1.325-1.707	2.623:2.319-2.967	3.085:2.677-3.356	1.929:1.255-2.967	2.077:1.280-3.369	2.510:2.376-2.653
	At discharge GAS score 24-74	1.573:1.338-1.850	1.243:1.152-1.341	1.310:1.186-1.447	1.366:1.263-1.476	1.208:1.031-1.411	1.397:1.047-1.865	1.362:1.305-1.423
	Time from the 1st diagnose in year	0.986:0.972-1.000	0.981:0.972-0.990	0.991:0.984-0.997	0.988:0.980-0.996	0.987:0.966-1.008	0.977:0.951-1.003	0.983:0.979-0.988
				Behaviour-specific				
	HIV_AIDS							
	No (Ref)							
	Yes	4.199:1.036-17.01	0.860:0.600-1.234	2.049:1.251-3.356	1.941:1.167-3.227	0.916:0.128-6.529	5.799:2.645-12.71	1.588:1.256-2.007
	Any substance use							
	No (Ref)							
	Yes	0.805:0.654-0.990	1.002:0.956-1.050	1.685:1.461-1.943	1.609:1.468-1.764	1.978:1.603-2.440	1.466:1.210-1.777	1.411:1.364-1.459
	Low motivation for treatment	0.991:0.975-1.008	1.050:1.028-1.074	0.987:0.976-0.998	1.019:1.000-1.039	1.049:0.972-1.134	1.022:0.953-1.095	1.005:0.997-1.013
Health service factors				Human resources				
	Negative beliefs/attitudes of staff							
	No of coercive method used							
	None (Ref)							
	One type	1.138:1.061-1.221	1.167:1.097-1.242	1.106:1.033-1.184	1.135:1.010-1.275	1.033:0.673-1.584	1.111:0.794-1.554	1.205:1.162-1.248
	Two types	1.257:1.102-1.435	1.199:1.072-1.342	1.143:1.008-1.296	1.193:0.939-1.516	1.527:0.379-6.153	1.703:0.781-3.712	1.237:1.157-1.323
	Three types	0.984:0.746-1.297	1.168:0.929-1.467	1.003: 0.782-1.287	1.088:0.726-1.630	1.668:0.230-12.08-	1.411:0.536-3.710	1.117:0.977-1.276
	Four types	1.237:0.810-1.888	1.531:0.947-2.475	1.088: 0.654-1.809	1.675:0.795-3.530	N/A	34.16:10.26-113.7	1.456:1.042-1.856
				Medication				
	Medication							
	None (Ref)							
	Psychosis drug Neurolepts	1.151:1.042-1.272	1.178:1.096-1.267	0.969:0.860-1.093	1.322:1.161-1.505	1.422:1.165-1.736	1.979:1.544-2.437	1.196:1.144-1.251
	Antidepressive	0.874:0.772-0.990	1.007:0.927-1.094	0.942:0.798-1.112	1.143:1.011-1.292	1.299:1.097-1.539	1.587:1.240-2.030	0.931:0.889-0.976
	Both neurolepts & antidepressive	1.158:1.038-1.291	1.193:1.094-1.230	0.988:0.871-1.120	1.306:1.153-1.480	1.585:1.316-1.908	2.139:1.673-2.736	1.143:1.091-1.198

	Other medication for psychiatric disorder	1.135:1.016-1.269	1.130:1.054-1.211	1.082:0.943-1.243	1.263:1.104-1.445	1.468:1.226-1.759	1.891:1.453-2.461	1.256:1.198-1.317
Social determinants of health				Social economic position				
	Unemployment							
	Employed (Ref)							
	Unemployment	1.315:1.071-1.616	1.281:1.209-1.358	1.454:1.300-1.625	1.323:1.230-1.423	1.579:1.358-1.836	1.407:1.127-1.756	1.504:1.448-1.561
	Student	1.112:0.600-2.060	0.990:0.871-1.126	1.490:1.282-1.731	1.125:0.995-1.272	0.903:0.712-1.145	1.053:0.783-1.416	1.104:1.031-1.182
	Retired	1.316:1.143-1.514	1.349:1.269-1.434	1.678:1.545-1.823	1.377:1.301-1.457	1.526:1.326-1.756	1.464:1.194-1.795	1.432:1.386-1.480
	Other	1.503:1.154-1.958	1.357:1.252-1.471	1.532:1.334-1.759	1.366:1.232-1.515	1.363:1.092-1.701	1.339:1.012-1.772	1.529:1.451-1.611
	Low health literacy							
	Higher degree (Ref)							
	Basic education	1.141:0.976-1.334	0.961:0.847-1.090	1.379:1.207-1.574	1.093:0.995-1.201	0.981:0.778-1.236	1.136:0.752-1.715	1.150:1.086-1.218
	Lower degree	1.128:0.957-1.330	0.939:0.819-1.076	1.182:1.024-1.365	1.041:0.942-1.150	0.880:0.682-1.135	1.051:0.670-1.646	1.061:0.998-1.129
	Unknown	1.199:1.032-1.393	1.046:0.922-1.186	1.556:1.364-1.775	1.221:1.112-1.341	1.169:0.926-1.473	1.529:1.014-2.305	1.294:1.222-1.369
	Environmental vulnerabilities							
	Participated rehab. (Ref)							
	Not participated rehab.	1.659:0.986-3.108	2.165:1.958-2.394	1.521:1.180-1.959	1.864:1.527-2.275	1.842:1.268-2.677	1.812:1.276-2.574	1.739:1.607-1.882
	Cultural & societal value							
	Not on income support (Ref)							
	On income support	1.092:1.029-1.158	1.088:1.035-1.145	1.170:1.125-1.217	1.309:1.255-1.365	1.334:1.207-1.481	1.421:1.096-1.688	1.239:1.212-1.266

