Scandinavian Journal of Public Health, 2022; 50: 686–692

SHORT COMMUNICATION

Changing characteristics over time of individuals receiving COVID-19 vaccines in Denmark: A population-based descriptive study of vaccine uptake

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Abstract

Aims: The Danish authorities implemented a differential rollout of the COVID-19 vaccines where individuals at high risk of COVID-19 were prioritized. We describe the temporal uptake and characteristics of COVID-19 vaccine recipients in Denmark. *Methods:* Using nationwide healthcare registries, we identified all Danish residents ⩾5 years of age who received at least one dose of a COVID-19 vaccine from 27 December 2020–29 January 2022. We charted the daily number of newly vaccinated individuals and the cumulative vaccine coverage over time, stratified by vaccine type, age groups and vaccination priority groups, and described characteristics of vaccine recipients during two-month-intervals and in vaccination priority groups. *Results:* By 29 January 2022, 88%, 86% and 64% of Danish residents ⩾5 years (n=5,562,008) had received a first, second and third dose, respectively, of a COVID-19 vaccine, most commonly the BNT162b2 vaccine (84%). Uptake ranged from 48% in 5–11-year-olds to 98% in 65–74-year-olds. Individuals vaccinated before June 2021 were older (median age 61–70 years vs 10–35 years in later periods) and had more comorbidities such as hypertension (22–28% vs 0.77–2.8% in later periods), chronic lung disease (9.4–15% vs 3.7–4.6% in later periods) and diabetes (9.3–12% vs 0.91–2.4% in later periods). ***Conclusions:*** **We document substantial changes over time in, for example, age, sex and medical history of COVID-19 vaccine recipients. Though these results are related to the differential vaccine rollout in Denmark, similar findings are probable in other countries and should be considered when designing and interpreting studies on the effectiveness and safety of COVID-19 vaccines.**

Keywords: *COVID-19, COVID-19 vaccine, differential rollout, epidemiology, population-based, patient characteristics*

Background

The initially limited supply capacity and high demand for coronavirus disease 2019 (COVID-19) vaccines forced authorities worldwide to implement a differential rollout of vaccines such that individuals at highest risk of severe COVID-19 were prioritized before younger and healthier individuals. To inform the design and interpretation of real-world studies on both the effectiveness and safety of the COVID-19 vaccines as well as on the course of the COVID-19 pandemic, we described the uptake of the COVID-19 vaccines in Denmark including characteristics of individuals receiving the COVID-19 vaccines at different time periods.

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Date received 1 April 2022; reviewed 28 April 2022; accepted 25 May 2022

DOI: 10.1177/14034948221108246
journals.sagepub.com/home/sjp
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Methods

Data sources

From the Danish Vaccination registry [1] we identified individuals who received a vaccine against COVID-19. Individual-level data were linked via a unique personal identifier to the Danish National Patient [2] and Prescription Registry [3] to obtain information on discharge diagnoses and prescription drug use. Information on positive and negative real-time reverse transcription polymerase chain reaction (RT-PCR) tests for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) was obtained from the Danish Microbiology Database [4].

Vaccine rollout strategy

Denmark began its COVID-19 vaccination programme on 27 December 2020 (**Supplemental Material Figure 1**). The Danish health authorities initially prioritized immunization of nursing home residents, frontline healthcare and social workers, and persons at particularly high risk of severe COVID-19 (see **Supplemental Material Appendix A** for a detailed description of vaccination priority groups). From mid-March to end-November 2021, the vaccination programme was gradually extended to the remaining population ⩾5 years of age. Four COVID-19 vaccines have been used in Denmark, mainly the BNT162b2 (Comirnaty, Pfizer BioNTech) and mRNA-1273 (Spikevax, Moderna) vaccine. The AZD1222 (Vaxzevria, AstraZeneca) vaccine was prioritized for healthcare and social workers, but removed from the vaccination programme on 11 March 2021, due to safety concerns [5] whereas the Ad26.COV2.S (COVID-19 Vaccine Janssen, Johnson & Johnson) vaccine was only available on a voluntary opt-in basis.

