The hospital and mortality burden of COVID-19 compared with influenza in Denmark: a national observational cohort study, 2022–24

Peter Bager, Ingrid Bech Svalgaard, Frederikke Kristensen Lomholt, Hanne-Dorthe Emborg, Lasse Engbo Christiansen, Bolette Soborg, Anders Hviid, Lasse S Vestergaard

Summary

Background **The COVID-19 pandemic has been on a downward trend since May, 2022, but it continues to cause substantial numbers of hospital admissions and deaths. We describe this burden in the 2 years since May, 2022, and compare it with the burden of influenza in Denmark.**

Methods **This observational cohort study included residents in Denmark from May 16, 2022, to June 7, 2024. Data were obtained from national registries, including admissions with COVID-19 or influenza (ie, having a positive PCR test for either virus from 14 days before and up to 2 days after the hospital admission date), deaths, sex, age, COVID-19 and influenza vaccination status, comorbidities, and residence in long-term care facilities. Negative binomial regression was used to estimate adjusted incidence rate ratios (aIRRs) to compare rates of hospital admissions between COVID-19 and influenza. To compare the severity of COVID-19 versus influenza among patients admitted to hospital, we used the Kaplan–Meier estimator to produce weighted cumulative incidence curves and adjusted risk ratios (aRRs) of mortality at 30 days between COVID-19 and influenza admissions.**

Findings **Among 5 899 170 individuals, COVID-19 admissions (n=24 400) were more frequent than influenza admissions (n=8385; aIRR 2·04 [95% CI 1·38–3·02]), particularly during the first year (May, 2022, to May, 2023) versus the second year (May, 2023, to June, 2024; p=0·0096), in the summer versus the winter (p<0·0001), and among people aged 65 years or older versus younger than 65 years (p<0·0001). The number of deaths was also higher for patients with COVID-19 (n=2361) than patients with influenza (n=489, aIRR 3·19 [95% CI 2·24–4·53]). Among patients admitted in the winter (n=19 286), the risk of mortality from COVID-19 was higher than for influenza (aRR 1·23 [95% CI 1·08–1·37]), particularly among those without COVID-19 and influenza vaccination (1·36 [1·05–1·67]), with comorbidities (1·27 [1·11–1·43]), and who were male (1·36 [1·14–1·59]).**

Interpretation **COVID-19 represented a greater disease burden than influenza, with more hospital admissions and deaths, and more severe disease (primarily among non-vaccinated people, those with comorbidities, and male patients). These results highlight the continued need for attention and public health efforts to mitigate the impact of SARS-CoV-2.**

Funding **Danish Government.**

Copyright **© 2025 Elsevier Ltd. All rights reserved, including those for text and data mining, AI training, and similar technologies.**

Lancet Infect Dis 2025

Published Online January 29, 2025 https://doi.org/10.1016/S1473-3099(24)00806-5

See Online/Comment https://doi.org/10.1016/S1473-3099(25)00001-5

Department of Infectious Disease Epidemiology and Prevention (F K Lomholt MD, H-D Emborg PhD, B Soborg PhD, Prof L S Vestergaard PhD) **and Department of Epidemiology Research** (P Bager PhD, I B Svalgaard MSc, L E Christiansen PhD, A Hviid PhD), **Statens Serum Institut, Copenhagen, Denmark; Pharmacovigilance Research Center, Department of Drug Design and Pharmacology, University of Copenhagen, Copenhagen, Denmark** (A Hviid)

Correspondence to: Dr Peter Bager, Department of Epidemiology Research, Statens Serum Institut, Copenhagen 2300, Denmark **pbg@ssi.dk**

Introduction

Although the COVID-19 pandemic is subsiding, infections with SARS-CoV-2 persist. These infections result in a substantial hospital and mortality burden that is moving towards a pattern resembling that of seasonal influenza. With decades of established data on influenza epidemiology, burden, and management, it is an ideal benchmark against which to assess the evolving impact of COVID-19, in turn informing public health strategies, resource allocation, and preparedness efforts.[1]

Only a few studies have compared the disease burden of COVID-19 with influenza in the 2 years elapsed since May, 2022, when the COVID-19 pandemic started on a downward trend,[2] all suggesting a higher disease severity of COVID-19, as measured by 30-day mortality among hospitalised patients. However, the generalisability of these studies was limited, because the studies included mostly older male patients from the US Veterans Affairs health-care system.[3,4]

In this study, we used data for the entire general population of Denmark and aimed to compare COVID-19 with influenza from 2022 to 2024 in terms of the number of hospital admissions, number of deaths, and disease severity.

