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Predictors of hospitalisation and death due to SARS-CoV-2 infection in Finland: A population-based register study with implications to vaccinations

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ABSTRACT

Introduction: The aim of this study was to investigate how age and underlying medical conditions affect the risk of severe outcomes following SARS-CoV-2 infection and how they should be weighed while prioritising vaccinations against COVID-19.
Methods: This population-based register study includes all SARS-CoV-2 PCR-test-positive cases until 24 Feb 2021, based on the Finnish National Infectious Diseases Register. The cases were linked to other registers to identify presence of predisposing factors and severe outcomes (hospitalisation, intensive care treatment, death). The odds of severe outcomes were compared in those with and without the prespecified predisposing factors using logistic regression. Furthermore, population-based rates were compared between those with a given predisposing factor and those without any of the specified predisposing factors using negative binomial regression.
Results: Age and various comorbidities were found to be predictors of severe COVID-19. Compared to 60–69-year-olds, the odds ratio (OR) of death was 7.1 for 70–79-year-olds, 26.7 for 80–89-year-olds, and 55.8 for $\geq$ 90-year-olds. Among the 20–69-year-olds, chronic renal disease (OR 9.4), malignant neoplasms (5.8), hematologic malignancy (5.6), chronic pulmonary disease (5.4), and cerebral palsy or other paralytic syndromes (4.6) were strongly associated with COVID-19 mortality; severe disorders of the immune system (8.0), organ or stem cell transplant (7.2), chronic renal disease (6.7), and diseases of myoneural junction and muscle (5.5) were strongly associated with COVID-19 hospitalisation. Type 2 diabetes and asthma, two very common comorbidities, were associated with all three outcomes, with ORs from 2.1 to 4.3. The population-based rate of SARS-CoV-2 infection decreased with age. Taking the 60–69-year-olds as reference, the rate ratio was highest (3.0) for 20–29-year-olds and < 1 for 70–79-year-olds and 80–89-year-olds.
Conclusion: Comorbidities predispose for severe COVID-19 among younger ages. In vaccine prioritisation both the risk of infection and the risk of severe outcomes, if infected, should be considered.

1. Introduction

Already during summer 2020, the first listings of predisposing conditions for severe COVID-19 were published to inform the public about the need to shield the most vulnerable [1–6]. Some of the first conditions listed were older age and various comorbidities. Furthermore, while efficacy studies of COVID-19 vaccines were still being carried out, more detailed research was published on predisposing conditions for severe infection outcomes leading to hospitalisation [7,8], intensive care [7,9,10], or death [7,8,11–14]. The implications from these studies have been valuable in planning the optimal allocation of the limited numbers of vaccine doses to prevent hospitalisations, need to intensive care and deaths.[15] For example, one of the questions was whether the elderly or individuals with certain background illnesses should be prioritised for COVID-19 vaccination.[15].

Along with the other European Union countries, Finland joined a common procurement system and subsequently commenced COVID-19 vaccinations on 27 December 2020. The groups to get vaccinated were prioritised in the following order: health care workers treating COVID-19 patients, residents and health care workers of long-term care facilities, the elderly aged $\geq$ 70 years and individuals aged 16–69 years with predisposing chronic

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conditions for severe COVID-19.[16] The vaccinations of those aged 16–69 years with predisposing conditions started on 24 February 2021.

We carried out a country-level pre-vaccination analysis of factors predisposing for severe COVID-19 outcomes, based on the possibility to link information across several national health care registers using the unique personal identifier. Vaccination programmes targeted solely by age (e.g. vaccinating all above 60 years of age) are straightforward to carry out but can lead to unjustified use of limited resources: a healthy individual above the age limit might have a lower risk but still be prioritised over a younger person with certain chronic conditions and thus higher risk for severe COVID-19. The specific aim of our study was to investigate how age and presence of underlying medical conditions affect the risk of severe COVID-19 outcomes and how age and medical conditions should be weighed against each other while prioritising vaccination. We assessed the predisposing factors for severe COVID-19 outcomes with specific attention to the elderly and persons with certain chronic illnesses and those taking potentially predisposing medications. The register-based analysis was conducted to answer three specific research questions. 1) Is there a specific age threshold at which the risk of severe COVID-19 outcomes increases considerably? 2) What are the medical conditions highly predisposing to severe COVID-19 outcomes in those with SARS-CoV-2 infection? 3) What predisposing factors are associated with the risk of infection and severe COVID-19 outcomes in the population? We here report the results with a particular focus on how these data were used to support effective COVID-19 vaccination intervention in Finland.

2. Material and methods

2.1. Study setting

The total population of Finland in 2019 was 5.5 million, 51% of which were women. Age- and sex-specific population sizes were obtained from the Finnish Population Information System, a computerised national database which registers individual-based information for all Finnish residents, including name, sex, personal identity code, address, date of birth and death. The personal identity code remains unchanged throughout the lifetime and is used for patient identification in all health care registers in Finland.

2.2. Case definitions

We established a dataset comprising virtually the entire Finnish population by linking data from multiple population-based and nationwide registers. This COVID-19 dataset included all individuals with a positive PCR test for SARS-CoV-2 identified between 1 January 2020 and 24 February 2021, based on the Finnish National Infectious Diseases Register. The pre-vaccination analysis was limited to the SARS-CoV-2 positive cases that were identified before the vaccinations of individuals with predisposing factors for severe COVID-19 started on 24 February 2021. The SARS-CoV-2 cases were linked to other registers to identify severe outcomes. The three severe outcomes were hospitalisation, admission to intensive care units (ICU) and death. All individuals hospitalised (according to the Care Register for Health Care) 14 days before or after the positive PCR test with a diagnosis indicating a respiratory infection, were considered as COVID-19 cases. Furthermore, the cases admitted to ICU were separated using the Finnish Intensive Care Consortium's Database (FICC). Any death (recorded in the Population Information System) that occurred within 30 days of the positive PCR test was considered as COVID-19 related.

2.3. Predisposing factors

Individuals with potential predisposing factors were identified from the registers by one or more of the following definitions: 1) having an entitlement to reimbursement of medicine expenses due to a specified comorbidity, 2) using specific medication or 3) using health care services due to the specified comorbidity. We used a pre-defined list of diagnoses and codes referring to specific comorbidities, medical conditions or the use of pharmacotherapy (Table 1). The following registers were employed: the Care Register for Health Care, the Register of Primary Health Care Visits, as well as the Special Reimbursement Register for Medicine Expenses and the Prescription Centre database, both maintained by the Social Insurance Institution of Finland. The registers used in the identification of each potentially predisposing factor are listed in the Table 1 at column 'Register'. The dataset covers for the most part all health care providers in Finland. The dataset was linked to the Finnish Population Information System in order to identify those without any of the factors potentially predisposing to severe COVID-19 listed in Table 1.

Individuals entitled to the specified special reimbursement of medicine expenses were identified from 1 January 2020 onwards. In Finland, all residents entitled to special reimbursement must have a condition that meets a set of specified medical criteria ensured by a medical certificate from a physician.[17] Individuals using medication predisposing to immunodeficiency or using medication for type 1 or 2 diabetes not more than two years prior to testing positive for SARS-CoV-2 were identified based on the Anatomical Therapeutic Chemical (ATC) codes.