DECLARATION OF INTEREST STATEMENT

Credit authorship contribution statement

All authors were involved in designing the study, interpreted the data and critically reviewed the manuscript. MY wrote the first draft of the manuscript and led interpretation of results. MV secured the grant for the study. MV and TL contributed to the writing. MY and TV analysed the data. SLN and MA provided critical comments to improve the manuscript. MV, TV and TL had full access to anonymised data.

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Declaration of competing interest

None.

Availability of Data and Materials

The data that support the findings of this study are available from The Finnish National Care Register for Health Care and Statistics Finland but restrictions apply to the availability of these data. The data are usable for this study only.

Author statement

Credit authorship contribution statement

All authors were involved in designing the study, interpreted the data and critically reviewed the manuscript. MY wrote the first draft of the manuscript and led interpretation of results. MV secured the grant for the study. MV and TL contributed to the writing. MY and TV analysed the data. SLN and MA provided critical comments to improve the manuscript. MV, TV and TL had full access to anonymised data.

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All authors were involved in designing the study, interpreted the data and critically reviewed the manuscript. MY wrote the first draft of the manuscript and led interpretation of results. MV secured the grant for the study. MV and TL contributed to the writing. MY and TV analysed the data. SLN and MA provided critical comments to improve the manuscript. MV, TV and TL had full access to anonymised data.

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Declaration of competing interest

None.

Availability of Data and Materials

The data that support the findings of this study are available from The Finnish National Care Register for Health Care and Statistics Finland, but restrictions apply to the availability of these data. The data are usable for this study only.

Abstract

This study aims to examine 20-year temporal trends in all-cause mortality among psychiatric patients and investigating impacts of risk factors on the time trends based on 218,703 Finnish adults with mental disorders who were discharged from 87 psychiatric hospitals between 1 Jan 1995 and 31 Dec 2014. The age-period-cohort analysis of Poisson model with random hospital effects estimated temporal trends in death rate and associated factors at individual, healthcare system, and society levels, following the WHO multilevel intervention framework model for six major psychiatric diagnosis. The adjusted annual mortality declined by 2.2% annually (RR: 0.978 [95% CI 0.976–0.980]) for all individuals, and by 2.8% after adjusting for all risk factors, with varied decreasing rate between 2.0% and 3.6% by diagnosis. Individual level factors accounted for the declining rate by 54.5% for all patients, with the highest impact on patients with personality disorders, followed by patients with affective disorders and patients with schizophrenia. Identified declining trends and associated factors which are preventable and modifiable for individuals with specific psychiatric diagnosis may lead to develop targeted service and intervention strategies in bringing down mortality further for the population.

Keywords: Mortality, Mental illness, Temporal trend, Risk factors

Temporal trends in mortality and associated factors among persons with mental disorders: a register-based cohort study