Methods

Study design and participants

This nationwide, observational cohort study included all residents of Denmark in the period from May 16, 2022, to June 7, 2024. The cutoff months allowed the period to be divided into two seasons (2022–23 and 2023–24), corresponding to the influenza season months from

Research in context

Evidence before this study

We conducted a search on PubMed with search terms of "COVID-19" AND "influenza" in titles, AND ("mortality" OR "burden" OR "admission") in any field (eg, title or abstract), restricted to publication dates between Jan 31, 2022, and Sept 20, 2024 with no language restrictions. The search was last updated on Sept 20, 2024, yielding 463 results. 171 mentioned European countries (13 mentioned Denmark specifically) and 292 did not. Only two studies included COVID-19 and influenza hospital admissions in the two seasons after May, 2022 (when the COVID-19 pandemic began its downward trend), and both suggested a higher disease severity (30-day mortality) of COVID-19. However, these studies had limited generalisability as the study populations were mostly older male patients. A study by the European Mortality Monitoring Network reported that excess all-cause mortality in the 2023–24 winter season among adults aged 45 years and older coincided with the widespread presence of COVID-19, influenza, and respiratory syncytial virus in many European countries.

Added value of this study

In this observational cohort study of the entire population of Denmark, COVID-19 represented a greater disease burden than influenza from 2022 to 2024, with more hospital admissions and deaths, particularly in the first year (May, 2022, to May, 2023), in the summer, and among older people. Our results also showed that COVID-19 conferred more severe disease than influenza, but not to the extent previously reported. More serious disease was observed especially among patients who were not vaccinated against either disease, those with comorbidities, and male patients.

Implications of all the available evidence

The results highlight the continued need for public health efforts to mitigate the impact of SARS-CoV-2, including the seasonal booster vaccination of older populations. By using influenza as a benchmark, our results on the continued hospital and mortality burden of COVID-19 can inform public health strategies, resource allocation, and preparedness efforts.

May to April, as defined by the US Centers for Disease Control and Prevention (CDC) and the European Centre for Disease Prevention and Control (ECDC).[5,6] Participants were considered hospitalised with COVID-19 or influenza if they had a positive PCR test from 14 days before and up to 2 days after the hospital admission date. The date of admission was used to calculate 30-day mortality. Participants with a positive PCR test for both COVID-19 and influenza in the 14 days before and up to 2 days after hospital admission were excluded.

This study was conducted as part of Statens Serum Institut's duties as a national public health agency. Ethical approval and individual consent were not acquired, as according to Danish law, they are not required for anonymised, aggregated, register-based studies. Due to the nature of this research, there was no direct involvement of patients or members of the public in the design or reporting of the study. Therefore, no approval from an ethics committee was required. The study is fully compliant with all legal and ethical requirements.

Data sources

This study was based on Denmark's national COVID-19 and influenza surveillance system and population-based registers with individual-level data that are updated and linked daily using the unique civil registration number given to all residents.[7] Details of all COVID-19 and influenza vaccinations administered in the country were obtained from the Danish National Vaccination Register.[8] Hospital admission and discharge dates, diagnoses, and referrals were obtained from the National Patient Registry.[9] Data on comorbidities based on ICD-10 diagnosis codes (haematological disease, cancers, neurological diseases, kidney diseases, cardiovascular diseases, respiratory diseases, and immunological conditions) were obtained from the National Patient Registry, and data on additional comorbidities (asthma, dementia, type 1 diabetes, type 2 diabetes, chronic obstructive pulmonary disease, rheumatoid arthritis, osteoporosis, and schizophrenia) were obtained from the Register of Selected Chronic Diseases and Severe Mental Disorders.[10] Data on living in a long-term care facility (LTCF) for older people (the majority being older than 65 years) were obtained from the LTCF address database.[11] Death dates (when applicable) and residency data were obtained from the Civil Registration System,[7] along with information on sex, age, address history, emigration, and disappearance from national registers. In adherence to Sex and Gender Equity in Research guidelines for reporting,[12] we derived the sex variable from the civil registration numbers assigned at birth or time of entry to Denmark, where an odd numerical value indicates male sex at birth and an even numerical value indicates female sex at birth. Details of all SARS-CoV-2 and influenza PCR tests conducted during the study period were obtained from the Danish Microbiology Database[13] and originated from one of three sources: routine clinical samples collected on indication at hospitals and primary care clinics country-wide;[14] clinical samples collected on indication in selected primary care clinics as part of the national sentinel surveillance system for influenza-like illness, based on ECDC and WHO guidelines;[15] and a self-sampling virus monitoring system (including SARS-CoV-2, influenza, and other viruses), known as virus monitoring in Denmark, implemented since May, 2022.[16,17] Clinical samples collected on indication at hospitals and primary care clinics were analysed by one of the country's ten departments of microbiology, and virus monitoring samples were analysed by Statens Serum Institut.[14]