Analysis

We identified all Danish residents ⩾5 years of age at the time of receiving the first dose of one of the four COVID-19 vaccines used in Denmark and described the daily number of recipients of a first vaccine dose as well as the cumulative vaccination coverage from 27 December 2020–29 January 2022, stratified by vaccine type, age groups and vaccination priority groups. We described the overall uptake of the first, second and third dose, and in age groups and vaccination priority groups. Finally, we described characteristics of recipients of a first vaccination dose within two-month-intervals. We stratified by type of vaccine, vaccination priority group, whether they received the second dose within 8 weeks and whether they had a prior positive SARS-CoV-2 PCR test. Codes used to define comorbidity and prior medical history are available in **Supplemental Material Table 1**.

Other

According to Danish law, studies based entirely on registry data do not require approval from an ethics review board [6]. The study was registered at the repository of the University of Southern Denmark (11.247) and the data were available from the Danish Health Data Authority (FSEID00005447). Due to legal reasons, individual-level data cannot be shared by the authors.

Results

By 29 January 2022, 88%, 86% and 64% of the Danish population ⩾5 years of age (n=5,562,008) had received a first, second and third dose, respectively, of a COVID-19 vaccine (data not shown). Uptake of the first vaccination dose ranged from 48% in 5–11-year-olds up to 98% in 65–74-year-olds (**Supplemental Material Figure 2**). Most received the BNT162b2 vaccine (n=4,114,960, 84%) (**Supplemental Material Figure 3**), primarily from March through July 2021 (**Supplemental Material Figure 4**). The rollout of the first vaccination dose in the highest prioritized groups was largely accomplished before April 2021 (**Figure 1(a)**) whereas most individuals ⩾75 years had received the first dose by the end of May 2021 (**Figure 1(b), Supplemental Material Figure 2**). Overall, 98% and 73% of vaccinated individuals received a second and third dose, respectively, before 29 January (**Supplemental Material Table 2**). Of these, 97% received homologous first and second doses, whereas 99% received homologous second and third doses (**Supplemental Material Table 3**).

The proportion of women among vaccine recipients changed from 70% in December 2020–January 2021 to ~50% after April 2021 (**Figure 2**) reflecting a high proportion of women among nursing home residents (62%), and healthcare and social workers (80%) (**Figure 3**). The median age at the time of vaccination was 61 years (interquartile range (IQR) 46–81) in December 2020–January 2021, increasing to 70 years (IQR 50–82) in February–March 2021, and decreasing to 10 years (IQR 8–13) in December 2021–January 2022 (**Figure 2**). Individuals vaccinated before June 2021 had more comorbidities than in later periods including hypertension (22–28% vs 0.77–2.8%), chronic lung disease (9.4–15% vs 3.7–4.6%) and diabetes (9.3–12% vs 0.91–2.4%) (**Figure 2**). The prevalence of comorbidities among

