Incidence of SARS-CoV-2 and all-cause mortality in persons with co-occurring substance use disorder and mental illness during the pandemic: A Norwegian cohort study

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#### Abstract

### Purpose

Most people were affected by the COVID-19 pandemic. Persons with co-occurring substance use disorder (SUD) and mental illness (MI) are already a marginalized group, with above average mortality. Thus, the study aim was to investigate SARS-CoV-2 incidence and mortality among persons with SUD/MI during the first two years of the pandemic.

## Methods

This historical cohort study merged data from the Norwegian Patient Register, the Norwegian Surveillance System for Communicable Diseases and census data from Statistics Norway. We calculated crude mortality rates for persons with SUD and mild/moderate vs. severe MI and compared them to persons with physical illnesses or healthy controls. The incidence rate ratios for SARS-CoV-2 infection and mortality were estimated using Poisson regression models.

#### Results

Compared to healthy controls, the SARS-Cov-2-infection rate was marginally lower in persons with SUD and mild/moderate MI (IRR,1.19 [95%CI,1.09-1.30]) as in persons with physical illness (IRR,1.35 [95%CI,1.23-1.47]), whereas persons with SUD and severe MI showed a lower rate compared to healthy controls. Crude mortality rates for persons with SUD/MI were substantially higher and increased much more during the pandemic than for persons with physical illnesses or healthy controls. The IRR for mortality in persons with SUD and mild/moderate MI was 10.61 (95%CI,7.19-15.67) and 11.44 (95%CI,7.50-17.45) for SUD and severe MI, compared to 5.03 (3.34-7.57]) for persons with physical illnesses only.

### Conclusion

The analysis showed excess mortality during COVID-19-pandemic for SUD/MI, but without higher SARS-CoV-2 infection rates in this group. Consequently, excess mortality among persons with SUD/MI was not due to SARS-CoV-2 infection.

## Introduction

Persons with co-occurring substance use disorders (SUD) and mental illness (MI) are among the most vulnerable individuals in modern welfare states. SUD/MI is associated with poorer than average health and increased mortality[1]. Persons with SUD/MI have a lower quality of life than persons with a single disorder[2] and low levels of functioning in important areas of life, such as poor living conditions, financial problems, social problems, and weak integration in their communities. They also have a much shorter life expectancy than the general population [3].

The global outbreak of SARS-CoV-2 in early 2020 affected the lives and health of most people worldwide. Females were generally more prone to a SARS-CoV-2 infection, while males had a greater proportion of treatment due to a SARS-CoV-2 infection in intensive care units [4]. Physical diseases such as cancer, cardiovascular disease, diabetes and acute kidney injury increased the risk of mortality related to SARS-CoV-2 infection [5]. In addition to pre-existing physical comorbidities, severe MI was a risk factor for severe outcomes and death among younger persons with SARS-CoV-2 infection [6]. Early COVID-19 studies concluded that persons with a SUD were at higher risk of hospitalization and intubation due to a SARS-Cov-2 infection. Further, as SARS-Cov-2 attacked the lungs, people who smoked or inhaled drugs were at particular risk [7, 8]. However, a greater probability of hospitalization for patients with co-occurring SUD and MI, compared with those with one or none of those disorders, was found in a US study of adults with a SARS-CoV-2 infection treated in emergency wards from April 2020 to August 2021. Otherwise, SUD appeared to involve a greater probability of hospitalization than MI [9]. Thus, SUD was associated with an increased risk for SARS-Cov-2 infection [10].

In the early phase of COVID-19, there was a fear that the virus would hit persons with SUD particularly hard [11]. However, a survey conducted among people with SUD in spring 2021 showed high compliance with the testing regime [12]. Only 2.5% of those tested were SARS-CoV-2 positive. This was in line with a study finding that persons with SUD were more often tested but were less likely to test positive than the general population [13].

General population excess mortality in 2020-2021 was highest in South Asia, North Africa, the Middle East, and in Eastern European countries [14]. In Norway, all-cause mortality decreased in 2020, the first year of the pandemic[15], whereas in the second year, death rates rose again [16]. All-cause mortality in the general Norwegian population was higher for men than women and total excess deaths were dominated by the age group 70-89 years in both 2020 and 2021 [16].