Test strategy, vaccinations, and circulating virus strains

Feb 1, 2022 marked the official date for removal of all COVID-19 restrictions in Denmark. The number of PCR and antigen COVID-19 tests performed weekly in Denmark hit a world record high of 4 million before and up to March, 2022. Since then, the number of tests has decreased, and PCR testing has been mainly focused on the health-care sector.[18,19] As of March 10, 2022, the guidelines on how to handle COVID-19 and influenza have both recommended that physicians perform PCR tests on people with symptoms and people at risk of a severe disease course (eg, due to immune deficiencies or hospital admission), considering also concurrent outbreaks.[20–22] The guidelines for COVID-19 differed from those for influenza in other cases—for example, until December, 2022, there was focused testing (ie, screening of patients admitted to hospital and having mild COVID-19 symptoms, acutely admitted medical patients, hospital outbreak-related patients, and testing related to LTCFs for older people). The COVID-19 guidelines were further relaxed in February and November, 2023. To assess the actual observable differences in test patterns, we describe the national PCR test patterns for COVID-19 and influenza by week, sex, age, and region.

Mass vaccination campaigns and virus strains circulating just before the COVID-19 pandemic began its downward trend in May, 2022 are described in the appendix (p 2). On Oct 1, 2022, mass vaccination targeting individuals aged 65 years and older was rolled out. More than 95% of adults aged 65 years and older received COVID-19 booster doses targeting both the ancestral strain and either omicron subvariant BA.1 or BA.4/5.[23,24] To protect against influenza, more than 81% of adults aged 65 years and older received the quadrivalent influenza vaccine targeting the A H1N1, A H3N2, B-Victoria, and B-Yamagata strains.[23] During the 2022–23 winter season, infections with recombinant XBB subvariants of omicron became dominant over other subvariants, including BA.1 and BA.4/5, while influenza A H1N1 (42%), A H3N2 (20%), and B (38%) infections co-circulated.[25] In the following winter season (2023–24), mass vaccination again started on Oct 1, 2023, and adults aged 65 years and older were offered booster doses targeting the XBB.1.5 subvariant, now with simultaneous administration of the quadrivalent influenza vaccine. More than 78% of this population received the two vaccines.[23] During the 2023–24 winter season, the hypermutated new omicron subvariant BA.2.86 began to dominate SARS-CoV-2 infections,[17,25] while influenza A H1N1 infections dominated (72%) influenza infections (followed by A H3N2 [28%]).

Statistical analysis

We used negative binomial regression to estimate sex-adjusted and age-adjusted incidence rate ratios (aIRRs) to compare rates of hospital admissions and deaths within 30 days of hospital admission between COVID-19 and influenza among all individuals living in Denmark (figure 1; appendix p 4).