We identified individuals who had used health care services due to any of the specified comorbidities not more than two years (cancer) or five years (all other comorbidities) prior to the positive PCR test. Secondary health care services were identified with the International Classification of Diseases 10th revision (ICD-10) codes and the Nordic Classification of Surgical Procedures (NCSP) codes. Primary health care services were identified with ICD-10 codes and the International Classification of Primary Care Second edition (ICPC-2) codes.

2.4. Statistical analysis

We assessed the proportion of severe outcomes in SARS-CoV-2 cases. In addition, we assessed the population-based incidences of SARS-CoV-2 infection and severe COVID-19 outcomes. Using logistic regression, we first estimated age-specific odds ratios (ORs) for each severe outcome in SARS-CoV-2 cases adjusting for sex. We next estimated odds ratios, comparing the odds of the severe outcomes in SARS-CoV-2 cases aged 20–69 years with and without each of the predisposing factors, adjusting for age and sex. In addition, negative binomial regression was used to estimate rate ratios (RR) for SARS-CoV-2 infection and the three severe outcomes in the Finnish population aged 20–69 years. For each predisposing factor, individuals with that factor were compared with individuals without any of the listed predisposing factors (Table 1). The negative binomial model was used instead of Poisson regression to account for overdispersion in the rates. The analysis was adjusted for age and sex. Both analyses were adjusted for sex, because the occurrence of severe COVID-19 outcomes had been shown to be associated with sex.[7] The ORs and RRs of the potentially predisposing factors related to severe COVID-19 outcomes were estimated only among the 20–69-year-olds, since the COVID-19 vaccinations of the elderly aged $\geq$ 70 years was anyway prioritised in Finland.

Table 1
Comorbidities and pharmacotherapies considered as potentially predisposing factors to severe COVID-19.

Potentially predisposing factor	Classification system	Codes	Registers
Organ or stem cell transplant	ICD-10	T86, Z94	1,2
Malignant neoplasms	ICD-10	C00–C43, C45–C80, C97, D05.1, D39	1,2
Hematologic malignancy	ICD-10	C81–C85, C88, C90–C96	1,2
Severe disorders of the immune system	ICD-10	D70.8, D80–D84, E31.00	2
Severe chronic renal disease	ICD-10	I12, I13, N00–N05, N07, N08, N11, N14, N18, N19, E10.2, E11.2, E14.2	1,2
Severe chronic liver disease	ICD-10	K70.2, K70.3, K70.4, K71–K74	2
Asthma	ICD-10	J45, J46	2, 3
	ICPC-2	R96	3
Chronic pulmonary disease	ICD-10	J41–J44, J47	2
Essential (Primary) Hypertension	ICD-10	I10	1, 3
	ICPC-2	K86	3
Hypertensive heart and/or renal disease, secondary hypertension	ICD-10	I11.9, I12, I13.1, I13.9, I15	1,2
Ischaemic heart diseases	ICD-10	I20-I25	1,2
Heart failure	ICD-10	I11.0, I13.0, I13.2, I50	1,2
Type 1 diabetes	ICD-10	E10	2, 3
	ICPC-2	T89	3
	ATC	A10A	4
Type 2 diabetes	ICD-10	E11, E13, E14	2,3
	ICPC-2	T90	3
	ATC	A10B	4
Diseases of myoneural junction and muscle	ICD10	G70–G73	2
Cerebral palsy and other paralytic syndromes	ICD10	G80–G83	2
Cerebrovascular diseases	ICD-10	I60–I69	2
Sleep apnea	ICD-10	G47.3	2, 3
Continuous positive airway pressure therapy	NCSP	WX723, WX780	2
Clozapine (prescription for)	ATC	N05AH02	4
Psychotic disorders	ICD-10	F20–F29	2, 3
	ICPC-2	P72	3
Autoimmune disease	ICD-10	D86, K50, K51, L40, M02, M05–M07, M13.9, M45, M46.0, M46.1, M46.9, M94.1	1, 2
Glucocorticoids (prescription for)	ATC	H02AB02, H02AB04, H02AB06, H02AB07	4
Biologic drugs (entitlement to reimbursement of medical expenses)	ATC	L04AA24, L04AB01, L04AB02, L04AB04, L04AB05, L04AB06, L04AC03, L04AC05, L04AC07, L04AC10, L04AC12, L04AC13, L04AC14, L04AC16, L04AC18	1
Biologic drugs, Tumor necrosis factor alpha (TNF-α) inhibitors (Prescription for)	ATC	L04AB	4
Biologic drugs, other (prescription for)	ATC	L01XC02, L04AA24, L04AA26, L04AA33, L04AC	4
Other Immunosuppressant drugs	ATC	L01BA01, L04AA06, L04AA10, L04AA13, L04AA18, L04AA29, L04AA37, L04AD01, L04AD02, L04AX01, L04AX03	4

ATC, Anatomical Therapeutic Chemical Classification System; ICD-10, International Statistical Classification of Diseases and Related Health Problems, tenth revision; ICPC-2, International Classification of Primary Care, second edition; NCSP, Nordic Nomesco Classification of Surgical Procedures.
Registers: 1, Special Reimbursement Register for Medicine Expenses; 2, Care Register for Health Care; 3, Register of Primary Health Care Visits; 4, Prescription Centre database.

3. Results

3.1. Characteristics of the study population

In Finland, a total of 52 502 SARS-CoV-2 cases aged ≥ 20 years occurred from 1 March 2020 through 24 February 2021, 2743 (5.2%) of which were hospitalised, 538 (1.0%) were admitted to ICU, and 801 (1.5%) died within 30 days after the positive PCR-test (Table 2). The incidence rates of SARS-CoV-2 cases, hospitalised cases, ICU cases and fatal cases were 822.4, 43.0, 8.4 and 12.5 per 100 000 person-years among adults aged ≥ 20 years, respectively. When restricting to 20–69-year-olds, there were 38 728 SARS-CoV-2 cases, 1 916 (4.9%) of which were hospitalised, 403 (1.0%) were admitted to ICU and 98 (0.3%) died within 30 days after the positive PCR-test.

3.2. Descriptive analysis: SARS-CoV-2 infection, COVID-19 outcomes and age

The proportion of fatalities among the SARS-CoV-2 cases increased with age (Fig. 1). In those aged 60–69 years, all fatal cases but one had at least one predisposing factor for severe COVID-19. By contrast, in those aged ≥ 70 years fatalities occurred also in individuals without any predisposing factors. In 20–69-year-olds, 28% of SARS-CoV-2 cases, 64% of hospitalised cases, 72% of ICU cases, and 87% of fatal cases had at least one predisposing factor.

The proportion of fatalities among SARS-CoV-2 cases increased with the number of predisposing factors (Fig. 1). In all age groups, the more predisposing factors there were, the higher the mortality was among the infected. With three or more predisposing factors the proportion of fatal cases varied from 4% (65–69 years) to 32% (75–89 years). In the oldest age group the proportion of fatal cases was even higher, irrespective of the number of predisposing factors.