1. INTRODUCTION

Excess mortality in persons with mental disorders has been well documented (Chesney et al., 2014), particularly in Nordic countries based on well-established register systems of patients admitted or discharged from hospitals, and cause of death (Wahlbeck et al., 2011, Nordentoft et al., 2013, Plana-Ripoll et al., 2019]. Evidence suggests that adults with mental disorders have risk to die earlier (Nordentoft et al., 2013], the risk is a two to three times higher than general population (Chesney et al., 2014, Crump et al., 2013a). They also live on average 7 to 23 years less than the general population (Chesney et al., 2014, Wahlbeck et al., 2011, Plana-Ripoll et al., 2020). The risk is even higher if a person is diagnosed with schizophrenia (Laurse et al., 2014, Crump et al., 2013b), bipolar disorder (Crump et al., 2013b), substance use or anorexia nervosa (Chesney et al., 2014, Nordentoft et al., 2013, Plana-Ripoll et al., 2019, Krupchanka et al., 2018). While life expectancy in the world has been increasing in the last 50 years, with fast and steady trajectories in Western European countries since 1980 (Leon 2011), studies on mortality trends of individuals with mental disorders were inconsistent. As part of health care reform in European countries in 90s, the de-institutionalisation and decentralisation of care for Finnish psychiatric patients (Chow & Priebe, 2016) resulted in 46% fewer psychiatric beds in 2014 compared to 1993 (Eurostat, 2019) and a reduction in life expectancy gap between patients and the general population (Wahlbeck et al., 2011). Improvements in social economics and health systems may also have contributed to this reduction (Liu et al., 2017). However, limited reports on changes in mortality trends have been conflicting. One research reported an increased standardized mortality ratio (SMR) among schizophrenia patients in Finland (Lumme et al., 2016) but another reported no change (Tanskanen et al., 2018). For all-cause mortality among individuals with any mental disorder, increased SMR was reported in Norway (Nome and Holsten., 2012), but decreased in both Denmark (Plana-Ripoll et al., 2020, Gissler et al., 2013) and Finland (Lumme et al., 2016, Gissler et al., 2013). A study that applied the age-period-cohort (APC) model examined the period effects of alcohol-related mortality based on data from four Nordic countries, France, and Germany in 1980–2009 (Kraus el., 2015). The study reported multiple trends of mortality, with increases in Denmark, Finland and Germany, a decrease in Sweden, and U-shaped trends in Norway and France. None of these studies examined how individual and societal determinants, health lifestyle and behaviours were associated with changes in mortality of psychiatric patients (Krupchanka et al., 2018).

1.1 Objective

This study aims to examine temporal trends of all-cause mortality in patients with mental disorders in Finland over two decades, and to quantify associations between risk factors and mortality trends. To provide guidance for targeted policies, we adopted the World Health Organization's Multilevel Intervention Framework (MIF) model (Liu et al. 2017), which classified risk factors into three categories: individual, health systems, and society.

2. METHODS

2.1 Study population

We identified 226,948 patients aged 18–102 years admitted to one of 87 psychiatric facilities with a primary diagnosis of mental disorders (ICD-10: F01 to F99) in Finland between 1 January 1995 and 31 December 2014. December 2014 was selected as the last observation year from the Care Register for Health Care held by the National Institute for Health and Welfare. For the current study, we also used registers from Statistics Finland, the Register of Social Assistance, the Infectious Diseases Register, and the Cause of Death Register to link individual information on socio-economic position, possible HIV infection or AIDS and death information of them. Individuals in the three register systems were linked using their unique personal identity code (Statistics Finland 2024), which is permanently issued to anyone registered in Finland's Population Information System. The personal identity code is a means of identification for individuals as there are no two persons with the exact same code. The code is used in registers and by healthcare service providers (Digital and Population Data Services Agency 2024). In our data, the personal codes were replaced by an encrypted coding system after data linkage by a data manager at the National Institute for Health and Welfare. Causes of death were identified using ICD-10 codes from 1998 in the register, were converted from ICD-9 to ICD-10 for patients admitted 1995–1997.

Individuals were followed from the date of discharge to the date of death, or to the end of the study on 31 December 2014, which ever came the first. At discharge, a majority (95%) of patients were classified in six primary diagnose groups: (1) known physiological conditions or organic disorders (D1:F01–F09), mental and behavioural disorders due to psychoactive substance use (D2:F10–F19), schizophrenia spectrum disorders (D3:F20–F29), mood/affective disorders (D4:F30–F39), anxiety/dissociative/stress-related somatoform and other nonpsychotic disorders (D5:F40–F49) and personality disorders (D6:F60–F69) (**Supplementary S1).** After excluding 6,701 (3%) cases without diagnose code, 147 (0.06%) cases with unspecified mental illness and 1,397 (0.62%) cases who died prior to the hospital discharge date, the final study sample included 218,703 patients (52.4% male and 47.6% female). Because individuals could be admitted more than once during our study period, only the most recent admission date of those with several admissions was selected as for the study cohort.

for the study.

2.2 Age, calendar time, cohort and mortality measures

The analysis used the patients age at discharge and calendar time from the last discharge year. The birth cohort was a difference between age and calendar year. The mortality rate was defined as *number of patients who died divided by total person years of all patients*100%* during a defined time period. The person year of each individual was calculated based on exact days of follow-up from the date of discharge to the date of death or date of censored or end of the study on 31 December 2014.

