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Deaths after confirmed SARS-CoV-2 in Norway

ORIGINAL ARTICLE

HANNE LØVDAL GULSETH

E-mail: hannelovdal.gulseth@fhi.no
Department of Chronic Diseases and Ageing
Norwegian Institute of Public Health
She has contributed to the idea, design, interpretation of results and drafting and revision of the manuscript, and has approved the submitted manuscript version.
Hanne Løvdal Gulseth, MD, PhD and head of department.
The author has completed the ICMJE form and declares no conflicts of interest.

EYVIND HELLAND

Department of Health Registries
Norwegian Directorate of Health
He has contributed to the analyses, interpretation of results and drafting and revision of the manuscript, and has approved the submitted manuscript version.
Eyvind Helland, PhD candidate in psychology at the Norwegian University of Science and Technology and advisor.
The author has completed the ICMJE form and declares no conflicts of interest.

KNUT IVAR JOHANSEN

Department of Health Registries
Norwegian Directorate of Health
He has contributed to the interpretation of results and drafting and revision of the manuscript, and has approved the submitted manuscript version.
Knut Ivar Johansen, sociologist and head of section.

The author has completed the ICMJE form and declares no conflicts of interest.

KIRSTEN GRAVNINGEN

Department of Infection Prevention and Preparedness, Norwegian Institute of Public Health
She has contributed to the interpretation of results and drafting and revision of the manuscript, and has approved the submitted manuscript version.
Kirsten Gravningen, PhD, specialist in medical microbiology and senior consultant.
The author has completed the ICMJE form and declares no conflicts of interest.

HELENA NIEMI EIDE

Department of Infection Prevention and Preparedness, Norwegian Institute of Public Health
She has contributed to the interpretation of results and drafting and revision of the manuscript, and has approved the submitted manuscript version.
Helena Niemi Eide, doctor and Master of Public Health.
The author has completed the ICMJE form and declares no conflicts of interest.

SIRI ELDEVIK HÅBERG

Centre for Fertility and Health
Norwegian Institute of Public Health
She has contributed to the idea, design, interpretation of results and drafting and revision of the manuscript, and has approved the submitted manuscript version.
Siri Eldevik Håberg, MD, PhD, deputy director.
The author has completed the ICMJE form and declares no conflicts of interest.

INGER JOHANNE BAKKEN

Department of Health Registries
Norwegian Directorate of Health
She has contributed to the idea, design, data analysis, interpretation of results and drafting and revision of the manuscript, and has approved the submitted manuscript version..
Inger Johanne Bakken, Dr.Eng. and senior adviser.
The author has completed the ICMJE form and declares no conflicts of interest.

BACKGROUND

Advanced age is the most important risk factor for death as a result of COVID-19, but there is a dearth of knowledge regarding the impact of chronic diseases. Using health registry data, we describe the disease profiles of persons who died after a confirmed infection with SARS-CoV-2 during the first three months of the pandemic in Norway.

MATERIAL AND METHOD

Data from the specialist health service (Norwegian Patient Registry, NPR) and the primary health service (Norwegian Registry for Primary Health Care, NRPHC) were linked to information on positive tests for SARS-CoV-2 from the Norwegian Surveillance System for Communicable Diseases (MSIS) and on deaths from the National Population Register. The data retrieval included the Norwegian population as of 1 March 2020 with data for confirmed infections, hospitalisations and deaths until 31 May 2020.

RESULTS

Of 8 412 persons with a confirmed SARS-CoV-2 infection, altogether 244 (2.9 %) died, whereof 133 (55 %) were men. Among those with a confirmed infection, the proportion who died varied from 0.2 % (age < 60 years) to 52 % (age ≥ 90 years). Altogether 92 (38 %) patients died in hospital. 25 (16 %) of those who died elsewhere had previously been hospitalised for COVID-19. The proportion with no registered chronic disease was 39 % in the age group < 70 years and 26 % in the age group ≥ 70 years. The disease distribution varied between those patients who had died in and outside of hospital, especially for diagnoses of diabetes, renal failure and dementia.