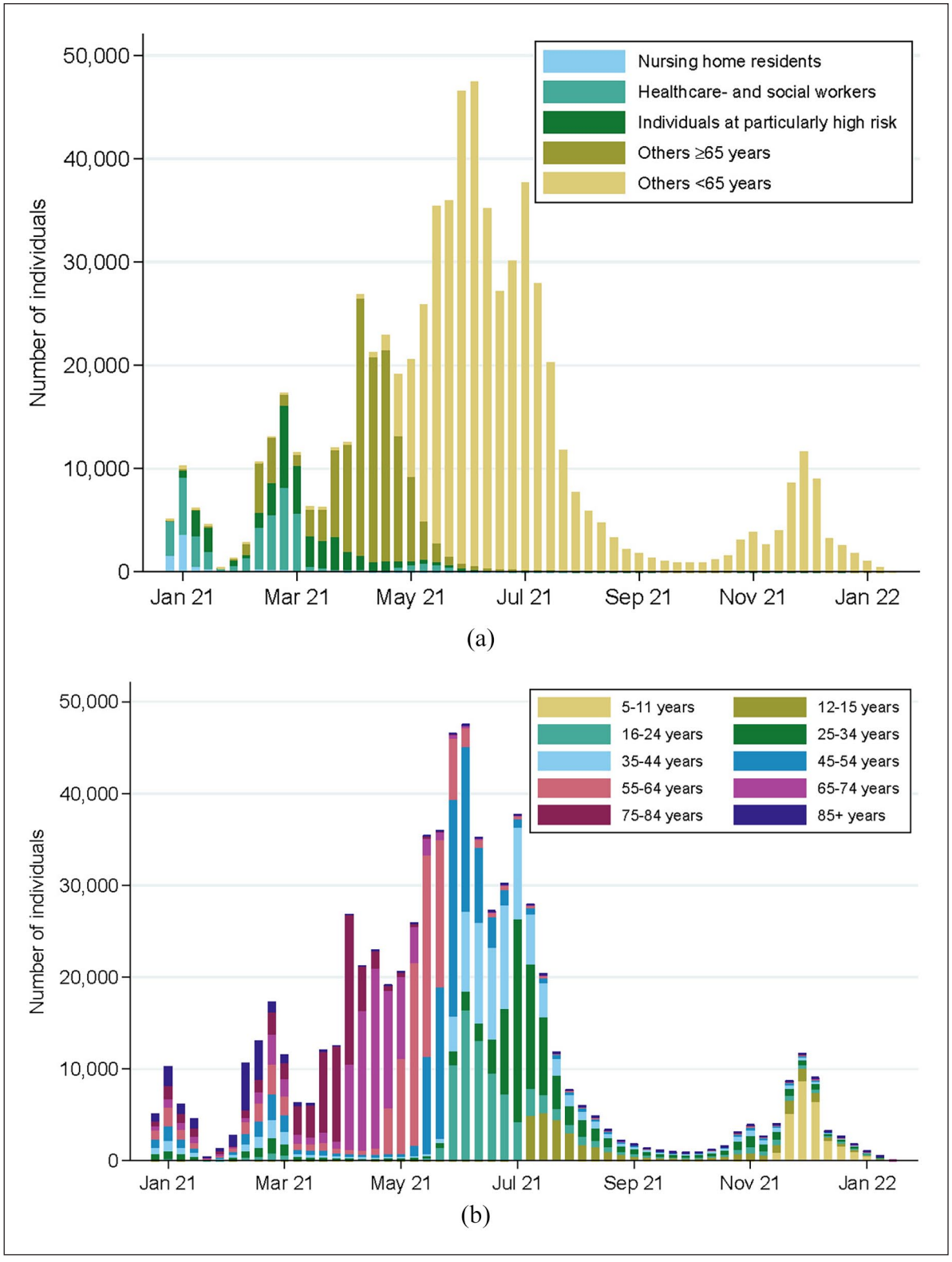