2.3 Risk factors

Based on the WHO MIF model, we extracted 13 variables from the register systems. Details of risk factors are in **Supplementary S2.** At individual level, four factors measured severity of disorders (length of hospital stay, number of previous hospital admissions, Global Assessment Scale [GAS] at discharge, and time from first diagnose to the latest treatment), and three individual risk behaviours (HIV/AIDS positive, substance use, and low motivation for treatment).

Two health system factors, workforce issue and medication, were created. The workforce issue was measured by number of coercive measures [Finnish Mental Health Act (1116/1990)] used by staff on each patient during the last treatment period. Medication was any type taken for psychosis or depression or both or others used during the period prior to the discharge date. Four social determinants measure for each individual included: (1) employment status, (2) education level; (3) rehabilitation program, and (4) income support.

2.4 Statistical analysis

We first examined the mortality rate over calendar year after discharge to observe the raw time trend and possible variation by discharge period, and then examined age specific crude mortality over time to observe difference in the time trend by age groups. We used Poisson regression models with random hospital effects of lognormal distribution to estimate relative rate (RR) of death based on exact follow-up days from discharge. The birth cohorts were defined as random effects in addition to the hospital effects according to the Intrinsic estimator approach.

To examine associations of risk factors with mortality and trends in mortality, we fitted six models in which the calendar time was coded from 0 to 19 for the 20-year period and fitted as a linear term in all models based on the observation of the descriptive analysis. In Model1 we estimated temporal trends, adjusted for patient's age and gender. A nonlinear term of age was fitted to reduce correlation between age and time. In Model 2 we added random effects of birth cohorts in Model 1. In Model 3, Model 4 and Model 5, we added individual level, health services level and societal level risk factors separately to Model 2 respectively. In Model 6 all factors were included. Likelihood ratio statistics determined the significance of cohort effects and the various sets of risk factors. The change rate of mortality was the estimated RR associated with the time variable minus 1, which indicates increasing over time in mortality if the sign is positive and declining over time if the sign is negative.

Analyses were conducted for all patients and then again for the six subgroups of different psychiatric diagnosis separately. We used IBM SPSS Statistics for Windows (version 26, IBM Corp., Armonk, NY) and SAS System for Windows (version 9.4, SAS Institute Inc., Cary, NC). The GLIMMIX procedure of SAS was used to fit all models.

2.5 Ethical standards

The authors assert that all procedures contributing to this work comply with the ethical standards of the relevant national and institutional committees on human experimentation and with the Helsinki Declaration of 1975, as revised in 2008.

Ethics approval for the register study were guaranteed by the Ethics Committee at the University of Turku (41/2015). The study plan was approved by the Data Protection Ombudsman (Dnro 3484/402/2015), National Institute for Health and Welfare (Dnro THL/1570/5.05.00/2015), and the Statistics Finland (Dnro TK52-691-16).

3. RESULTS

3.1 Mortality rate and change pattern

The mean age was 44.3 (SD=16.3) for male (52.4%) and 47.9 (SD=18.5) for female (47.6%). Over the 20-year period, 54,236 (24.6 %) patients died (59.1% male; 40.9% female). The total follow-up time was 1,660,399 person years with median 5.71 years (min/max: 0.0/19.99), and 165,862 were alive and censored at the end of study period.

Mortality was higher in male than in female as expected (Table 1). Among discharge periods, the overall mortality was similar, ranging from 3.67% (1995–1999) to 3.35% (2010–2014). Within each period the mortality declined linearly for both male and female. Across periods, the mortality of all patients showed a markedly declining trend from 7.42% down to 3.35% in the first five-year period of discharge, less declining from 3.61% to 2.69% in the second five-year period, and the least declining from 2.58% to 2.27% in the third five-year period.

(Table 1 Crude death rate over time by discharge period)

3.2 Temporal trends, age and cohort effects

The annual rate of death corrected for age and sex (Model 1) decreased overall by 2.3%, with no decline in the group with personality disorders (D6) (RR: 0.995, 95% CI 0.983–1.007), and the largest decline rate of 2.7% in D4 of mood affective disorder (RR:0.973, 0.969–0.976), followed by D3 of affective non-psychotics group at 2.6%. These patterns remained the same after taking into account the birth cohort effects (Model 2) (Table 2, Figure 1a).

A nonlinear (quadratic) effects of age was demonstrated for patients with any diagnose and for all, with slow increase in mortality before 60 years old and a rapid increase after the age of 60 (**Supplementary S3**). A large difference in age effects between models 2 and 6 suggested that risk factors at different levels accounted for large amount of age effects. Effects of birth cohort were minor and fracture, which were not affected by risk factors (**Supplementary S3**).