During the study period, SARS-CoV-2 infections were most frequent among 20–29-year-olds, hospitalised cases among 50–59-year-olds, ICU cases among 60–69-year-olds, and fatal cases among 80–89-year-olds (Table 2). The age-specific incidence rates per 100 000 person-years peaked for SARS-CoV-2 infections in those aged 20–29 years (1475), for hospitalised cases in those aged 80–89 years (79.6), for ICU cases in those aged 60–69 years (17.6) and for fatal cases in those aged ≥ 90 years (289.1) (Fig. 2). Severe COVID-19 outcomes were thus clearly over-represented among the elderly. Only 6% (3390/52502) of all SARS-CoV-2 cases were detected in individuals aged ≥ 70 years (Table 2). Yet 28% (766/2 743) of hospitalised cases, 25% (132/538) of ICU cases and 88% (702/801) of the fatal cases occurred in this age group.

Table 2
Baseline characteristics of SARS-CoV-2 infection cases identified between 1 January 2020 and 24 February 2021 in the Finnish National Infectious Diseases Register.

	SARS-CoV-2 PCR-positive	Hospitalised	Hospitalised, ICU	Fatal cases
n = 52502 (100%)	n = 2743 (100%)	n = 538 (100%)	n = 801 (100%)	
Age, years				
0–9	3447 (6.6%)	33 (1.2%)	0 (0%)	<5
10–19	6937 (13.2%)	28 (1%)	<5	0 (0%)
20–29	11,168 (21.3%)	120 (4.4%)	11 (2%)	<5
30–39	9376 (17.9%)	242 (8.8%)	39 (7.2%)	6 (0.7%)
40–49	7773 (14.8%)	389 (14.2%)	75 (13.9%)	7 (0.9%)
50–59	6837 (13%)	627 (22.9%)	134 (24.9%)	26 (3.2%)
60–69	3574 (6.8%)	538 (19.6%)	144 (26.8%)	58 (7.2%)
70–79	1782 (3.4%)	470 (17.1%)	115 (21.4%)	183 (22.8%)
80–89	1151 (2.2%)	245 (8.9%)	17 (3.2%)	324 (40.4%)
90+	457 (0.9%)	51 (1.9%)	0 (0%)	195 (24.3%)
20–69	38,728 (73.8%)	1916 (69.9%)	403 (74.9%)	98 (12.2%)
Sex				
male	26,881 (51.2%)	1516 (55.3%)	353 (65.6%)	398 (49.7%)
female	25,621 (48.8%)	1227 (44.7%)	185 (34.4%)	403 (50.3%)
Number of potentially predisposing factors, all ages				
0	37,407 (71.2%)	808 (29.5%)	131 (24.3%)	45 (5.6%)
1	9200 (17.5%)	797 (29.1%)	150 (27.9%)	166 (20.7%)
2	3771 (7.2%)	594 (21.7%)	139 (25.8%)	272 (34%)
3+	2124 (4%)	544 (19.8%)	118 (21.9%)	318 (39.7%)
Number of potentially predisposing factors, 20–69-year-olds				
0	27,940 (72.1%)	696 (36.3%)	112 (27.8%)	13 (13.3%)
1	7236 (18.7%)	589 (30.7%)	105 (26.1%)	29 (29.6%)
2	2429 (6.3%)	351 (18.3%)	97 (24.1%)	29 (29.6%)
3+	1123 (2.9%)	280 (14.6%)	89 (22.1%)	27 (27.6%)
Potentially redisposing factors, 20–69-year-olds				
Organ or stem cell transplant	59 (0.2%)	21 (1.1%)	9 (2.2%)	<5
Malignant neoplasms	596 (1.5%)	87 (4.5%)	18 (4.5%)	18 (18.4%)
Hematologic malignancy	112 (0.3%)	23 (1.2%)	7 (1.7%)	<5
Severe disorders of the immune system	36 (0.1%)	10 (0.5%)	<5	0 (0%)
Severe chronic renal disease	152 (0.4%)	53 (2.8%)	17 (4.2%)	9 (9.2%)
Severe chronic liver disease	65 (0.2%)	9 (0.5%)	<5	<5
Asthma	1823 (4.7%)	249 (13%)	77 (19.1%)	11 (11.2%)
Chronic pulmonary disease	122 (0.3%)	38 (2%)	12 (3%)	6 (6.1%)
Primary or secondary hypertension	2585 (6.7%)	455 (23.7%)	131 (32.5%)	35 (35.7%)
Essential (primary) hypertension alone	669 (1.7%)	54 (2.8%)	9 (2.2%)	<5
Secondary hypertension (hypertensive heart and/or renal disease) alone	878 (2.3%)	170 (8.9%)	63 (15.6%)	19 (19.4%)
Ischaemic heart diseases	498 (1.3%)	103 (5.4%)	33 (8.2%)	11 (11.2%)

Table 2 (*continued*)

	SARS-CoV-2 PCR-positive	Hospitalised	Hospitalised, ICU	Fatal cases
Heart failure	66 (0.2%)	12 (0.6%)	<5	<5
Type 1 diabetes	312 (0.8%)	28 (1.5%)	5 (1.2%)	<5
Type 2 diabetes	1293 (3.3%)	271 (14.1%)	87 (21.6%)	25 (25.5%)
Diseases of myoneural junction and muscle	56 (0.1%)	16 (0.8%)	7 (1.7%)	<5
Cerebral palsy and other paralytic syndromes	70 (0.2%)	11 (0.6%)	<5	<5
Cerebrovascular diseases	247 (0.6%)	54 (2.8%)	15 (3.7%)	8 (8.2%)
Sleep apnea	1403 (3.6%)	230 (12%)	68 (16.9%)	11 (11.2%)
Psychotic disorders	60 (0.2%)	11 (0.6%)	<5	<5
Clozapine (prescription for)	362 (0.9%)	54 (2.8%)	5 (1.2%)	9 (9.2%)
Glucocorticoids (prescription for)	2989 (7.7%)	385 (20.1%)	84 (20.8%)	26 (26.5%)
Biologic drugs (entitlement to reimbursement of medical expenses)	163 (0.4%)	14 (0.7%)	<5	0 (0%)
Biologic drugs, Tumor necrosis factor alpha (TNF-α) inhibitors (prescription for)	135 (0.3%)	9 (0.5%)	<5	0 (0%)
Biologic drugs, other (prescription for)	50 (0.1%)	8 (0.4%)	<5	0 (0%)
Other Immunosuppressant drugs	486 (1.3%)	69 (3.6%)	16 (4%)	<5
Autoimmune disease with immunosuppressive drug therapy	709 (1.8%)	94 (4.9%)	18 (4.5%)	8 (8.2%)
Autoimmune disease without immunosuppressive drug therapy	651 (1.7%)	51 (2.7%)	13 (3.2%)	<5

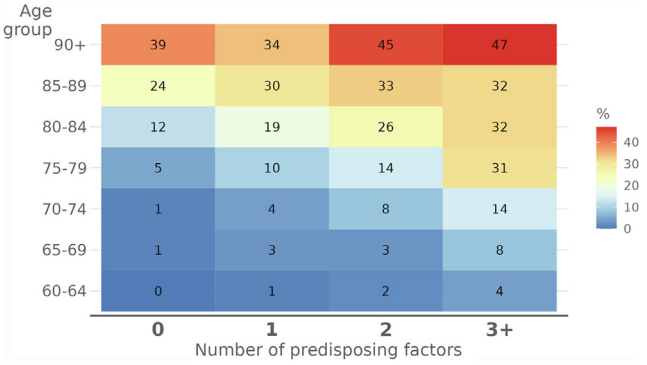

Fig. 1. Proportion (%) of fatal outcomes in cases of SARS-CoV-2 infection by age group and number of comorbidities.