INTERPRETATION

Among those who had a SARS-CoV-2 infection confirmed during the first three months of the pandemic in Norway, only a small proportion died. The majority of those who died were 70 years or older and had at least one chronic disease, but the disease profile varied between patients who died in and outside of hospital. Health registry data can help provide a better overview of and advice to risk groups in the population during an ongoing pandemic.

Main findings

As of 31 May 2020, a total of 224 deaths had been registered among persons with a confirmed SARS-CoV-2 infection in Norway, i.e. 2.9 % of all those who had tested positive.

Of 145 persons aged 90 years or older in whom the infection had been confirmed, more than one-half died.

Linking of multiple health registries showed that of those who died, three of four were registered with one or more chronic diseases.

There were major differences in terms of the age and disease profiles between those who died in hospitals and those who died elsewhere.

The first death to occur in Norway as a result of COVID-19, the disease caused by the SARS-CoV-2 virus, was reported on 12 March 2020. As of 10 June 2020, the Norwegian Institute of Public Health reported that altogether 239 deaths associated with COVID-19 had been registered in the Norwegian Surveillance System for Communicable Diseases (MSIS) (1, 2), and on the same day, the World Health Organization reported more than 370 000 deaths attributable to the COVID-19 pandemic worldwide (1). Many European countries have reported a higher mortality rate (excess mortality) during the pandemic (2), while general mortality in the Norwegian population remained normal until June, including among persons over 70 years of age (3).

Figures from Norway and other countries show that advanced age is the most important risk factor for a severe clinical course and death in patients with COVID-19, and that underlying diseases appear to increase the risk even further (4–7). Studies from other countries have shown that non-communicable diseases such as diabetes, cardiovascular diseases, cancer and chronic pulmonary and renal diseases combined with age, sex (male) and obesity can be risk factors for a fatal outcome of COVID-19 (6).

Identifying population groups with an elevated risk of a severe clinical course and death from an infection with a novel virus that spreads easily is required to provide evidence-based advice on targeted measures. The Norwegian Institute of Public Health has drawn on existing evidence from other countries (6, 8) to prepare advice on preventive measures for groups with underlying conditions, and these recommendations are updated on a regular basis.

An overview of the population's health, disease prevalence, mortality and use of health services is essential for appropriate management of disease outbreaks and epidemics. Data from national health registries assist in the planning of healthcare service provision and can also be used to analyse the possible consequences and effects of measures (9).

In this article we describe deaths among patients with a confirmed SARS-CoV-2 infection in Norway by linking national registry data. We have investigated the prevalence of chronic diseases and underlying conditions in this population.

Material and method

In association with the outbreak of COVID-19, the Norwegian Directorate of Health and the Norwegian Institute of Public Health have established a collaborative project, the objective of which is to use health registry data to quickly obtain an overview of the situation with regard to COVID-19 in Norway. Particular emphasis is placed on disease development and death in risk groups (10, 11).

The Department of Health Registries in the Norwegian Directorate of Health has adapted the statistics based on data from the MSIS registry (12), the Norwegian Patient Registry (NPR) and the Norwegian Registry for Primary Health Care (NRPHC) (9). The regulations for these registries provide the legal basis for the handling of data. Staff at the directorate had no access to national identity numbers or other personally identifiable characteristics. Staff at the Norwegian Institute of Public Health have access only to aggregated data that cannot be traced back to individuals.

The sample includes 8 412 persons with a SARS-CoV-2 infection confirmed with a PCR test and reported to the MSIS registry before 31 May 2020. The data set was restricted to all persons who were registered with a date of death in the Persons Registry (PREG, a copy of the National Population Registry used by the Norwegian Health Net) (13), altogether 244 persons as of 10 June 2020. The last date of death in this update was 29 May 2020.