(Table 2 Associations of time with mortality and attribution by risk factors by primary diagnosis from Poisson random effects models)

3.3 Temporal trends and risk factors

Comparing with Model 2, time trends of Model 6 that adjusted for all risk factors demonstrated further decline in mortality for any diagnose group by 27.3% (RR: 0.972-1 VS 0.978-1) with the largest change in decline rate for the Personality disorder group (D6) by 350% (RR: 0.973-1 VS 0.994-1), followed by D5 of anxiety non-psychotics by 50.0% (RR: 0.979-1VS 0.986-1) and then D4 of mood affective disorders by 38.5% (RR: 0.964-1 VS 0.974-1). The

decline rate of the D1 group, organic disorders, seemed unaffected by any risk factors as the RR estimates of Model 2 and Model 6 were almost the same (Table 2, Figure 1b). The accountability of individual risk factors on the decline rate was the largest for the group with personality disorders (D6) at 467.7%, followed by the group of anxiety non-psychotics (92.9%), psychoactive substance use (85.7%), schizophrenia spectrum (61.5%) and mood affective disorders (51.9%). For all patients, adjusting for individual level factors (Model 3) brought down decline rate by 54.5% (RR: 0.966-1 VS 0.978-1) (Table 2 and Figure 1c), while as health services (Model 4) and societal factors (Model 5) accounted for the decline trends only by 4.5% and 4.1% respectively. The overlapping 95% CIs of Model 4 and Model 5 with that of Model 2 suggested no significant impacts of health service and societal factors on the declining trends of mortality over time (Table 2 and Figure 1d).

3.4 Effects of risk factors on death risk

All risk factors at individual level demonstrated associations with death risk in the expected direction except for low motivation for treatment, with varied impacts by diagnosis group (Table 3). Severity of disorders in the GAS score and frequency of hospital admission were associated with increased risk of death for all patients, while longer hospital stay and longer time from the year of first diagnose to the year of recent hospital admission were associated with lower risk of death except for patients in groups of anxiety non-psychotics (D5) and of personality disorders (D6). Patients who were admitted to hospitals more than ten times and in the lowest GAS band at discharge would have cumulative death risk as high as 9.3 (95%CI:7.2–11.4) times in the mood effective disorders (D4) and as low as 3.2 (2.0–4.9) times in the group of organic disorders (D1) than their counterparties. HIV positive was associated with increased RR except for patients with psychoactive substance use (D2) and with anxiety non-psychotics (D5). Use of any substance was associated with increased RR for most groups of patients but negatively associated with the group of organic disorders (D1). Low motivation for treatment was a risk factor for patients with psychoactive substance use or with mood affective disorders only.

(Table 3 Estimated associations of factors with relative rate (RR) of mortality from Model 6)

At the health service level, use of coercive measures was weakly associated with increased death risk for patients with organic disorders (D1), psychoactive substance use (D2), schizophrenia spectrum (D3) and mood affective disorders (D4). No dose-response effect of multiple use coercive type was observed. Any medication use was associated with higher death risk than not using them for most groups except for patients with schizophrenia (D3). Use of antidepressants reduced RR in patients with organic disorders (D1), and increased RR in patients with mood affective disorders (D4), with anxiety disorders (D5) and personality disorders (D6). Use of both neurolepts and antidepressants increased hazard ratio (HR) for all groups except for the schizophrenia group (D3).

Among social determinants, employment was associated with lower relative risk (RR) for all six major diagnose groups. Low education was a risk factor for schizophrenia patients (D3) but not for other diagnose groups. Both not participating rehabilitation program and not on income support after discharge were associated with increased death risk of patients in all groups.

4. DISCUSSION

Previous literature reported overall declined mortality among psychiatric patients admitted to hospitals in Finland. However, from literature review to update, we found hardly any literature that examined the association between the temporal trend and the impacts of multiple risk factors at individual, societal and health care levels on the change trends in death risk for individuals with different psychiatric diagnosis. The national health care information system in Finland has been well established and managed with high quality (Sund 2012). The data consists of treatment notifications with personal identity codes from healthcare units (The Finnish Institute for Health and Welfare 2020). Valid codes identifying various psychiatric diagnoses under the ICD-10 system and are linked with ICD-9 for the purpose of this study

This study only used data from 1995 to 2014 that were available to examine the mortality trend and risk factors associated with the trend. Since the period effect reflects environment change such as national healthcare policy change that was aimed to impact on mortality over an implementing time (Smith & Wakefield, 2016), the finding of this study, in particular, the change trend related to healthcare system and social policy factors may not be extendable to the later ten years. Instead, future study in examining impacts of the national healthcare changes in recent period on mortality trend in specific psychiatric population may use this study as a reference. However, previous literature in mortality trend among this population in Finland were also up to 2014, which gives a sound comparative base for the study.