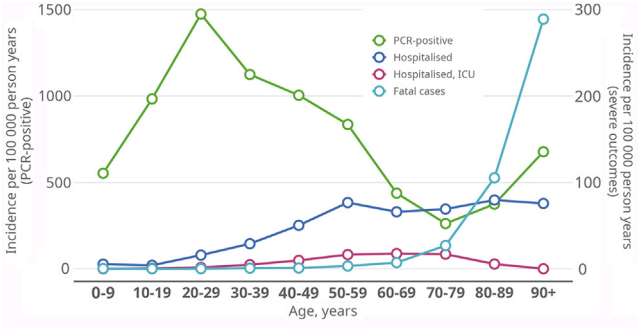

Fig. 2. Incidence (per 100 000 person-years) of the SARS-CoV-2 infection and COVID-19 outcomes by age group in the Finnish population. SARS-CoV-2 cases on the left side Y axis and the remainder on right side Y axis.

3.3. Predictors of hospitalisation, ICU admission and death among the SARS-CoV-2 infected

According to the logistic regression analysis, the risk of severe COVID-19 outcomes in an individual infected with SARS-CoV-2 increased with age. Compared to 60–69-year-olds, the odds ratio (OR) of death, adjusted for sex, was 7.1 (95% CI 5.3, 9.7) for the 70–79-year-olds, 26.7 (95% CI 20, 36) for the 80–89-year-olds, and 55.8 (95% CI 40.5, 77.9) for the ≥ 90-year-olds (Table 3a). Furthermore, the OR of hospitalisation was 2.0 (95% 1.8, 2.3) and of ICU admission 1.7 (95% CI 1.3, 2.2) for those aged 70–79 years (Table 3a). In addition, male sex was identified as a predisposing factor for all severe outcomes: hospitalisation (OR 1.3; 95% CI 1.2, 1.4), ICU admission (OR 1.9; 95% CI 1.6, 2.3), and death (OR 1.9; 95% CI 1.6, 2.2).

The more predisposing factors a person had, the higher was the risk of severe COVID-19. The effect was even stronger when the analysis was restricted to 20–69-year-olds (Table 3b). Comparing SARS-CoV-2 cases with three or more predisposing factors with cases without any of the predisposing factors in question, the age- and sex-adjusted ORs of severe outcomes were 6.6 for hospitalisation (95% CI 5.6, 7.7), 9.5 for ICU admission (95% CI 7.0, 12.9), and 16.1 for death (95% CI 8.1, 33.4).

Many of the individual predisposing factors were clear risk factors for death. Among the 20–69-year-olds the strongest risk factors for death related to COVID-19 were severe chronic renal disease (OR 9.4; 95% CI 4.2, 18.8), malignant neoplasms (OR 5.8; 95% CI 3.3, 9.7), hematologic malignancy (OR 5.6; 95% CI 1.6, 14.1), chronic pulmonary disease (OR 5.4; 95% CI 2.0, 11.9), and cerebral palsy and other paralytic syndromes (OR 4.6; 95% CI 0.3, 22.6), when comparing the odds between individuals with and without the predisposing factor in question (Table 3b). Likewise, cerebrovascular diseases, type 2 diabetes, autoimmune diseases treated with immunosuppressive drugs, use of glucocorticoids,

Table 3a
Relative risk of severe COVID-19 (hospitalisation, ICU and death) in cases of SARS-CoV-2 infection by age group and sex. The reference category is 60–69-year-old females. Relative risks are presented in terms of odds ratios (OR) and their 95% confidence intervals (CI 95%).

	Hospitalised		Hospitalised, ICU		Fatal cases	
	Crude	Adjusted for sex	Crude	Adjusted for sex	Crude	Adjusted for sex
Age, years						
0–9	0.1 (0, 0.1)	0.1 (0, 0.1)	0 (0, 0)	0 (0, 0)	0 (0, 0.1)	0 (0, 0.1)
10–19	0 (0, 0)	0 (0, 0)	0 (0, 0)	0 (0, 0)	0 (0, 0)	0 (0, 0)
20–29	0.1 (0, 0.1)	0.1 (0, 0.1)	0 (0, 0)	0 (0, 0)	0 (0, 0)	0 (0, 0)
30–39	0.1 (0.1, 0.2)	0.1 (0.1, 0.2)	0.1 (0.1, 0.1)	0.1 (0.1, 0.1)	0 (0, 0.1)	0 (0, 0.1)
40–49	0.3 (0.3, 0.3)	0.3 (0.3, 0.3)	0.2 (0.2, 0.3)	0.2 (0.2, 0.3)	0.1 (0, 0.1)	0.1 (0, 0.1)
50–59	0.6 (0.5, 0.6)	0.6 (0.5, 0.6)	0.5 (0.4, 0.6)	0.5 (0.4, 0.6)	0.2 (0.1, 0.4)	0.2 (0.1, 0.4)
60–69	1.0 (ref)	1.0 (ref)	1.0 (ref)	1.0 (ref)	1.0 (ref)	1.0 (ref)
70–79	2 (1.8, 2.3)	2 (1.8, 2.3)	1.6 (1.3, 2.1)	1.7 (1.3, 2.2)	6.9 (5.2, 9.5)	7.1 (5.3, 9.7)
80–89	1.5 (1.3, 1.8)	1.6 (1.3, 1.9)	0.4 (0.2, 0.6)	0.4 (0.2, 0.6)	23.7 (17.9, 32)	26.7 (20, 36)
90+	0.7 (0.5, 1)	0.8 (0.6, 1)	0 (0, 0)	0 (0, 0)	45.1 (33, 62.5)	55.8 (40.5, 77.9)
Sex						
Male		1.3 (1.2, 1.4)		1.9 (1.6, 2.3)		1.9 (1.6, 2.2)
Female		1.0 (ref)		1.0 (ref)		1.0 (ref)

secondary hypertension alone, ischaemic heart diseases and asthma increased the risk of death, with ORs between 2 and 5. Some of the predisposing factors were very rare, thus, it was not possible to calculate reliable OR estimates.