Information on these 244 individuals was retrieved from registries of health service use managed by the Norwegian Directorate of Health: NPR for the specialist health service and NRPHC for the primary health service. Diseases and conditions that could entail an elevated risk for a severe course of COVID-19 were defined based on knowledge from other countries about the course of COVID-19, the infection risk for influenza and the course of diseases, as well as about treatment and possible effects on the immune system (8). We included a wide range of diseases, since emergency preparedness and surveillance were the main objectives of the project and there was limited knowledge about COVID-19 (11). The definition of risk factors is based on the registered codes, ICD-10 (the international statistical classification of diseases and associated health problems) in NPR and ICPC-2 (international classification for primary care) in the NRPHC. We have primarily looked at non-communicable diseases such as diabetes, cardiovascular diseases, cancer and chronic pulmonary diseases, as defined in Table 1. We also conducted a broader analysis where we included obesity and gastrointestinal, rheumatic and neurological diseases; see (11) for a more detailed definition. For some chronic diseases we used all available past data, while for others we went seven or five years back in time, depending on the knowledge of the clinical course (11). We had no access to data on general drug use, but the Norwegian Directorate of Health has an overview of drugs that have been funded by the health trusts and used in hospitals and elsewhere. These include, for example, biological drugs such as infliximab and adalimumab, as well as some cancer drugs.

Table 1

Definitions of relevant chronic diseases and conditions investigated for persons who died after a confirmed SARS-CoV-2 infection.

Disease/condition	Period	Data source	
		Norwegian Patient Registry (ICD-10 codes)	**Norwegian Registry for Primary Health Care (ICPC-2 codes)**
Diabetes	All available data[1]	E10, E11	T89, T90
Cardiovascular disease	Last five years	G45, H34, I00–99	K74–80, K82, K83, K85–87, K89–92
Cancer	Last five years	C00–97, D32–33, D35.2–35.4, D42, D43, D44.3–44.5, D45–47	
Chronic pulmonary disease	Last five years	J41–47, J84, J98	R95, R96
Dementia	All available data[1]	F00–03, G30, G31.0, G31.2, G31.8,	
Renal failure	All available data[1]	N18.3–18.5	
Liver failure	All available data[1]	K70.4, K72	
Conditions that affect the immune function (transplantation, immune failure)	All available data[1]	D80–D84, Z94.0–94.4, Z94.8	

[1]2008–19 in the Norwegian Patient Registry and July 2016–March 2020 in the Norwegian Registry for Primary Health Care.

Microsoft SQL Server was used to retrieve data from the databases and prepare the first adaptations of the variables. Linking of data and adaptation of tables were undertaken with the R analysis tool (www.rstudio.com). We present descriptive statistics by sex, age and deaths that have occurred in and outside of hospitals. For reasons of data protection, no information on place of residence or details on age and sex distribution are included. We have grouped all the risk groups together and show statistics for number and proportion without any registered chronic disease or condition. In addition, we show how many were registered with at least one of the diseases or conditions defined in Table 1 and at least one or two of the non-communicable diseases (diabetes, cardiovascular disease, cancer and chronic pulmonary disease).

Results

Of 8 412 persons in Norway with a confirmed SARS-CoV-2 infection, 244 (2.9 %) were registered in the National Population Register as deceased as of 31 May 2020 in an update carried out on 10 June 2020. Their median age at death

was 85 years (interquartile range 77–90 years), and 133 (55 %) were men. Most of the deaths occurred in the age group 80–89 years, and the fewest among patients under 60 years. The lethality, defined as the proportion of deaths among those with a confirmed infection, was highest in the oldest age groups and varied from 0.2 % in patients younger than 60 years to 52 % in those older than 90 (Table 2). The median number of days from the confirmation of a SARS-CoV-2 infection to death was 10 (interquartile range 6–16 days). In four cases, the test date was the same as or later than the date of death.