Several important findings emerge from the study. First, decline trends in mortality differed by primary diagnosis, although the overall mortality trend declined. Second, more than 50% of the declining trend in mortality was counted by risk factors of mortality in psychiatric patients at individual level. Finally, we provided further evidence that multilevel risk factors as identified by the WHO MIF model were associated with mortality of individuals with psychiatric diagnoses and could have large impact on time trend of mortality.

The declined time trend in this study aligns with the declining mortality trend for the period 1987–1996 reported by Gissler et al. (2013), is consistent with a Finnish study based on all psychiatric patients aged 25–75 years in 1990–2010 (Lumme et al., 2016) and is in line with a previous study analysing SMRs by age group in a Finnish birth cohort (Gissler et al., 2013). However, the subgroup analysis demonstrated different declining rate in patients with different diagnoses before adjusting for any risk factors. The annual decline rates were 2.4%–2.6% in patients with organic disorders (D1), schizophrenia (D2) and mood disorders (D4), of 1.4% in D2 group of psychoactive substance use and D5 anxiety non-psychotics, and no decline in group D6 of personality disorders. After adjusting for all risk factors, the annual decline rates were between 2% (D2) and 3.6% (D4). The declining trend of death risk in the schizophrenia group is opposite to the study based on psychotic patients aged 25–75 years in Finland during 1990–2010 (Lumme et al., 2016), and is different from another Finnish study showing no change of mortality in SMRs among schizophrenia patients during 1984–2014 (Tanskanen et al., 2018), but seemingly consistent with a study in Sweden in 1987–2010 (Osby et al., 2016). However, the declined death risk for the group with personality disorders (D6) in this study was opposite to a Swedish study that reported an increasing trend of SMR for the period 1987–2011 (Bjorkenstam et al., 2015). The declining trend for individuals in the group of psychoactive substance use is also opposite to the Finnish study (Lumme et al., 2016). Our result should not be directly comparable with studies that included patients of different ages, from different time periods, and not adjusted for cohort effect or for risk factors.

The declining trend in the group of schizophrenia could be attributed to several reasons. Evidence consistently indicated high death risk of suicide and cardiovascular diseases (Tanskanen et al., 2018) among people with schizophrenia in Finland and other nations (Saha et al., 2007). Use of antipsychotic treatment significantly reduced death risk of both suicide and cardiovascular diseases in a 20-year follow-up study based on 62,250 schizophrenia patients in Finland (Taipale et al., 2020). The suicide prevention program in Finland was shown effective (Lewitzka et al., 2019) and our study also suggested that controlling for risk factors of disease severity and health behaviour of individuals could lead to a reduced mortality trend over time by 61.5% for individuals with schizophrenia. Among group with substance use disorders (D2), the main cause of death was alcohol induced followed by cardiovascular diseases, then accidents (**Supplementary S4**), in line with a Swedish (Fugelstad et al., 2014 and a Danish study (Plana-Ripoll et al., 2019). Changes in alcohol policy led to a decrease in prevalence of alcohol-related problems (Bloomfield et al., 2010).

The decline trend was the least varied in the range of 2.2%–2.4% in the group of organic disorders, and the change rate in mortality was not affected by risk factors at any level. This group of patients had an average age of 77.3 years old (SD 11.7) at death. The life span of individuals in this group was slightly shorter than general population until 2010 for men and 2005 for women when the gap significantly increased (**Supplementary S4**). Their main causes of death were of dementia/Alzheimer's and circulatory diseases (**Supplementary S4**). The mortality pattern in dementia/Alzheimer's was inconsistent according to a global literature review (Prince et al., 2016). Although death risk from diseases of circulatory system among persons with psychiatric disorders was two times more than general population in Finland (Karald et al., 2008, the time trend in cardiovascular mortality was not explained by traditional risk factors (Laursen et al., 2013). Further research could examine risk factors in association with dementia/Alzheimer's of these populations and review quality of current healthcare systems for them in order to develop a well-targeted care plan to fill the gap in health inequality.

Based on the study data, the main causes of death in the anxiety group (D5) were circulatory diseases, suicide and neoplasms (**Supplementary S4**). Although the mortality rate decreased over the study period, those individuals lived a life about 20 years' shorter than general population with average age at death 57.7 years old and the gap was increasing continually (**Supplementary S3**). Similarly, the first three causes of death in personality disorder group (D6) in the study population were suicide, circulatory disease and accidents which is consistent to a previous study (Shmuel et al., 2022). Other known causes of death for individuals with personality disorders were substance abuse, comorbid conditions and poor health. These factors are all at individual level. The mortality rate did not show change over time for group 6 before adjusting for risk factors, and presented significantly declining after adjusting for risk factors at individual level (Model 3). The reduced mortality rate overtime maintained for the full adjustment (Model 6). The evidence from this study clearly showed that once controlled for clinical severity at individual level that were associated with high risk of death, the mortality rate declined rather fast over time for the two groups, particularly for group D6. Although personality disorders were underdiagnosed (Tyrer et al., 2015) and evidence on which treatment would benefit an individual with personality disorders is incomplete and scarce, personality disorder itself cannot lead to death but other comorbid conditions. This finding suggested that effective clinical care to reduce severity of comorbid conditions of patients with personality disorders or anxiety might have reduced mortality of those individuals. Therefore, continuously providing high quality clinical care as well as social supports for those people should be warranted to reduce their mortality rate further.