Strong risk factors for COVID-19 hospitalisation among the 20–69-year-olds were severe disorders of the immune system (OR 8.0; 95% CI 3.5, 17.2), organ or stem cell transplant (OR 7.2; 95% CI 4.0, 12.5), chronic renal disease (OR 6.7; 95% CI 4.6, 9.6), diseases of myoneural junction and muscle (OR 5.5; 95% CI 2.9, 10.2) (Table 3b). Likewise, psychotic disorders, chronic pulmonary disease, paralytic syndromes, asthma, hematologic malignancy, type 2 diabetes, cerebrovascular diseases, cardiovascular diseases, autoimmune diseases treated with immunosuppressive drugs, sleep apnea, and the use of clozapine, immunosuppressants or biologic drugs increased the risk of hospitalisation, with ORs between 2 and 5. The severity of the comorbidity was associated with severe disease outcomes: the risk of hospitalisation and admission to ICU was higher for asthma and type 2 diabetes cases that had been treated in secondary health care (Fig. 3).

3.4. Population based relative rates of SARS-CoV-2 infection and COVID-19 outcomes

According to the negative binomial regression model, the population-based rate of SARS-CoV-2 infection decreased with age. Compared to the 60–69-year-olds, the relative rate was 3.0 in 20–29-year-olds (95% CI 2.8, 3.3) and 2.4 in 30–39-year-olds (95% CI 2.2, 2.5), but < 1 in 70–79-year-olds (RR 0.7; 95% CI 0.6, 0.7) and 80–89-year-olds (RR 0.9; 95% CI 0.9, 1). The higher rate of SARS-CoV-2 infection in the ≥ 90-year-olds (RR 1.5; 95% CI 1.4, 1.7) can be explained by local epidemics which occurred in nursing homes. However, the rate of SARS-CoV-2 infection did not differ between females and males. Compared to the 60–69-year-olds, the population-based rate of hospitalisation (RR 1.3; 95% CI 1.2, 1.4) and the risk of ICU admission (RR 1.2; 95% CI 1.0, 1.4) were higher among the 50–59-year-olds. The population-based rate of death increased with age. Compared to the 60–69-year-olds, the relative rate was 3.2 in 70–79-year-olds (95% CI 2.7, 3.8), 8.5 in 80–89-year-olds (95% CI 7.2, 10.1) and 21.5 in the ≥ 90-year-olds (95% CI 17.9, 25.9).

In addition, we assessed the relative rate of hospitalisation, ICU admission and death in the 20–69-year-olds for each predisposing factor, comparing individuals with the predisposing factor with those without any of the specified predisposing factors (Table 4). The relative rates of SARS-CoV-2 infection was roughly the same for most of the predisposing factors. However, individuals using clozapine (RR 0.5; 95% CI 0.4, 0.7), with psychotic disorders (RR 0.6; 95% CI 0.5, 0.7) and heart failure, (RR 0.7; 95% CI 0.6, 0.9) had clearly lower rates of SARS-CoV-2 infection. The relative rate of severe COVID-19 outcomes varied across the studied predisposing factors. The relative rate of hospitalisation was 5.1–8.9 for organ or stem cell transplant, severe chronic renal disease, severe disorders of the immune system, diseases of myoneural junction and muscle and type 2 diabetes.

In the upper part of Table 4, 60-69-year-olds are the reference, and the rate ratios presented for each predisposing factor and outcome in the lower part of the table can be taken to present relative risks in that age group. The additional risk caused by a specific predisposing factor in any other age group can be obtained by multiplying the factor-specific rate ratio by the age-specific rate ratio. For almost all predisposing factors, the relative rates of death for 50–59-year-olds with predisposing factors, were greater than for 60–69-year-olds without any predisposing factors. For example, the risk of a 55-year-old person with chronic pulmonary disease to die of COVID-19 is almost 10 times (0.5 × 19.5) the risk of a 65-year-old person without any of the studied factors.

4. Discussion

In this population-based setting we estimated the risks for four entities: SARS-CoV-2 infection and COVID-19-related hospitalisation, ICU admission and death by multiple potentially predisposing factors. Age, certain comorbidities and medical conditions were found to be predictors of severe COVID-19 in individuals with

Table 3b
Relative risk of severe COVID-19 (hospitalisation, ICU and death) in cases of SARS-CoV-2 infection by number of potentially predisposing factors and by individual factor, adjusted for age and sex. Relative risks are presented in terms of odds ratios (OR) and their 95% confidence intervals (CI 95%).