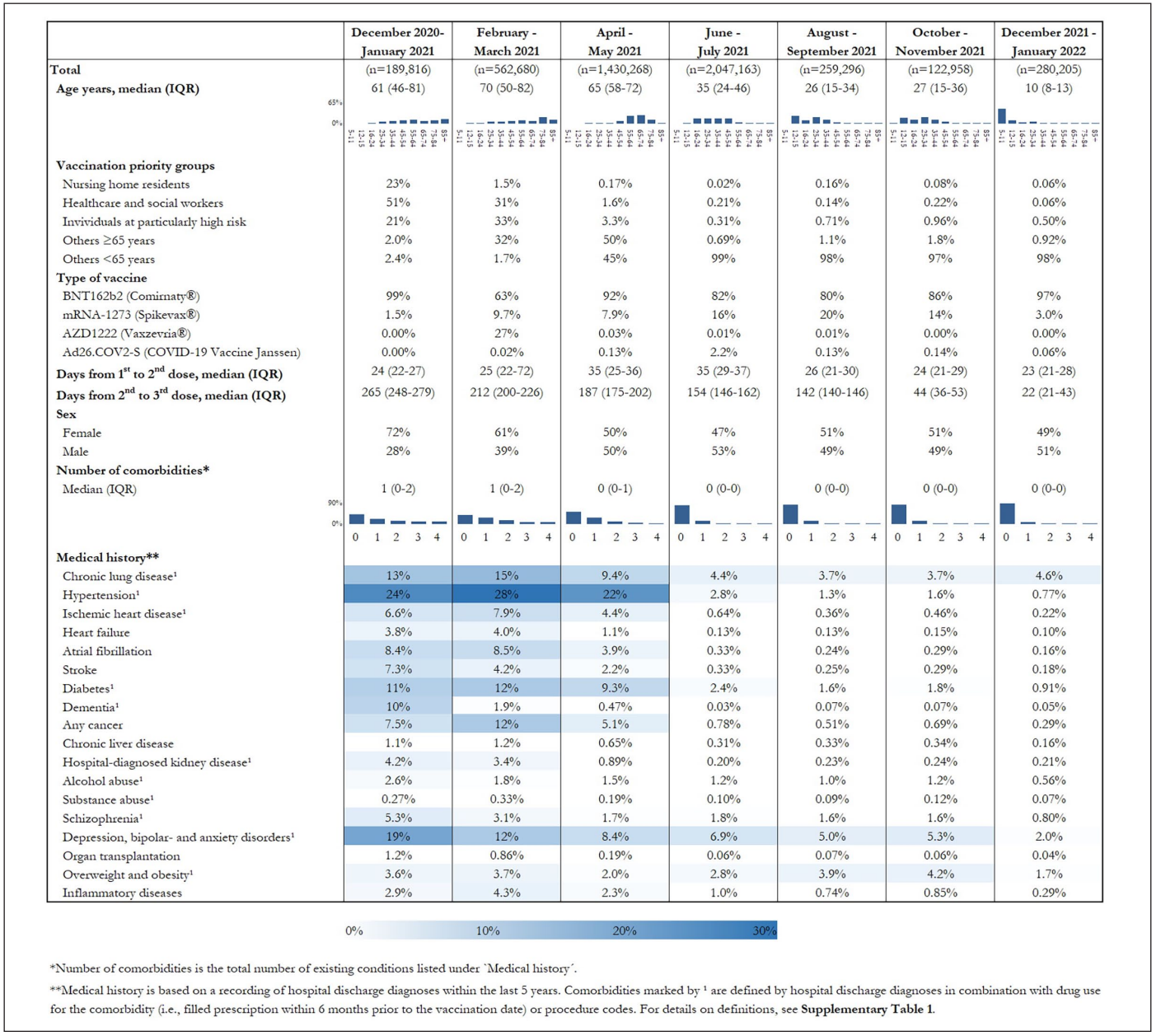