The association of risk factors with mortality in our sample was expected and well recognized globally (Liu et al., 2017). High quality healthcare aimed to improve clinical conditions at individual level with any diagnose of mental disorders could not only led to a reduced mortality, but also bring down the curve of death risk considerably. Although the health problems are well known in Finnish population with serious mental disorders, monitoring and treatment of somatic health problems is still insufficient (Eskelinen et al., 2017). It has also reported that individuals with mental disorders often were at lower social economic level (Kivimaki et al., 2020). Among our study individuals, 13.7% was unemployed, 40.1% had only basic education and 57.9% on income support. These social determinants of health were associated with premature mortality (Liu et al., 2017), which was also evidence in this study. But the impact of social determinants on the time trend of mortality in this study was minor at about 4.7%. In our study population, individuals with basic education were younger with similar crude mortality rate to the reference group, and individuals on income support were younger with lower mortality than those in the reference group. Interactions between social determinants and other individual factors could also let to a reduced impact on the time trend. Further research to identify risk factors with significant power to predict death risk of individuals with different psychiatric diagnosis should help in developing clinical service tools for monitoring and reducing preventable death in the future. Research on risk factors for the raising gap in life expectancy between individuals with specific psychiatric disorders and general population in Finland, and on developing targeted intervention plans in healthcare service should be a priority.

Our study found no association between any medication use and death risk for individuals with schizophrenia. A Finish population-based cohort study in patients with schizophrenia between 1996–2006 found that long-term treatment with any antipsychotic drugs was associated with lower mortality of all causes compared with no antipsychotic use (HR 0.81, 95% CI 0.77–0.84), but a higher risk of mortality for the use of quetiapine than the use of perphenazine (HR 1.41, 95%CI 1.09–1.82) (Tiihonen et al., 2009), which suggested varied impact on mortality by different type of medication. A Swedish register data-based follow-up study on antipsychotic treatment and mortality in schizophrenia demonstrated a U-shaped relationship between mortality and dosage of medication, i.e. both no use and high dosage use of the medication had high risk of mortality (Torniainen et al., 2015). Other studies suggested that for this population, medication compliance with antipsychotics, lipid-modifying agents, antidepressants, and lithium is the most important factor in reducing all-cause mortality (Correll et al. 2022). Proper dosage and adherence to long-term use as well as good family or social supports are also key factors (Liu et al., 2017) for reducing all-cause mortality. However, for this study we did not have detailed information on what specific antipsychotic drugs used by individuals and for how long as well as at what dosage. Information on compliance of individuals to medication were also not available. Based on literature, one possible explanation of our finding could be that these individuals might not have taken the right medication, they may not have had good adherence to their medication, or their average dosage was at the bottom of the U shape, having no direct impact on mortality. Further research is needed to investigate this finding.

The study also found that use of antidepressants reduced RR in patients with organic disorders (D1), and increased RR in patients with mood affective disorders, which further indicated complexity of treatments for people with mental disorders. Large population-based studies suggest that long-term use of antidepressants is associated with increased mortality due to suicide (Choi 2021), cardiovascular disease and cerebrovascular disease (Bansal et al. 2022). The longer the use of antidepressants lasted, the higher the risk for diabetes and hypertension was (Bansal et al. 2022). New cardiovascular events increased too (Maslej et al. 2017). As opposite, for people with cardiovascular diseases, antidepressants do not seem to increase the risk for mortality, possibly due to the anticlotting properties of

antidepressants (Maslej et al. 2017). This might explain why people with organic disorders were different in our study in terms of mortality and use of antidepressants. Further study is required to investigate specific medication treatment and association with mortality for people with different diagnosis.

Although health services factor did not show significant impact on temporal changes in death rates, the use of coercive measures of one or two types significantly increased the risk of death for patients in the groups with organic disorders, psychoactive substance use disorders and schizophrenia. Future research should identify risk factors associated with coercion in psychiatric hospitals. The knowledge derived can be used to design and test the effectiveness of interventions to decrease the use of coercive treatment and improve quality of care for those patients.