In sum, physical illness, MI and SUD were risk factors for a SARS-CoV-2 infection, and for greater mortality than in the general Norwegian population. Less is known about how this played out for people with SUD/MI. Were they at greater risk? Thus, we hypothesize that people with compromised health due their SUD/MI were at increased risk of a SARS-CoV-2-infection and that all-cause mortality in this group increased during the pandemic. Following this, the aims of the present study were 1) to estimate the incidence of SARS-CoV-2 infection among persons with SUD/MI, and 2) to examine how the first two years of COVID-19 affected the all-cause mortality of persons with SUD/MI, separated into those with mild/moderate MI and with severe MI, and persons with only physical illness, compared with the general population.

## Methods

#### **Data sources**

We conducted a historical cohort study based on a data file constructed by merging individual-level information from the Norwegian Patient Register, the Norwegian Surveillance System for Communicable Diseases and register data managed by Statistics Norway. The Norwegian Patient Register collects data about all contacts with and admissions to specialist health care in Norway, such as date of referral, length of stay, diagnosis, whether hospital admission was acute or planned, treatment codes, and whether the outcome was discharge or death. The register data administered by Statistics Norway include a wide range of socio-demographic information such as age, gender, country of birth, educational level, employment status, disability pension and death. Linking these data is possible due to the unique 11-digit personal identifier assigned to all Norwegian residents. For the present study we used register data from 2019 to 2021.

The study was approved by the South-Eastern Norway Regional Committee for Medical and Health Research Ethics (reference number 158909) and from the data protection office of Inland Hospital Trust (reference number 135540).

## Sample

The population of interest was defined as all patients diagnosed with at least one SUD and MI between 2019 and 2021. The ICD-10 main diagnosis (Chapter V) was used to identify persons with SUD/MI. Persons who were registered with F10-F19 as a main or secondary diagnosis with any other concurrent main or secondary F-diagnosis (excluding organic, symptomatic, mental disorders (F00-F09)) were specified as persons with SUD/MI. Within this group, all patients with schizophrenia-like psychotic disorder (F20–F29), bipolar disorder (F30–F31), and depressive disorder with psychotic features (F32.3, F33.3) were grouped as persons with SUD and severe MI. These two subpopulations with either SUD and mild/moderate MI (N=33427) or persons with SUD and severe MI (N=3516) were compared to a random cohort of persons with no SUD/MI, who had been matched by sex, five-year

age bands and health region based on place of residence to the persons with SUD/MI. The control population was then split into A) healthy persons with no record in the Norwegian Patient Register between 2019 and 2021 (as healthy controls, N=13806), B) persons with a physical illness only (any ICD-10 code except F-codes, N=21265), C) persons with only MI (F20-F99, N=1640) and D) persons with only SUD (F10-19, N=196). Due to the random sampling, the numbers of persons with MI only or SUD only were so low that they were not included for further analysis (see appendix page 1-2 for the cohort selection process and cohort characteristics). Persons in all cohorts were at least 18 years old in 2019.

## Measures

Month and year of death registered between January 1, 2019 and December 31, 2021 were obtained from data from Statistics Norway. The first SARS-CoV-2 infection, confirmed by a polymerase chain reaction test between March 2020 and December 2021, was obtained from the Norwegian Surveillance System for Communicable Diseases.

Covariates included sex, age (categorized into three age groups: 18-40 years, 41-60 years and 61-82 years) and health region. Age was defined as age reached at the end of each calendar year. We also included social benefits paid by the local Norwegian Labour and Welfare Administration as a marker of low socio-economic status. Social benefits refer here to loans and financial support received by people unable to support themselves. In Norway such financial assistance is provided if there is an imbalance between a person's expenses and income as determined by the government. Dummy variables were constructed to indicate whether participants had received social benefits in 2018-2019. The study cohort was followed from the date of their first consultation or admission with an MI and/or

SUD diagnosis from January 2019 to December 2021. Follow-up ended on December 31, 2021, or on the date of death, whichever came first.

## Statistical analysis

The characteristics of the study population were described by frequencies and percentages if categorical. Comparisons between the different patient groups and the healthy controls were made using the  $\chi^2$ -test for categorical data.

Further, we calculated crude mortality rates (CMR) by dividing the total number of deaths in a patient group by the total number of persons in the group by the end of the years 2019, 2020 and 2021. These were compared to the CMRs calculated for the Norwegian population, aged 18-82 years, retrieved from SSB in those years. All CMRs are reported per 1,000 persons with 95% Poisson confidence intervals (CI).