We analysed disease severity (approximated as 30-day mortality) among individuals living in Denmark who were admitted to hospital with either COVID-19 or influenza (figure 1), with the positive test taken between Dec 1 and May 31 (referred to here as the winter season) of 2022–23, 2023–24, or both. We thereby excluded individuals admitted from June 1 to Nov 30, for brevity referred to as the summer season. This exclusion was made as the influenza mortality numbers in the summer season were too small for meaningful comparison with COVID-19. Furthermore, individuals with missing information on region of residence were excluded. The cohort was followed up for 30 days or until death, emigration, disappearance from national registers, or the end of study period, whichever occurred first. Baseline characteristics between patients hospitalised with COVID-19 and influenza were compared using standardised mean differences (SMDs), with an SMD less than 0·1 indicating good balance (data not shown).[26] An overview of baseline variables is provided in the appendix (p 3). Differences in baseline characteristics between the two groups were adjusted for using inverse probability weighting. A propensity score, calculated using logistic regression to estimate the probability of being assigned to the COVID-19 group, was applied to balance the groups on the following variables: sex, age at test (10-year intervals), season, origin (eg, Danish, born abroad, second-generation immigrant), region of residence, vaccination status, and a range of comorbidities (appendix p 3). Weights were constructed as 1 for the COVID-19 group and propensity score/(1–propensity score) for the influenza group. Both unweighted and weighted cumulative incidence curves were produced by the Kaplan–Meier estimator. Additionally, the adjusted risk difference (aRD; measured in percentage points) and adjusted risk ratio (aRR) between COVID-19 and influenza groups were estimated using the cumulative incidences of deaths at 30 days post-admission with corresponding 95% CIs calculated by the delta method. We conducted stratified analyses based on the following variables: sex, age (<65 years *vs* ≥65 years), comorbidity (any *vs* none) and vaccination status within 180 days of the test date of the admission (vaccinated against both diseases, vaccinated against the disease the individual tested positive for, or not vaccinated). A sensitivity analysis was conducted to investigate immortal time bias by setting the start of follow-up as the date of the PCR test for individuals who tested positive after admittance to hospital in the analysis of disease severity. Furthermore, as a sensitivity analysis of risk over time in

See Online for appendix

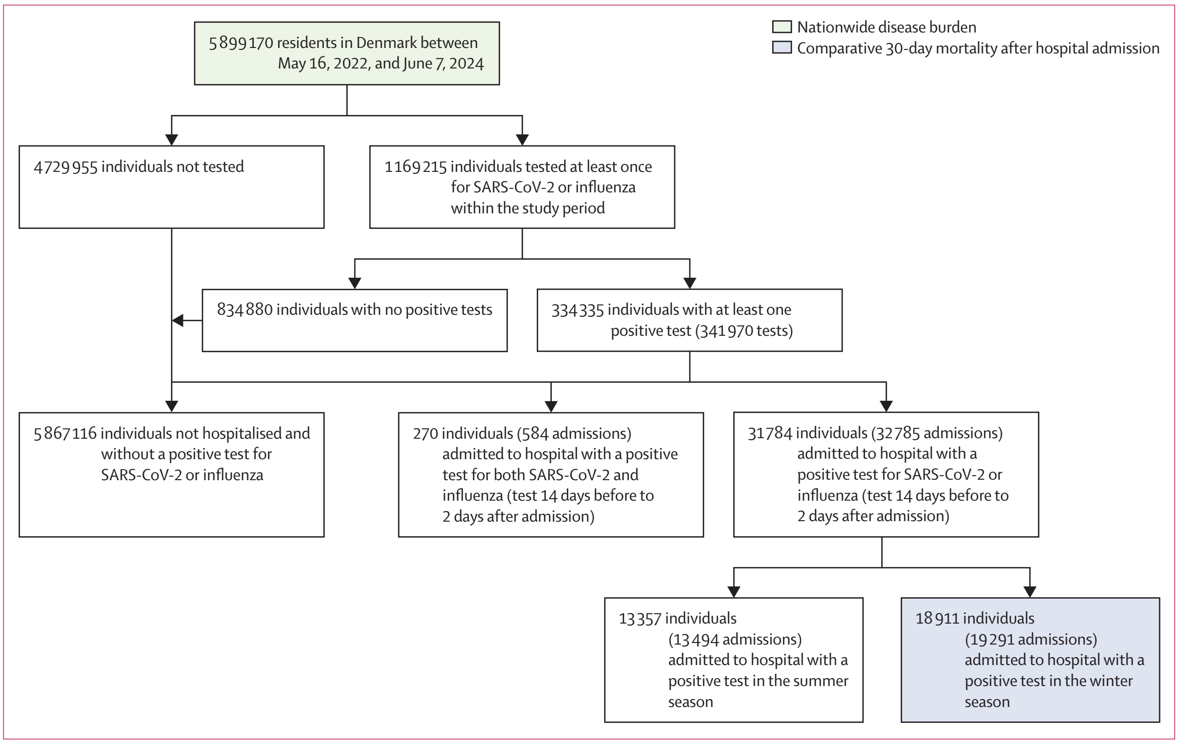

Figure 1: **Flowchart of study population**
Summer season refers to June 1–Nov 30, and winter season refers to Dec 1–May 31 (appendix p 7).