Table 2

Number of deaths registered among persons with a confirmed SARS-CoV-2 infection in Norway as of 31 May 2020. Lethality is the proportion of deaths out of the total number of positive tests.

	Number of deaths (% of the total)	Number of men (%)	Number of deaths in hospital (%)	Number who tested positive (lethality, %)
All	244	133 (55)	92 (38)	8 412 (2.9)
Age groups (years)[1]				
0–69	31 (13)	26 (84)	26 (84)	7 287 (0.4)
70–79	46 (19)	29 (63)	22 (48)	602 (8)
80–89	91 (37)	49 (54)	28 (31)	378 (24)
≥ 90	76 (31)	29 (38)	16 (21)	145 (52)

[1]In the age group under 70 years, the figures are small, and all details can therefore not be reported for reasons of data protection. Altogether 11 deaths (4.5 %) occurred in the age group under 60 years, lethality 0.2 %, and 20 deaths (8.2 %) in the age group 60–69 years, lethality 2.1 %.

Altogether 92 persons (38 %) were registered as having died in hospital. In the age group under 70 years, 26 of 31 (84 %) deaths occurred in hospital, while the equivalent proportion was 21 % (16 of 76) among those aged 90 years or older. Of those 152 patients who died outside hospital there were 25 (16 %) who were registered with a previous hospitalisation for COVID-19, and 15 of these patients died in the course of the first seven days after discharge.

Of those who died, altogether 67 persons (27 %) had not previously been registered with a chronic somatic disease or condition (Table 3). The proportion with no registered chronic disease was virtually identical in and outside of hospital; 28 % vs. 27 %. The most common conditions registered were cardiovascular disease (55 %), diabetes (21 %), cancer (16.8 %) and pulmonary disease (16.4 %). Among persons under 70 years, the proportion with no registered chronic disease was larger (39 %) than among persons aged more than 70 years (26 %), but the proportion with diabetes and renal failure was larger in patients under 70 years.

Table 3

Chronic diseases and risk factors among persons who had died after a confirmed SARS-CoV-2 infection in Norway as of 31 May 2020. Subgroups of small figures that cannot be reported for reasons of data protection are indicated by a dash.

	Number among all deaths (%), n = 244	Number among deaths outside hospital (%), n = 152	Number among deaths in hospital (%), n = 92	Number among deaths < 70 years (%), n = 31	Number among deaths ≥ 70 years (%), n = 213
No registered chronic disease with an assumed elevated risk[1]	67 (28)	41 (27)	26 (28)	12 (39)	55 (26)
At least one non-communicable disease[2]	169 (69)	104 (68)	65 (71)	18 (58)	151 (71)
At least two non-communicable diseases[2]	77 (32)	43 (28)	34 (37)	7(23)	70 (33)
Cardiovascular disease	134 (54)	88 (58)	46 (50)	12 (39)	122 (57)
Diabetes	50 (21)	22 (14)	28 (30)	8 (26)	42 (20)
Cancer	41 (17)	25 (16)	16 (17)		– [3]
Chronic pulmonary disease	40 (16)	24 (16)	16 (17)		– [4]
Dementia	36 (15)	36 (24)	0		– [5]
Renal failure	16 (7)	– [6]		5 (16)	11 (5)
Conditions that affect the immune system (transplantation, immune failure)	5 (2)	0	5 (5)		– [7]

[1]Chronic diseases as defined in Table 1, the numbers are too small to be reported for liver failure separately.

[2]Collective designation for diabetes, cardiovascular disease, cancer and chronic pulmonary disease.

[3]Most of those registered with cancer were in the oldest age group.

[4]The difference in the proportion with pulmonary disease varied relatively little between the age groups.

[5]The vast majority of those previously registered with dementia were in the oldest age group.

[6]The vast majority of those previously registered with renal failure died outside hospital.

[7]Of those who died with previously registered conditions related to their immune function, the majority were in the youngest age group.