We applied Poisson regression models to estimate incidence rate ratios (IRR) for the comparison of rates of SARS-CoV-2 infection and mortality between persons with SUD and mild/moderate MI, persons with SUD and severe MI, persons with physical illness only and healthy controls. This procedure allowed us to control for various covariates [35]. Due to the matched design, the Poisson regression was controlled for the matching factors of sex, age group, receiving social benefits, and health region as a proxy for place of residence. The regression model can be written as follows:

$$\ln\left(\frac{Y}{exposure}\right) = \beta 0 + \beta 1 X1 + \beta 2 X2 + \beta 3 X3 + \beta 4 X4 \epsilon, \quad \epsilon \sim \text{Poisson}$$

In this equation, Y is the number of first-time SARS-CoV-2 infections (Table 2) or deaths (Table 3). Exposure is the number of person-months at risk, thus the number of months from the start of the pandemic in March 2020 until the first confirmed SARS-CoV-2 infection or the end of the observation period in December 2021 (Table 2), or the number of months from birth until month of death or the end of the observation period (Table 3). Further,  $\beta$ 1-4 are the coefficients and X1-4 the covariates sex, age group, health region and receiving social benefits.

Results with p < 0.05 were considered statistically significant. All analyses were performed using Stata SE/17.

#### Results

### Sociodemographic characteristics

There was a male majority in all subpopulations and most belonged to the youngest age band (18-40 years). In the groups of persons with SUD and mild/moderate or severe MI, about twice as many received social benefits (45.1% and 47.2%) as the healthy controls (22.6%). Comparisons between all groups were significant (p<0.001). Table 1 presents the characteristics of the sample.

#### \*\*\*please insert table 1 here\*\*\*

#### **SARS-CoV-2** infection

For first-time SARS-CoV-2 infection, bivariate analysis showed significant differences between the various subpopulations, although these were clinically marginal. SARS-CoV-2 infection was most prevalent among persons with only a physical illness at 6.8%, followed by persons with SUD and mild/moderate MI (6.2%) and healthy controls (5.6%). Among persons with SUD and severe MI, 175 (5.0%) were infected from March 2020 to 2021 for the first time (Table 1). In table 2, we present crude an adjusted IRR for SARS-CoV-2 infection in the period March 2020 to December 2021. Adjusted IRR (Table 2) indicated that the SARS-CoV-2-infection rate among persons with only physical illness is 1.35 (95%CI,1.23-1.47) times as high as the rate among healthy controls, while the rate for persons with SUD and mild/moderate MI was 1.19 (95%CI,1.09-1.30) times greater. Although persons with SUD and severe MI showed a 0.90 (95%CI,0.77-1.07) lower rate of infection with SARS-Cov-2 in the first two years of the pandemic, this result was not significant. Further, sex and receiving social benefits were likewise not significant.

#### \*\*\*please insert table 2 here\*\*\*

#### Mortality

Between 2019 and 2021 the percentage of cases of death was highest among persons with SUD and mild/moderate MI (3.9%, 1293 cases) and persons with SUD and severe MI (3.7%, 130 cases), followed by persons with physical illness only (1.0%, 222 cases), see table 1.

CMRs in the year before the pandemic were at least three times higher among persons with a SUD and MI (CMR,19.54 [95%CI,17.08-22.25] for SUD and mild/moderate MI, and CMR, 24.37 [95%CI,16.44-34.79] for SUD and severe MI) than among persons with physical illness only (CMR, 7.74 [95%CI 5.85-10.02]) or the average in the Norwegian population (CMR, 5.08 [95%CI,5.01-5.15]), see figure 1 and supplementary table 2 in the appendix. The mortality rate for persons with SUD and mild/moderate MI nearly tripled from the year before the pandemic (CMR,19.54 [95%CI 17.08-22.25]) to the year 2021 (CMR, 54.07 [95%CI,49.83-58.57]). As for persons with SUD and severe MI, CMRs doubled from 2019 (CMR, 24.37 [95%CI,16.44-34.79]) to 2020 (CMR,47.14 [95%CI,35.20-61.82]) but showed a small decrease in 2021 (CMR,40.60 [95%CI,29.94-53.84]). The rates for persons with only physical illness increased less in the same period (from CMR,7.74 [95%CI,5.85-10.02] in 2019 to CMR,13.23 [95%CI,10.74-16.10] in 2021). For the Norwegian population between 18-82 years, CMRs remained stable over the three years, fluctuating between CMR,5.08 (95%CI,5.01-5.15) in 2019 and CMR,5.18 (95%CI,5.11-5.25) in 2021, with a slight decrease in 2020 (CMR,5.06 [95%CI,4.99-5.12]).