	Hospitalised		Hospitalised, ICU		Fatal cases	
	Crude	Adjusted for age and sex	Crude	Adjusted for age and sex	Crude	Adjusted for age and sex
Number of predisposing factors, all ages[1]						
1	4.3 (3.9, 4.8)	2.4 (2.2, 2.7)	4.7 (3.7, 6)	2.5 (2, 3.2)	15.3 (11.1, 21.5)	2.6 (1.9, 3.8)
2	8.5 (7.6, 9.5)	3.5 (3.1, 4)	10.9 (8.6, 13.9)	4.5 (3.4, 5.8)	64.5 (47.5, 89.8)	4.4 (3.1, 6.3)
3+	15.6 (13.8, 17.6)	5.3 (4.6, 6.1)	16.7 (13, 21.5)	6.2 (4.6, 8.2)	146.2 (107.8, 203)	6.2 (4.4, 9)
Number of predisposing factors, 20–69-year-olds[1]						
1	3.5 (3.1, 3.9)	2.5 (2.2, 2.8)	3.7 (2.8, 4.8)	2.4 (1.8, 3.2)	8.6 (4.6, 17.2)	4.7 (2.5, 9.6)
2	6.6 (5.8, 7.6)	3.8 (3.3, 4.4)	10.3 (7.8, 13.6)	5.4 (4, 7.2)	26 (13.8, 51.7)	9.9 (5.1, 20.3)
3+	13 (11.1, 15.2)	6.6 (5.6, 7.7)	21.4 (16.1, 28.4)	9.5 (7, 12.9)	52.9 (27.8, 106.2)	16.1 (8.1, 33.4)
Predisposing factors, 20–69-year-olds[2]						
Organ or stem cell transplant	10.7 (6.2, 18.1)	7.2 (4, 12.5)	17.5 (8, 34.1)	9.8 (4.3, 19.8)	6.9 (0.4, 31.6)	2.8 (0.2, 13.5)
Malignant neoplasms	3.4 (2.7, 4.3)	1.7 (1.4, 2.2)	3.1 (1.8, 4.8)	1.4 (0.9, 2.3)	14.8 (8.6, 24.3)	5.8 (3.3, 9.7)
Hematologic malignancy	5 (3.1, 7.8)	2.9 (1.7, 4.6)	6.4 (2.7, 12.9)	3.1 (1.3, 6.4)	15.2 (4.6, 37.1)	5.6 (1.6, 14.1)
Severe disorders of the immune system	7.4 (3.4, 14.9)	8 (3.5, 17.2)	2.7 (0.2, 12.6)	2.5 (0.1, 12.4)	0 (0, 5211.9)	0 (0, 4720.9)
Severe chronic renal disease	10.5 (7.5, 14.7)	6.7 (4.6, 9.6)	12.5 (7.2, 20.2)	6.1 (3.5, 10.2)	27.2 (12.5, 52.2)	9.4 (4.2, 18.8)
Severe chronic liver disease	3.1 (1.4, 6)	1.5 (0.7, 3)	4.6 (1.1, 12.5)	2.1 (0.5, 5.7)	26.9 (8.1, 67)	9.8 (2.9, 25.7)
Asthma	3.3 (2.9, 3.8)	3 (2.5, 3.4)	4.9 (3.8, 6.3)	4.3 (3.3, 5.6)	2.6 (1.3, 4.6)	2 (1, 3.7)
Chronic pulmonary disease	8.8 (6, 12.9)	3.7 (2.5, 5.5)	10.7 (5.5, 18.7)	3.8 (1.9, 6.7)	21.7 (8.3, 46.5)	5.4 (2, 11.9)
Primary or secondary hypertension	5.1 (4.5, 5.7)	2.3 (2.1, 2.7)	7 (5.7, 8.7)	2.9 (2.3, 3.7)	7.9 (5.1, 11.8)	2.2 (1.4, 3.4)
Essential (primary) hypertension alone	1.7 (1.3, 2.2)	0.8 (0.6, 1.1)	1.3 (0.6, 2.4)	0.6 (0.3, 1.1)	1.2 (0.2, 3.8)	0.5 (0.1, 1.5)
Secondary hypertension (hypertensive heart and/or renal disease) alone	5 (4.2, 5.9)	2.1 (1.7, 2.5)	8.5 (6.4, 11.2)	3.2 (2.4, 4.3)	10.6 (6.2, 17.1)	2.7 (1.6, 4.5)
Ischaemic heart diseases	5.2 (4.2, 6.5)	2 (1.6, 2.6)	7.3 (4.9, 10.3)	2.4 (1.6, 3.4)	9.9 (5, 17.9)	2.1 (1, 3.9)
Heart failure	4.3 (2.2, 7.7)	2.3 (1.1, 4.3)	3 (0.5, 9.6)	1.3 (0.2, 4.1)	6.1 (0.3, 28.1)	1.8 (0.1, 8.6)
Type 1 diabetes	1.9 (1.3, 2.8)	1.9 (1.2, 2.8)	1.6 (0.6, 3.4)	1.4 (0.5, 3.1)	1.3 (0.1, 5.7)	1 (0.1, 4.8)
Type 2 diabetes	5.8 (5, 6.6)	2.8 (2.4, 3.3)	8.5 (6.6, 10.8)	3.7 (2.8, 4.7)	10.1 (6.3, 15.7)	3.2 (2, 5.1)
Diseases of myoneural junction and muscle	7.7 (4.2, 13.6)	5.5 (2.9, 10.2)	13.8 (5.7, 28.7)	8.1 (3.2, 17.9)	14.9 (2.4, 48.7)	5.8 (0.9, 20.4)
Cerebral palsy and other paralytic syndromes	3.6 (1.8, 6.6)	3.3 (1.6, 6.2)	5.8 (1.8, 14.1)	4.9 (1.4, 12.4)	5.8 (0.3, 26.4)	4.6 (0.3, 22.6)
Cerebrovascular diseases	5.5 (4, 7.4)	2.5 (1.8, 3.4)	6.3 (3.6, 10.4)	2.4 (1.3, 4)	14.3 (6.3, 28)	3.8 (1.7, 7.6)
Sleep apnea	4.1 (3.6, 4.8)	2.2 (1.9, 2.6)	5.6 (4.3, 7.3)	2.7 (2, 3.5)	3.4 (1.7, 6.1)	1.2 (0.6, 2.2)

(*continued on next page*)

Table 3b (*continued*)

	Hospitalised		Hospitalised, ICU		Fatal cases	
	Crude	Adjusted for age and sex	Crude	Adjusted for age and sex	Crude	Adjusted for age and sex
Psychotic disorders	3.4 (2.5, 4.6)	3.4 (2.5, 4.7)	1.3 (0.5, 2.9)	1.2 (0.4, 2.7)	11 (5.1, 20.8)	10.2 (4.6, 20)
Clozapine (prescription for)	4.3 (2.1, 8)	4.2 (2, 8)	3.3 (0.5, 10.6)	2.9 (0.5, 9.7)	6.7 (0.4, 31)	6.1 (0.3, 30.6)
Glucocorticoids (prescription for)	3.3 (2.9, 3.7)	2.6 (2.3, 2.9)	3.2 (2.5, 4.1)	2.4 (1.8, 3)	4.3 (2.7, 6.7)	3 (1.9, 4.7)
Biologic drugs (entitlement to reimbursement of medical expenses)	1.8 (1, 3)	1.7 (0.9, 2.9)	0.6 (0, 2.6)	0.5 (0, 2.4)	0 (0, 0.8)	0 (0, 76.3)
Biologic drugs, Tumor necrosis factor alpha (TNF-α) inhibitors (prescription for)	1.4 (0.6, 2.6)	1.4 (0.6, 2.6)	0.7 (0, 3.2)	0.7 (0, 3.3)	0 (0, 2.4)	0 (0, 462.3)
Biologic drugs, other (prescription for)	3.7 (1.6, 7.4)	2.9 (1.2, 5.9)	1.9 (0.1, 8.9)	1.4 (0.1, 6.5)	0 (0, 46.4)	0 (0, 0)
Other Immunosuppressant drugs	3.3 (2.5, 4.2)	2.5 (1.9, 3.3)	3.3 (1.9, 5.4)	2.4 (1.4, 3.9)	3.4 (1, 8.1)	2.2 (0.7, 5.3)
Autoimmune disease with immunosuppressive drug therapy	3 (2.4, 3.8)	2.3 (1.8, 2.9)	2.5 (1.5, 4)	1.8 (1.1, 2.8)	4.8 (2.1, 9.3)	3.1 (1.4, 6.1)
Autoimmune disease without immunosuppressive drug therapy	1.7 (1.2, 2.2)	1.2 (0.9, 1.6)	2 (1.1, 3.3)	1.4 (0.8, 2.4)	0.6 (0, 2.7)	0.4 (0, 1.7)

[1] Compared to the individuals without any of the predisposing factor in question.
[2] Comparing the odds of each outcome with and without the predisposing factors in question.

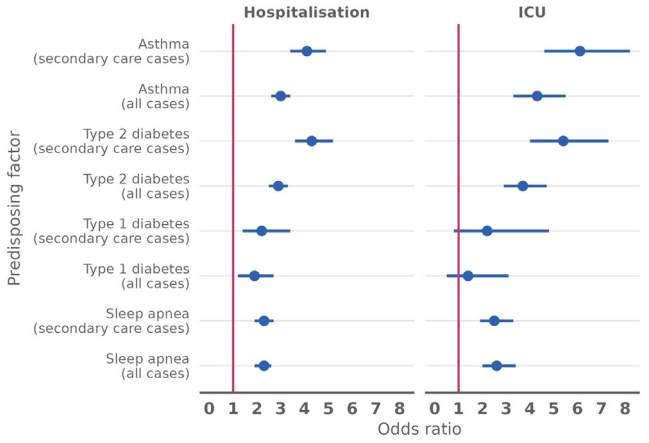

Fig. 3. Predictors of severe COVID-19 (hospitalisation and ICU) in cases of SARS-CoV-2 infection. Odds ratios (OR) and 95% confidence intervals (CI 95%).