It is well known that effective, targeted and long-term health care policies aimed at reducing death among patients are reflected in the change of mortality over time. By examining the temporal trend in mortality for six major groups of psychiatric diagnosis, this study provides reference for adjusting existing policies or making new policies for specific populations. For example, the overall mortality decline from 1995 to 2014 in Finland could be partly due to the national plan to prevent suicides among individuals with mental disorders implemented in the 1970s and which led to a steady decline of suicide rates since the 1990s (Statistics Finland 2020). However, the overall mortality declined in groups D2 and D5 with diagnoses involving psychoactive substance use and anxiety non-psychotics was the slowest. Similarly, the change rate in the two groups was only impacted by individual risk factors, not by social and health service factors. The top three causes of death in D2 were alcohol, circulatory diseases and accidents, and in D5 circulatory diseases, suicide and neoplasms. Hence, these individuals might not have particularly benefited from the suicide prevention strategy. A health care strategy on preventing alcohol-related death would be mostly relative for the D2 group. In 2014, the national plan for mental health and substance abuse was implemented in Finland; it set joint objectives for mental health and substance abuse work at the national level (Ministry of Social Affairs and Health 2014). Extending the current research to the last ten years, one would be able to assess the effect of government policy, particularly on individuals in group D2. The same principle of implementation may apply to groups with other diagnoses.

4.1 Limitations

The study has limitations. First, the psychiatric diagnosis based on a register of patients recently discharged from hospitals during the study period means that the time period from onset of the condition to the recent discharge for some patients were not included in the follow-up time. However, mortality rate was a relative measure, the difference due to different starting points of follow-up should not make large difference in the outcome. A national study based on a cohort of 1st admission of patients (Plana-Ripoll et al., 2019) reported a mortality rate ratio of patients with substance use disorders as same as another national study based on the discharge cohort of patients with the same diagnose (Krupchanka et al., 2018) on the same population. Moreover, this study was focused on the time trend in the death risk, which was also relative and should not be affected by the choice of admission or discharge cohort.

Second, we only examined linear trend over 20-year period based on initial observation in the data for all patients, which could limit its relevance to today's climate. In the current situation, however, the data analysis could not be extended beyond 2014 due to practical obstacles (Ketchen et al., 2023) and new national regulations on the secondary use of health and social data (the Ministry of Social Affairs and Health 2024). If new data of recent years were included to explore the trend, a nonlinear trend is possible for some diagnosis groups, which might alter the change rate in mortality in either

direction, increasing or declining to a small degree. Further exploration of change mechanisms would be needed. However, a nonlinear trend may not have implications if one could not establish its association with impacts of the national healthcare changes in recent period (the Ministry of Social Affairs and Health, 2023) on mortality trend in specific psychiatric population.

Third, we excluded individuals dying prior to hospital discharge which may have made our observed cohort appear healthier than all individuals hospitalized. As this study was interested in the change in mortality over time and not in the absolute mortality at each time point, this limitation should not impact the interpretation of the key findings.

Fourth, some important risk factors at the health systems and societal levels, such as leadership, financing and information as well as personal income, were not available. They could have impact on mortality trends. For example, personal income as a social determinant factor was known to be associated with mortality. Changes in the factor over time might impact a change in mortality, too. However, single risk factors usually had rather small impacts on mortality. Other similar factors reflecting the financial situation of individuals, such as employment or whether one's income is enough to meet their needs, could have similar impacts on mortality. Given that the study already included many factors in the same category, adding one or two more factors may not alter the findings a great deal. Nevertheless, including more factors in this kind of study in the future would provide stronger evidence for targeted mortality reduction intervention.

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Figure Citations

Figure 1 Comparing time trends in estimated RR among models

a Model 2 estimated trends adjusted for age, sex and birth year by diagnose group

b Model 6 estimated trends adjusted for all risk factors by diagnose group

c Estimated trends after adjusting for various risk factors (all diagnosis)

d Estimated trends with 95% confidence intervals before and after adjusting for all factors (all diagnosis)

Figure Legends

(Model 1 adjusted for age and sex; Model 2 adjusted for age, sex and birth year; Model 3 adjusted for risk factors at individual level based on Model 2; Model 4 adjusted for health services factors based on Model 2; Model 5 adjusted for societal factors based on Model 2; Model 6 adjusted for all factors based on Model 2)

Title: Temporal trends in mortality and associated factors among persons with mental disorders: a register-based cohort study

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All authors were involved in designing the study, interpreted the data and critically reviewed the manuscript. MY wrote the first draft of the manuscript and led interpretation of results. MV secured the grant for the study. MV and TL contributed to the writing. MY and TV analysed the data. SLN and MA provided critical comments to improve the manuscript. MV, TV and TL had full access to anonymised data.

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Declaration of competing interest

None.

Availability of Data and Materials

The data that support the findings of this study are available from The Finnish National Care Register for Health Care and Statistics Finland, but restrictions apply to the availability of these data. The data are usable for this study only.