Figure 1. The number of individuals who received their first dose of COVID-19 vaccine each day from 27 December 2020–29 January 2022, stratified by (a) vaccine priority groups and (b) age groups.



	December 2020-January 2021	February - March 2021	April - May 2021	June - July 2021	August - September 2021	October - November 2021	December 2021 - January 2022
Total	(n=189,816)	(n=562,680)	(n=1,430,268)	(n=2,047,163)	(n=259,296)	(n=122,958)	(n=280,205)
Age years, median (IQR)	61 (46-81)	70 (50-82)	65 (58-72)	35 (24-46)	26 (15-34)	27 (15-36)	10 (8-13)
Vaccination priority groups							
Nursing home residents	23%	1.5%	0.17%	0.02%	0.16%	0.08%	0.06%
Healthcare and social workers	51%	31%	1.6%	0.21%	0.14%	0.22%	0.06%
Invividuals at particularly high risk	21%	33%	3.3%	0.31%	0.71%	0.96%	0.50%
Others ≥65 years	2.0%	32%	50%	0.69%	1.1%	1.8%	0.92%
Others <65 years	2.4%	1.7%	45%	99%	98%	97%	98%
Type of vaccine							
BNT162b2 (Comirnaty®)	99%	63%	92%	82%	80%	86%	97%
mRNA-1273 (Spikevax®)	1.5%	9.7%	7.9%	16%	20%	14%	3.0%
AZD1222 (Vaxzevria®)	0.00%	27%	0.03%	0.01%	0.01%	0.00%	0.00%
Ad26.COV2-S (COVID-19 Vaccine Janssen)	0.00%	0.02%	0.13%	2.2%	0.13%	0.14%	0.06%
Days from 1st to 2nd dose, median (IQR)	24 (22-27)	25 (22-72)	35 (25-36)	35 (29-37)	26 (21-30)	24 (21-29)	23 (21-28)
Days from 2nd to 3rd dose, median (IQR)	265 (248-279)	212 (200-226)	187 (175-202)	154 (146-162)	142 (140-146)	44 (36-53)	22 (21-43)
Sex							
Female	72%	61%	50%	47%	51%	51%	49%
Male	28%	39%	50%	53%	49%	49%	51%
Number of comorbidities*							
Median (IQR)	1 (0-2)	1 (0-2)	0 (0-1)	0 (0-0)	0 (0-0)	0 (0-0)	0 (0-0)
Medical history**							
Chronic lung disease[1]	13%	15%	9.4%	4.4%	3.7%	3.7%	4.6%
Hypertension[1]	24%	28%	22%	2.8%	1.3%	1.6%	0.77%
Ischemic heart disease[1]	6.6%	7.9%	4.4%	0.64%	0.36%	0.46%	0.22%
Heart failure	3.8%	4.0%	1.1%	0.13%	0.13%	0.15%	0.10%
Atrial fibrillation	8.4%	8.5%	3.9%	0.33%	0.24%	0.29%	0.16%
Stroke	7.3%	4.2%	2.2%	0.33%	0.25%	0.29%	0.18%
Diabetes[1]	11%	12%	9.3%	2.4%	1.6%	1.8%	0.91%
Dementia[1]	10%	1.9%	0.47%	0.03%	0.07%	0.07%	0.05%
Any cancer	7.5%	12%	5.1%	0.78%	0.51%	0.69%	0.29%
Chronic liver disease	1.1%	1.2%	0.65%	0.31%	0.33%	0.34%	0.16%
Hospital-diagnosed kidney disease[1]	4.2%	3.4%	0.89%	0.20%	0.23%	0.24%	0.21%
Alcohol abuse[1]	2.6%	1.8%	1.5%	1.2%	1.0%	1.2%	0.56%
Substance abuse[1]	0.27%	0.33%	0.19%	0.10%	0.09%	0.12%	0.07%
Schizophrenia[1]	5.3%	3.1%	1.7%	1.8%	1.6%	1.6%	0.80%
Depression, bipolar- and anxiety disorders[1]	19%	12%	8.4%	6.9%	5.0%	5.3%	2.0%
Organ transplantation	1.2%	0.86%	0.19%	0.06%	0.07%	0.06%	0.04%
Overweight and obesity[1]	3.6%	3.7%	2.0%	2.8%	3.9%	4.2%	1.7%
Inflammatory diseases	2.9%	4.3%	2.3%	1.0%	0.74%	0.85%	0.29%

*Number of comorbidities is the total number of existing conditions listed under `Medical history´.

Medical history is based on a recording of hospital discharge diagnoses within the last 5 years. Comorbidities marked by [1] are defined by hospital discharge diagnoses in combination with drug use for the comorbidity (i.e., filled prescription within 6 months prior to the vaccination date) or procedure codes. For details on definitions, see **Supplementary Table 1.

Figure 2. Characteristics within two-month intervals of individuals receiving their first dose of a COVID-19 vaccine. IQR: interquartile range.