## \*\*\*please insert figure 1 here\*\*\*

The IRRs in persons with SUD and MI showed a similar tendency to the CMRs. Table 3 presents the crude and adjusted IRRs for mortality in persons with SUD and mild/moderate MI, with SUD and severe MI, and with physical illness only for January 2019 to December 2021 compared to the healthy controls. After adjusting for the matching factors of sex, age group and health region, and for receiving social benefits, IRR for mortality in persons with SUD and severe MI was slightly higher (IRR,11.44 [95%CI,7.50-17.45]) than in persons with SUD and mild/moderate MI (IRR,10.61 [95%CI,7.19-15.67]). Although the IRR for persons with a physical illness only (IRR,5.03 [95%CI,3.35-7.58]) was likewise higher than for healthy controls, their IRR was still half of those with a SUD and MI. Mortality for females was lower than for males in 2019-2021 (IRR,0.85 [95%CI,0.77-0.94]), while the oldest age group (61-82 years) showed a 4.12 [95%CI,3.62-4.68] times higher IRR than the youngest age group. Receiving social benefits increased the rate about 6.56 times compared to non-recipients of social benefits.

#### \*\*\*please insert table 3 here\*\*\*

### Discussion

Our study identified a greatly increased general mortality rate during the first two years of COVID-19 among persons with SUD/MI despite a low incidence of SARS-CoV-2. This suggests that a SARS-CoV-2 infection was not the reason for high excess mortality among persons with SUD/MI. With the onset of the pandemic in 2020, the CMR in both SUD/MI groups doubled compared to before COVID-19. This might have several reasons. In Norway, the first national lockdown and other infection control measures were implemented from March 2020. This also meant the discharge of persons with SUD from long-term inpatient care. Non-SARS-CoV-2 hospital treatment was deprioritized, and nurses and social workers in mental health care were given new tasks to control the virus. People also found more barriers to healthcare during lockdown [17]. This may have been an additional challenge for persons with SUD/MI. The International Society of Addiction Medicine Practice and Policy Interest Group raised the concern that people who use drugs may have been especially vulnerable during the pandemic [18]. Increasing difficulty in accessing physical health care for persons with SUD/MI may have meant that diseases were left untreated, which may be an explanation for excess mortality in this group [19]. Furthermore, some health care services became digital during COVID-19. Persons with SUD/MI might have had limited access to smart phones and digital tools [20]. In a study of persons with SUD/MI, they reported challenges in participating in online health consultations due to their limited digital skills [21].

Another possible reason is that the first lockdown in spring 2020 led to the closure of low-threshold facilities for persons with SUD/MI [22]. Opportunities for counselling, contact and socialisation suddenly disappeared. As persons with SUD/MI are generally weakly integrated in society and have little meaningful activity[23], the loss of such facilities might have exacerbated social isolation and increased the sense of loneliness. Social isolation and loneliness have been identified as risk factors for increased mortality[24], and this has been confirmed in a meta-analysis even after stratification by gender, quality, and by studies that controlled for the effect of depression [25]. The decline in mental

health as a consequence of the lockdowns was not only seen in persons with SUD/MI [21], but also those with pre-existing MI [26] reported a worsening of their mental condition during COVID-19. Increased substance use may also have contributed to the excess mortality among persons with SUD/MI during the pandemic [27]. The present study only includes all-cause mortality, being unable to identify drug-related deaths. Other studies, however, have found evidence of this increase[28], and persons with SUD/MI are reported to have consumed stronger substances than usual to cope with the pandemic [21]. With restricted access to syringe services, persons who inject drugs might have re-used or shared syringes, which could have caused infections. During the first six months of the pandemic, the Norwegian borders were basically closed [29], which led to a shortage of pure drugs and persons with SUD/MI might have consumed contaminated or "stretched" drugs. These two factors may have placed an extra burden on the health of persons with SUD/MI.

The finding that the CMR for persons with SUD and severe MI decreased from 2020 to 2021, whereas CMR for persons with SUD and mild/moderate MI rose, is somewhat puzzling. After a year of strict restrictions, health care services in 2021 established strategies to provide care and treatment to those with the greatest needs, such as people with SUD and severe MI. This may explain the decrease in CMR in this group, although it is still higher than in persons with only a physical illness.