SARS-CoV-2 infection. Old age was strongly associated with mortality, and having multiple comorbidities was associated with both mortality and hospitalisation in the SARS-CoV-2 infected. In the oldest, the proportion of fatal cases was highest irrespective of the number of predisposing factors (Fig. 1). The estimation of population-based rates of hospitalisation and death related to SARS-CoV-2 infection allowed an even more detailed characterisation of the relative roles of age and underlying medical conditions as risk factors for severe COVID-19. The risk of a ≥ 70-year-old person to die of COVID-19 was 3.2 to 21 times the risk of a 60–69-year-old person. Based on these analyses, vaccination of the elderly aged ≥ 70 years was prioritised in Finland, followed by vaccination of those aged 16– 69 years with highly predisposing medical conditions.[18].

During the study period in Finland, SARS-CoV-2 infections occurred most frequently in young adults and the early middle-aged (Fig. 2). The age distribution of SARS-CoV-2 infections was thus similar to the one observed in Denmark, Norway and Sweden during that period.[19] As expected, immunosuppressive states such as organ or stem cell transplantation, severe disorders of the immune system or severe renal disease were associated with increased risks of hospitalisation and ICU admission due to COVID-19. Similar results were obtained in a population-based Danish study where organ transplantation and severe kidney disease were the two medical conditions associated with the highest risks of severe COVID-19.[7] Also in an English study, which recorded nearly 11 000 deaths in a cohort of more than 17 million SARS-CoV-2 positive patients, organ transplantation was associated with the highest risk of death due to COVID-19 (hazard ratio 6.0; 95% CI 4.7, 7.6) among the studied medical conditions, after the analysis was adjusted for age and sex.[11] Furthermore, our study demonstrated that among patients with an autoimmune disease, those receiving immunosuppressive drug therapy were more prone to severe outcomes than patients without such therapy (Table 3b, Table 4). Potential reasons for the increased risk are the immunosuppressive medication itself and the increased severity of the underlying disease that necessitated an immunosuppressive drug therapy.

Among SARS-CoV-2 cases aged 20–69 years, the relative risk of death was higher in patients with chronic renal or liver disease, diseases of myoneural junction and muscle, cerebral palsy or other paralytic syndromes as well as in those with psychotic disorders, especially with prescription for the psychiatric medication clozapine. The association of psychiatric disorders and high COVID-19 mortality has been explained only partly by the presence of other comorbidities. [20] Other reasons such as socioeconomic factors, delays in treatment seeking and certain deficits in cellular immunity in schizophrenia have been implicated.[20] Although it is known that clozapine causes neutropenia and predisposes for pneumonia[21] its role in COVID-19 infections has not been assed broadly.

In our analysis, asthma, similarly to other chronic pulmonary diseases, was associated with higher risk of hospitalisation and intensive care treatment, but it was not associated with higher mortality. The association with hospitalisation was weaker but present even when asthma had been treated in primary health care only, indicating a presumably less severe manifestation. However, in a review and *meta*-analysis where 76 studies and more than 17

Table 4
Relative rate of SARS-CoV-2 infection and severe COVID-19 outcomes (hospitalisation, admission to ICU and death) in the Finnish population aged 20–69, based on a negative binomial regression model. The table presents rate ratios (RR) and 95% confidence intervals (CI 95%).

	SARS-CoV-2 PCR-positive	Hospitalised	Hospitalised, ICU	Fatal cases
Age, years				
20–29	3.1	0.4	0.2	0.1
	(2.9, 3.3)	(0.3, 0.5)	(0.1, 0.3)	(0, 0.3)
30–39	2.4	0.8	0.5	0.2
	(2.3, 2.5)	(0.7, 0.9)	(0.4, 0.7)	(0.1, 0.3)
40–49	2.3	1.2	0.9	0.3
	(2.2, 2.4)	(1, 1.3)	(0.8, 1.2)	(0.2, 0.4)
50–59	1.8	1.3	1.2	0.5
	(1.8, 1.9)	(1.2, 1.5)	(1, 1.4)	(0.4, 0.7)
60–69	1.0	1.0	1.0	1.0
	(ref)	(ref)	(ref)	(ref)
Sex				
Male	1	1.3	1.2	2.1
	(1, 1)	(1.2, 1.4)	(1.1, 1.3)	(1.8, 2.3)
Female	1.0	1.0	1.0	1.0
	(ref)	(ref)	(ref)	(ref)
Predisposing factors, 20–69-year-olds[1]				
Organ or stem cell transplant	1	8.9	20.7	15.2
	(0.8, 1.3)	(5.5, 13.8)	(9.7, 38.6)	(0.8, 76.6)
Malignant neoplasms	1	3.1	3.6	20.7
	(0.9, 1.1)	(2.3, 4)	(2.1, 5.7)	(10, 43.9)
Hematologic malignancy	1	4.7	7.6	25.9
	(0.8, 1.2)	(2.9, 7.2)	(3.2, 15.3)	(7.2, 73.9)
Severe disorders of the immune system	0.9	7.5	4.7	NA
	(0.6, 1.2)	(3.7, 13.5)	(0.3, 20.8)	
Severe chronic renal disease	1	8.3	14.3	46.4
	(0.8, 1.1)	(6, 11.3)	(8.2, 23.2)	(19, 108.7)
Severe chronic liver disease	0.9	2.7	4.8	38.6
	(0.7, 1.1)	(1.3, 4.9)	(1.2, 12.7)	(10.8, 110.3)
Asthma	1.1	4.8	9.5	9.8
	(1.1, 1.2)	(4, 5.9)	(7.1, 12.7)	(4.3, 22.1)
Chronic pulmonary disease	0.8	4.6	7.4	19.5
	(0.7, 1)	(3.1, 6.6)	(3.9, 13)	(6.8, 50.1)
Primary or secondary hypertension	0.9	3.5	4.9	7.5
	(0.9, 1)	(2.8, 4.2)	(3.8, 6.4)	(4, 15)
Essential (primary) hypertension alone	1	1.8	1.6	2.2
	(0.9, 1.1)	(1.3, 2.4)	(0.8, 3)	(0.4, 8.2)
Secondary hypertension (hypertensive heart and/or renal disease) alone	0.8	2.9	5.6	9.1
	(0.7, 0.9)	(2.3, 3.7)	(4, 7.7)	(4.4, 19.1)
Ischaemic heart diseases	1	3.4	5.2	8.9
	(0.9, 1.1)	(2.6, 4.5)	(3.4, 7.7)	(3.8, 20.2)
Heart failure	0.7	2.8	2.4	6.6
	(0.6, 0.9)	(1.5, 4.9)	(0.4, 7.4)	(0.4, 33.6)
Type 1 diabetes	0.8	2.5	2.6	4.1
	(0.7, 0.9)	(1.6, 3.7)	(0.9, 5.8)	(0.2, 20.7)
Type 2 diabetes	1.1	5.1	7.9	12.8
	(1.1, 1.2)	(4.1, 6.3)	(5.9, 10.5)	(6.5, 26.1)
Diseases of myoneural junction and muscle	0.9	7	17	31.5
	(0.7, 1.1)	(4, 11.3)	(7.2, 34)	(4.9, 114.8)
Cerebral palsy and other paralytic syndromes	1	5	10.7	19.9
	(0.7, 1.2)	(2.5, 8.7)	(3.3, 25.5)	(1.1, 100.2)
Cerebrovascular diseases	0.9	4.2	6	17.9
	(0.8, 1.1)	(3, 5.8)	(3.3, 10)	(7, 43.1)
Sleep apnea	1	3.7	5.6	6.1
	(0.9, 1)	(3, 4.6)	(4.1, 7.6)	(2.6, 13.7)
Psychotic disorders	0.6	3.1	1.7	24.6
	(0.5, 0.7)	(2.2, 4.1)	(0.6, 3.7)	(10.2, 57.2)
Clozapine (prescription for)	0.5	2.9	3	12.7
	(0.4, 0.7)	(1.5, 5)	(0.5, 9.5)	(0.7, 63.7)
Glucocorticoids (prescription for)	1.1	3.9	5.1	11.5
	(1, 1.1)	(3.2, 4.7)	(3.8, 6.8)	(6, 23.2)
Biologic drugs (entitlement to reimbursement of medical expenses)	0.9	2.4	1	NA
	(0.8, 1.1)	(1.3, 4)	(0.1, 4.6)	
Biologic drugs, Tumor necrosis factor alpha (TNF-α) inhibitors (prescription for)	0.9	1.9	1.3	NA
	(0.8, 1.1)	(0.9, 3.5)	(0.1, 5.7)	
Biologic drugs, other (prescription for)	1	4.7	3.4	NA
	(0.8, 1.3)	(2.1, 8.9)	(0.2, 15)	
Other Immunosuppressant drugs	0.8	3.3	4.4	7.9
	(0.8, 0.9)	(2.4, 4.3)	(2.5, 7.3)	(2.2, 22.3)
Autoimmune disease with immunosuppressive drug therapy	0.9	3.1	3.6	11.4
	(0.8, 0.9)	(2.4, 4.1)	(2.1, 5.7)	(4.5, 27.2)
Autoimmune disease without immunosuppressive drug therapy	0.9	1.9	2.8	1.6
	(0.8, 0.9)	(1.4, 2.6)	(1.5, 4.8)	(0.1, 8)