The disease profiles of those who died in hospital differed from the profiles of those who died elsewhere. Those who died in hospital more often had at least two previously registered non-communicable diseases. The proportion with diabetes was 30.4 % among those who died in hospital and 14.5 % among those who died outside hospital. The vast majority of the diabetes patients had type-2 diabetes. There were no cases of death among persons registered with type-1 diabetes in the age group under 80 years. All persons with a registered diagnosis of dementia died outside hospital. Five deaths occurred among persons registered with a disease or condition that affects the immune system. All these deaths occurred in hospital, and most of the persons concerned had undergone a transplantation. None of the deceased had been prescribed with an h-prescription drug in 2019, and no deaths occurred among patients undergoing active cancer therapy. When we used a broader search for definition of chronic disease that also included obesity and gastrointestinal, rheumatic and neurological diseases, we found another eleven persons. In other words, only 23 % (56 of 244) had no chronic somatic condition.

Discussion

In our data set, which includes deaths until 1 June 2020, the median age at death after a confirmed SARS-CoV-2 infection was 85 years. The proportion of deaths (lethality) was low (2.9 %) in Norway, but increased significantly with age. In our data, the lethality among persons aged 90 years and over was 52 %. High lethality among the oldest patients has been shown in several countries, proving the importance of protecting the most vulnerable segments of the population (14). Not all those infected with SARS-CoV-2 develop symptoms, and some have symptoms that are so mild as to evade testing. The test criteria and capacity may also vary over time and across regions and countries. The number of people who are tested and have the disease confirmed is decisive for determining its lethality (14). In countries where many persons with a mild or no disease have been tested, this will lower the lethality rate. As of 7 June 2020, Iceland, where widespread testing has been undertaken, reported a lethality of 0.6 %, Finland 4.6 %, Denmark 4.9 % and Sweden, which has been severely affected by the pandemic, reported a lethality of 10.4 % (15, 16).

We found that two of every three deaths after a confirmed SARS-CoV-2 infection occurred outside of hospitals. Figures from the MSIS registry show that the majority of these deaths occurred in other healthcare institutions, most likely in nursing homes, and only a minority died outside an institution. Since positive tests for SARS-CoV-2 were retrieved from the MSIS registry and linked to deaths recorded in the National Population Register, the location of the test was assumed to be the same as the place where the patient died. In most cases this will be correct, but we cannot exclude the possibility of erroneous classifications. Reporting to the MSIS registry includes information on whether the patient was at home at the time when the test was taken or admitted to a

hospital, nursing home or other healthcare institution, but does not indicate the type of healthcare institution in question, nor whether persons have been long-term nursing home residents, have been admitted for short-term periods from their homes or have been transferred from a hospital for a temporary stay in a nursing home. In our study, 15 patients died during the first week after discharge from a hospitalisation episode with a COVID-19 diagnosis, but we have no information on their clinical histories or functional status. The Norwegian Directorate of Health recommends that nursing home residents who fall ill with COVID-19 be treated in the nursing home without being hospitalised, unless there are especially strong grounds to indicate that a hospitalisation will significantly prolong their lives and enhance their quality of life (17). The nursing home population is especially vulnerable to a serious trajectory and death from COVID-19 due to their advanced age, underlying chronic diseases and general frailty, and a high risk of rapid spread of the virus among nursing home residents has also been shown (18, 19). Old and frail patients often have atypical symptoms, which increase the risk that the disease goes unnoticed or is discovered at a late stage. High-quality infection control, good monitoring of symptoms, a low threshold to testing for SARS-CoV-2 and isolation of infected patients are therefore especially important to prevent outbreaks in nursing homes.