	Nursing home residents	Healthcare and social workers	Individuals at particularly high risk	Others ≥65 years	Other <65 years	No 2nd dose within 8 weeks	Prior pos SARS-CoV-2 PCR test
Total	(n=56,242)	(n=300,494)	(n=285,541)	(n=923,867)	(n=3,326,242)	(n=311,325)	(n=253,868)
Age years, median (IQR)	84 (77-90)	48 (35-57)	69 (55-77)	74 (69-79)	37 (22-51)	35 (21-51)	34 (20-52)
Days from 1st to 2nd dose, median (IQR)	24 (22-26)	63 (26-83)	23 (21-27)	26 (22-35)	35 (28-37)	83 (76-89)	34 (25-37)
Days from 2nd to 3rd dose, median (IQR)	234 (225-240)	209 (182-264)	218 (205-238)	203 (191-212)	161 (149-172)	187 (164-203)	166 (151-187)
Sex							
Female	62%	80%	51%	53%	47%	63%	50%
Male	38%	20%	49%	47%	53%	37%	50%
Number of comorbidities*							
Median (IQR)	2 (1-3)	0 (0-1)	2 (1-3)	1 (0-2)	0 (0-0)	0 (0-0)	0 (0-0)
Medical history**							
Chronic lung disease[1]	16%	6.5%	23%	11%	4.8%	5.9%	6.4%
Hypertension[1]	41%	6.5%	36%	32%	4.2%	4.7%	6.2%
Ischemic heart disease[1]	11%	1.3%	12%	6.5%	0.93%	1.2%	1.6%
Heart failure	6.5%	0.18%	7.5%	1.9%	0.17%	0.42%	0.52%
Atrial fibrillation	17%	0.76%	11%	7.2%	0.50%	0.94%	1.4%
Stroke	18%	0.45%	6.8%	3.3%	0.46%	0.72%	0.86%
Diabetes[1]	17%	3.6%	20%	11%	3.0%	3.1%	4.3%
Dementia[1]	35%	0.03%	3.0%	0.93%	0.03%	0.45%	0.49%
Any cancer	8.7%	2.1%	23%	6.8%	1.1%	1.8%	1.9%
Chronic liver disease	1.4%	0.37%	2.8%	0.50%	0.35%	0.49%	0.44%
Hospital-diagnosed kidney disease[1]	5.1%	0.27%	7.7%	1.4%	0.22%	0.49%	0.64%
Alcohol abuse[1]	5.8%	0.77%	3.8%	1.2%	1.2%	1.5%	0.85%
Substance abuse[1]	0.44%	0.06%	0.74%	0.12%	0.12%	0.20%	0.08%
Schizophrenia[1]	15%	0.95%	6.4%	1.2%	1.7%	1.8%	1.2%
Depression, bipolar- and anxiety disorders[1]	41%	7.3%	18%	8.5%	6.5%	7.2%	5.7%
Organ transplantation	0.38%	0.09%	2.3%	0.23%	0.06%	0.10%	0.16%
Overweight and obesity[1]	1.9%	4.2%	5.9%	1.5%	2.7%	3.5%	2.6%
Inflammatory diseases	2.5%	1.9%	9.5%	2.0%	1.1%	1.3%	1.3%

0% 10% 20% 30% 40% 50%

*Number of comorbidities is the total number of existing conditions listed under `Medical history´.

Medical history is based on a recording of hospital discharge diagnoses within the last 5 years. Comorbidities marked by [1] are defined by hospital discharge diagnoses in combination with drug use for the comorbidity (i.e., filled prescription within 6 months prior to the vaccination date) or procedure codes. For details on definitions, see **Supplementary Table 1.

Figure 3. Characteristics of individuals receiving their first dose of a COVID-19 vaccine, stratified by priority group, whether they did not receive their second dose within 8 weeks, and whether they had a positive severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) polymerase chain reaction (PCR) test prior to receiving their first vaccination dose. IQR: interquartile range.

vaccinated individuals generally decreased over time (**Figure 2**). The prevalence and type of comorbidities varied markedly across vaccination priority groups (**Figure 3**).