[1] Comparing the rate of each outcome in individuals with the predisposing factor in question to those without any of the specified factors.

million SARS-CoV-2 positive patients were included, asthma was not associated with severe COVID-19.[22] In our study, 4.7% of 20–69-year-old SARS-CoV-2 cases were recognized as having asthma although the overall prevalence in Finland is twice as high.[18] Our estimate is likely to represent the risk for more severe asthma. In line with that, recent treatment of asthma with corticosteroids, indicating a more severe manifestation, has been reported to be associated with an increased risk of severe COVID-19 in some studies.[7,11].

Although they are no typical predictors for other infectious diseases, it has been widely noted that metabolic syndrome and obesity as well as type 2 diabetes are strongly associated with higher risks of severe COVID-19.[11,12,14,23] In our study, type 2 diabetes, which often occurs together with obesity and metabolic syndrome, was associated with higher risks of severe COVID-19 and death than the more serious disease, type 1 diabetes. In addition to obesity, regulation of blood glucose levels might play a role in the progression of SARS-CoV-2 infections among type 2 diabetes patients as high blood sugar levels have been shown to predict severe COVID-19.[11,23,24] Moreover, type 2 diabetes has been identified as a prognostic factor for survival among COVID-19 cases requiring critical care especially among the middle-aged and younger.[14].

In many studies, hypertension has been more prevalent among severe or fatal COVID-19 cases than among milder cases.[25] Also in our study, hypertension was more prevalent among severe cases; while only 7% of the SARS-CoV-2 positive 20–69-year-old individuals were hypertensive, 25%, 32% and 36% of the hospitalised, ICU and fatal 20–69-year-old cases suffered from hypertension. However, patients who had only hypertension were not at increased risk of severe outcomes according to our study; similar results have been obtained elsewhere.[26] Since hypertension is common in patients who also have other factors predisposing for severe COVID-19, such as obesity, hypertension alone is thus not an appropriate indicator for the prioritisation of COVID-19 vaccination.

The main strength of our study is the utilisation of multiple national registers, across which individual-level data were linked via a unique personal identifier. Information on possible predisposing comorbidities and conditions could therefore be verified from different sources. Furthermore, not only the conditional risk of hospitalisation given SARS-CoV-2 infection but also the rate of SARS-CoV-2 infection could be evaluated based on our nationwide dataset. It is a strength of our study that the effect of comorbidities on the risk of severe COVID-19 was analysed among the 20–69-year-olds, excluding the elderly, which should be prioritised by their age in any case.

Our study is solely based on register data. Therefore, we could not address the severity of the underlying comorbidities to any further extent than what could be deduced from the recorded diagnoses and medications. Another weakness is the rather limited number of cases, although we included all laboratory-confirmed SARS-CoV-2 cases that had occurred by 24 February 2021. During the study period, non-pharmaceutical interventions reduced the spread of COVID-19 in Finland considerably. Additionally, not all national registers are adequate for real-time use. For example, the Finnish Cancer Register is updated only annually, so that, at the time of the study, data from 2019 and beyond were not yet available. Therefore, we could not utilise more detailed data from this register on the status or treatment of cancers and, therefore, could not identify all individuals receiving immunosuppressive treatment due to cancer. Furthermore, the national registers used to identify individuals with the specified predisposing factors did not contain private or occupational health care visits. However, if any disease entitling a special reimbursement is diagnosed at those visits, it is registered in the Special Reimbursement Register for Medicine Expenses and thus included in our study.

When vaccinations are targeted to prevent severe COVID-19 among those with very common comorbidities, the number of vaccine doses needed is reasonably high. However, if we assume that vaccination prevents all severe cases (e. g. hospitalisations) and that the whole population, without vaccinations, would eventually acquire SARS-CoV-2 infection, the number needed to vaccinate to prevent one COVID-19 hospitalisation would remain small even for common comorbidities: only 4.8 (1293 infections / 271 hospitalisations; Table 2) for type 2 diabetes, 6.1 for sleep apnea and 7.3 for asthma.

According to our study, vaccination of the more critically ill is in fact slightly less effective in preventing severe COVID-19 than vaccination of individuals with less severe, more prevalent conditions: the risks of hospitalisation, intensive care treatment and death, conditional on SARS-CoV-2 infection, among patients with heart failure or type 1 diabetes are lower than among type 2 diabetes patients. Furthermore, in Finland patients with heart failure and type 1 diabetes were less likely to have a SARS-CoV-2 infection than patients with type 2 diabetes or asthma. These findings may follow from effective shielding of the most vulnerable, i.e., strict adherence to the nonpharmaceutical interventions recommended. If in the future we are in a similar situation again (new pathogen, vaccine scarcity), this kind of study is the key.

Authors' contributions

HS, TL (Tuija), TL (Toni) conceptualized the study. TL (Toni) and UB conducted the statistical analysis. TL (Tuija) reviewed the literature. HS, TL (Tuija) and KA drafted the manuscript. All authors discussed the results and contributed to the final manuscript.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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