The similarity between the SARS-Cov-2 IRRs of persons with SUD and mild/moderate MI and those with only a physical illness might be explained by the general high compliance with the national infection prevention measures by the Norwegian population [29]. This is also in line with previously published research [12]. However, the lower rate of a SARS-Cov-2 infection in persons with an SUD and severe MI than in healthy controls is more difficult to interpret. This cannot be explained by the higher proportion of men in this group, since the analysis was adjusted for sex. Onn explanation could be that persons with SUD and severe MI often live isolated lives due to their severe impairment and were thus not as exposed to the virus as the other groups. Further, a qualitative study of 21 persons with SUD/MI found that most of the participants performed the recommended actions such as washing and disinfecting their hands, maintaining physical distance, and having little contact with others to avoid infection [21]. There is evidence that persons with MI [30] and SUD [31] are of low socio-

economic status. This is also confirmed by our analysis, which shows that over 45% of persons with SUD/MI were receiving social benefits. As for the general impact of socio-economic status on the likelihood of a SARS-CoV-2 infection, recent research is ambiguous. On the one hand, there is evidence that high infection rates correlate with low socio-economic status [32], whereas a German [33] study did not identify any negative associations between low socio-economic position and incidence of SARS-CoV-2, similarly to our research. This analysis, like most of the published research to date, sheds light on the first two years of the pandemic (2020 and 2021). In those years, more virulent SARS-CoV-2 variants were circulating than the Omicron variant that emerged in late 2021, which spreads more easily but usually causes less severe illness. Thus, our incidence rates might not be representative for the third year of COVID-19.

To our knowledge, this is the first study to assess mortality and SARS-CoV-2 incidence among persons with SUD/MI. A major strength of this analysis is that we could include all persons in Norway who were registered as having SUD/MI in specialist health care services in 2019-2021, and then identify those with a SUD and severe MI. This number of patients concurs with a previous Norwegian assessment [34] of this vulnerable group, which means that our study is representative. Further, the use of data from the pre-COVID year to compare with data from two entire years of COVID-19 strengthens this study. However, there are several limitations. First, we were not able to assess cause-specific mortality, because we could not link the data to the Norwegian Cause of Death Registry. Due to the COVID-19 pandemic and reallocation of resources, data from this register is currently not available. Secondly, due to the use of a dataset in which persons with SUD/MI were matched to a random population without SUD/MI, the control population showed a small number of patients with MI only or SUD only, which would have made rate comparisons difficult to interpret, and those patients were therefore omitted from the analysis. However, this bias is unlikely to have affected our main conclusions because the number of cases used in the regression models is sufficient.

# Conclusion

In summary, although we did not find elevated SARS-CoV-2 incidence in our target group in comparison to persons with only physical illness, we found greater mortality associated with both SUD and mild/moderate MI and SUD and severe MI in the first two years of the pandemic than in healthy controls and patients with physical illness only. This suggests that excess mortality among persons with SUD/MI in the COVID-19 years 2020-2021 was not due to a SARS-CoV-2 infection. Further studies are needed to investigate the causes of excess mortality among persons with SUD/MI during the COVID-19 pandemic.

## Contributors

The study was conceived by ML and LL. ML and LL verified the data. ML analysed the data and wrote the manuscript. ML, JGB and LL interpreted the data. ML and LL had full access to the raw data. ML and LL take responsibility for the integrity of the data and the accuracy of the statistical analysis. All authors contributed to preparing the manuscript. All authors had final responsibility for the decision to submit for publication.

## **Declaration of interests**

We declare no competing interests.

### **Data sharing**

The data used in the study are not publicly available. Data from the used health registers can be obtained from the Norwegian Directorate for e-Health which has the authority to process applications and grant access to health data from eleven central health registers, and the authority to grant exemption from confidentiality from the Norwegian Directorate of Health and the Regional Committees for Medical and Health Research Ethics. The application form can be accessed via <a href="https://helsedata.no/en/">https://helsedata.no/en/</a>. The data from Statistics Norway may be applied via <a href="https://www.ssb.no/en/data-til-forskning">https://helsedata.no/en/</a>. The STATA codes are available from the first author on request.