Discussion

We have documented an extensive uptake of COVID-19 vaccines in Denmark where 88% of the eligible population had received at least one dose by 29 January 2022. Individuals vaccinated before April 2021 were more often women, people of older age and had more comorbidities compared to those vaccinated in the remaining period, reflecting the differential rollout which initially prioritized individuals at particularly high risk of COVID-19.

The high validity of Danish health registries [2] enabled a nationwide description of the COVID-19 vaccine uptake including a comprehensive description of medical history among individuals receiving the COVID-19 vaccine at different time points. Though data from clinical databases and on diagnoses from primary care were not available, we have been able to identify the most relevant medical history by use of hospital discharge diagnoses and drug use from primary care. Information on individuals not accepting a COVID-19 vaccine was not available. Also, we did not have access to data on socioeconomic factors such as income, educational level and migration status which have been shown to be associated with vaccine acceptance in both low- and middle-income [7] and high-income countries [8].

Though the observed changes in patient characteristics over time among those vaccinated are specifically related to the vaccine rollout strategy applied in Denmark, similar strategies were implemented in other countries. As such, most countries initially prioritized vaccination of high-risk individuals and healthcare workers, and later expanded vaccine rollout, primarily vaccinating the oldest before the youngest [9–12].

The Danish health registries are well-suited for timely analyses of COVID-19 vaccine safety and effectiveness, due to their high validity and frequently updated information on vaccine uptake. However, the analyses and interpretation of such studies should carefully consider how to address confounding due to the marked differences in patient characteristics over time and across vaccine priority groups. For example, self-controlled designs are vulnerable to temporal confounding [13], and cohort studies of vaccine effectiveness should carefully take calendar time into account, for example by using proportional hazard analyses that are anchored in calendar time. Since important differences in patient characteristics also exist across recipients of different vaccines, similar considerations should be undertaken in head-to-head comparisons of vaccine effectiveness. Importantly, changes over time in characteristics of patients receiving the COVID-19 vaccines should be considered in any study relying on data from countries that implemented a differential rollout strategy. Similar considerations of changes in characteristics also applies for individuals not accepting the vaccine.

Conclusions

COVID-19 vaccines had a high uptake in Denmark, though showing noticeable differences in characteristics over time among vaccine recipients. This should be considered when designing and interpreting studies on the course of the COVID-19 pandemic, and on the effectiveness and safety of COVID-19 vaccines.

Acknowledgements

Sissel Mogensen is acknowledged for help producing Supplemental Material Figure 1.

Declaration of conflicting interests

The author(s) declared the following potential conflicts of interest with respect to the research, authorship and/or publication of this article: H Støvring has received personal consulting fees from Bristol-Myers-Squibb, Novartis, Roche, Merck and Pfizer outside the submitted work. He has received teaching fees from Atrium. J Hallas and A Pottegård report participation in studies funded by Alcon, Almirall, Astellas, AstraZeneca, Boehringer-Ingelheim, Novo Nordisk, Servier, Pfizer, Menarini Pharmaceuticals and LEO Pharma, all regulator mandated phase IV studies, all with funds paid to their institution (no personal fees) and with no relation to the work reported in this article. J Hallas has received teaching fees from Atrium. LC Lund reports participation in research projects funded by Menarini Pharmaceuticals and LEO Pharma, all with funds paid to the institution where he was employed (no personal fees) and with no relation to the current work. M Reilev and PB Jensen report participation in research funded by LEO Pharma A/S (no personal fees) outside the submitted work. L Rasmussen reports funds paid to her institution for participation in research projects funded by Novo Nordisk, outside the current work. JH Andersen, H Kildegaard, P Damkier, MT Ernst, M Olesen and L Ladebo declare no conflicts of interest.

Funding

The author(s) received no financial support for the research, authorship and/or publication of this article.

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Supplemental material

Supplemental material for this article is available online.

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