In deaths that occurred outside hospitals, cardiovascular diseases and dementia were the most common underlying diseases. We have previously investigated the prevalence of underlying diseases in persons hospitalised for COVID-19 (11). In that study, the proportion of patients in the hospital population with a diagnosis of dementia was identical to the proportion of persons with a diagnosis of dementia in the general population. It is therefore interesting to note that no diagnoses of dementia could be identified in any of the patients who died while in hospital. This could indicate that the recommendations from the Norwegian Directorate of Health regarding treatment of nursing home residents with severe COVID-19 outside hospital are being complied with (17). In a study of COVID-19 outbreaks in Bergen, very few nursing home residents were hospitalised. The authors discussed whether the reason could be that the nursing homes had made thorough efforts to establish the treatment level for each resident prior to the COVID-19 epidemic (19). In line with Danish (5) and Italian studies (20), we found a larger proportion of patients with diabetes among those who died while in hospital than among those who died elsewhere. During the first weeks of the pandemic there was special concern about persons with underlying conditions or undergoing treatment that affects the immune system. In our study, only five persons with such conditions were registered as deceased after a confirmed SARS-CoV-2 infection, and there were no deaths among persons receiving active cancer therapy or users of biological drugs prescribed and paid for by the hospital (h-prescription).

The strength of this study is that it includes all persons resident in Norway and all deaths among people with a confirmed SARS-CoV-2 infection. The registry linkages provide us with data for prospectively registered somatic diagnoses from both the specialist and the primary health service. Even though the quality of some diagnoses varies between the health registries, their advantage

is that these diagnoses have been registered on an ongoing basis, thus avoiding the biases that may arise when the risk factors are reported by the deceased person's doctor.

A weakness of this study is that we cannot know whether COVID-19 was the direct cause of death. Theoretically, the patient could have recovered from the infection and later died from another cause. However, for several reasons we assume it is likely that the vast majority of the persons included in the statistical base in fact died from SARS-CoV-2, because only a short time had passed between confirmation of the infection and death, all those who had a confirmed infection and died while in hospital had COVID-19 as their main or secondary diagnosis, and the number of deaths from COVID-19 reported to the MSIS registry was numerically quite equal to our sample; 239 and 244 persons respectively. A review of patient records to verify COVID-19 as the cause of death would have strengthened the validity of the study.

In September 2020, the Norwegian Institute of Public Health published preliminary data from the Causes of Death Registry on COVID-19 as a cause of death and the correlation with chronic diseases (21). These analyses encompass the period March–May 2020, and the Causes of Death Registry reports that COVID-19 was registered as the underlying cause of death in 215 (91 %) of the 236 cases that had been confirmed by a laboratory and reported to the registry. Chronic diseases had been registered in the death certificates for 89 % of all deaths associated with COVID-19, and by registering chronic diseases in this manner, the Causes of Death Registry has applied a wider definition of chronic disease than we have done in our analysis.

The disease profile differs to some extent from what we found, with less reported diabetes and more dementia in the data from the Causes of Death Registry. This underscores the need for using multiple sources in parallel when studying such complex issues.

Aggregated data based on registry linkages can be a good source of information on risk groups during a pandemic, but are not sufficient for more refined analyses. A major research project is therefore now being established, in which individual-level data on underlying disease and risk factors are also being linked to causes of death from the Causes of Death Registry, drug use from the Prescription Registry and data on socioeconomic conditions and country of origin from Statistics Norway.

Conclusion

Only a small proportion of the patients with a confirmed SARS-CoV-2 infection died during the first three months of the pandemic in Norway (2.9 %), but the lethality exceeded 50 % in the age group over 90 years. Most of those who died were registered with at least one chronic disease, but in the age group under 70 years no previous chronic disease or condition had been registered in four out of ten deceased persons. No patients with a registered dementia diagnosis died while in hospital. Persons who died while in hospital were younger and more often registered with diabetes or conditions that affect the immune system, and

often suffered from multiple conditions in parallel. Norwegian health registries are good sources to obtain an overview of risk factors and trajectories during an ongoing pandemic.

The article has been peer reviewed.

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