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# **Tables and Figure**

	Persons with SUD and mild/moderate MI		Persons with SUD and severe MI		Persons with physical illness only		Healthy controls	
	n=33427		n=3516		n=21265		n=13806	
	n	(%)	n	(%)	n	(%)	n	(%)
Sex								
Male	20346	(60.9)	2501	(71.2)	11544	(54.3)	10318	(74.7)
Female	13081	(39.1)	1014	(28.8)	9720	(45.7)	3488	(25.3)
Age group								
18-40 years	17359	(51.9)	1878	(53.5)	9723	(45.7)	8284	(60.0)
41-60 years	11153	(33.4)	1373	(39.1)	7402	(34.8)	4573	(33.1)
61-82 years	4915	(14.7)	263	(7.4)	4139	(19.5)	949	(6.9)
Recipient of social	15081	(45.1)	1661	(47.2)	1586		3114	(22.6)
benefit								
SARS-CoV-2	2087	(6.2)	175	(5.0)	1443	(6.8)	778	(5.6)
infection								
Deaths (2019-	1293	(3.9)	130	(3.7)	222	(1.0)	26	(0.2)
2021)								

# Table 1. Characteristics of the final cohort, n=72014

Data are n (%), Differences between groups are all significant (p<0.001)

<b>Table 2</b> Incidence rate ratio (IRR) for SARS-CoV-2 infection in the period March 2020 to							
December 2021, n = 72014							
	Events	Person	Crude IPP	Adjusted IRR (050			

	Events	Person-	Crude IRR	Adjusted IRR (95%
	(SARS-	years		CI)
	CoV-2			
	infection)			
Patient group				
Healthy controls	778	26.15	REF	REF
Persons with SUD and	2087	63.24	1.11 (1.02-1.20)	1.19 (1.09-1.30)*
mild/moderate MI				
Persons with SUD and	175	6.67	0.88 (0.75-1.04)	0.90 (0.77-1.07)
severe MI				
Persons with physical	1443	40.13	1.21 (1.11-1.32)*	1.35 (1.23-1.47)*
illness only				
Sex				
Male	2818	84.56	REF	REF
Female	1783	51.62	1.03 (0.97-1.09)	1.01 (0.95-1.07)
Age group				
18-40 years	2960	70.22	REF	REF
41-60 years	1388	46.41	0.72 (0.67-0.76)*	0.69 (0.65-0.74)*
61-82 years	253	19.56	0.31 (0.28-0.36)*	0.29 (0.26-0.33)*
Recipient of social assistance				
No	3213	95.64	REF	REF
Yes	1388	40.55	1.03 (0.97-1.10)	0.97 (0.90-1.04)

The model is additionally adjusted for health region due to the matched design

REF = reference category

IRRs were estimated using Poisson regression accounting for different observation durations

<sup>1</sup>For the purpose of better readability, person-month which have been used in the equitation, have been converted into 1000 person-years in this table.

\* p < 0.05

	Events	Person- years <sup>1</sup>	Crude IRR	Adjusted IRR
	(dead)	-		(95% CI)
Patient group				
Healthy controls	26	550	REF	REF
Persons with SUD and	1293	144167	18.95 (12.85-27.94)*	10.61 (7.19-
mild/moderate MI				15.67)*
Persons with SUD and	130	147	18.72 (12.29-28.52)*	11.44 (7.50-
severe MI				17.45)*
Persons with physical	222	97500	4.83 (3.19-7.25)*	5.03 (3.34-7.57)*
illness only				
Sex				
male	1113	191667	REF	REF
female	568	120000	0.81 (0.73-0.89)*	0.85 (0.77-0.94)*
Age group				
18-40 years	330	115000	REF	REF
41-60 years	513	1241667	1.46 (1.27-1.68)*	1.70 (1.48-1.95)*
61-82 years	838	719	4.17 (3.67-4.74)*	7.27 (6.37-8.29)*
Recipient of social welfare				
No	543	226667	REF	REF
Yes	1138	841667	5.68 (5.13-6.29)*	6.56 (5.85-7.35)*

**Table 3.** Incidence rate ratio (IRR) for mortality in the period January 2019 -December 2021, n = 72014

The model is additionally controlled for health region, due to the matched design

REF = reference category

IRRs were estimated using Poisson regression accounting for different observation durations

<sup>1</sup>For the purpose of better readability, person-month which have been used in the equitation, have been converted into 1000 person-years in this table.

\* p < 0.05

## Figure 1: All-cause crude mortality rate (CMR) per 1000 by group