the 30-day period, a weighted Cox proportional hazards model (with time since admission as the underlying time scale) was used to estimate the hazard of death between COVID-19 and influenza groups, with results reported as adjusted hazard ratios (aHRs) with 95% CIs. The proportional hazards assumption was assessed using the scaled Schoenfeld residuals, both graphically and by testing for independence between residuals and time. If the assumption was violated, appropriate timepoints were determined, and step-wise models were fitted.

All analyses were carried out in R version 4.1.1. The packages MASS (version 7.3–54), performance (version 0.12.0), and survival (v3.2–11) were used for modelling and ggplot2 (version 3.5.1) and forestploter (version 1.1.1) for visualisations.

Role of the funding source

The funders of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the report.

Results

The study cohort consisted of 5 899 170 individuals living in Denmark from May 16, 2022, to June 7, 2024. During this period, 1169 215 (19·8%) individuals were tested for COVID-19 or influenza, of whom 334 335 (28·6%) tested positive. Among those who tested positive, 31 784 (9·5%) were defined as being admitted to hospital with COVID-19 (n=24 400) or influenza (n=8385), constituting 32 785 hospital admissions (figure 1).

Compatible with guidelines recommending decreased but still some COVID-19 screening in the health sector until December, 2022, the number of tests performed per week (ie, the weekly test rate) was higher for COVID-19 than influenza until December, 2022, after which the test rate for COVID-19 drops sharply and aligns closely with the influenza test rate from February, 2023 (appendix p 4). The number of tests that were positive among all tests performed per week (ie, the test-positive rate) was higher year round for COVID-19 than influenza, except in January, 2023, and January to June, 2024 (appendix p 4), when the test-positive rate for influenza was similar to COVID-19. This observation is compatible with a similar precision of identification of people with symptoms of COVID-19 and influenza, and also reflects that COVID-19 occurred year round whereas influenza occurred seasonally. Female individuals were tested for COVID-19 more often than males, and differences in test intensity by age groups and region were also evident (appendix p 5). These findings supported adjusting for age, sex, and region to improve the validity of comparisons of COVID-19 and influenza admissions by accounting for potential test-related over-representation (eg, of COVID-19 admissions of older people) in the entire study cohort.

31 637 (96·5%) of the 32 785 admitted patients had their samples collected at hospitals or primary care

clinics (note that some patients were admitted more than once). Most patients were tested at the hospital on or 2 days after admission (ie, 21 926 [90%] of 24 400 patients with COVID-19 and 7966 [95%] of 8385 patients with influenza), and most were tested for both COVID-19 and influenza on the same date (ie, 19 989 [81·9%] patients with COVID-19 and 8198 [97·8%] patients with influenza; appendix p 6). Among admissions for patients with influenza, 7333 were influenza A (87·5%) and 1052 were influenza B (12·5%). The mean length of hospital stay was slightly longer for patients with COVID-19 (4·71 days [SD 6·33]) than for patients with influenza (4·07 days [6·11]).

Overall, in the study cohort (ie, the entire Danish population), the absolute numbers of COVID-19 admissions and deaths within 30 days of admission were higher than for influenza (24 400 *vs* 8385 admissions, 2361 *vs* 489 deaths; table). This was the case during most months of the 2 years (exceptions were February, 2023, and February, 2024; figure 2). The difference was most pronounced in the first year, during the summer season, among males, and among patients older than 65 years (appendix p 7). Except for the results on sex, these results were consistent with the aIRRs based on 11·9 million person-years of follow-up (table). The national incidence rate per 100 000 person-years for COVID-19 admissions was 204·64 and for influenza admissions was 70·23 (aIRR 2·04, 95% CI 1·38–3·02). For 30-day mortality, the incidence rates were 19·76 per 100 000 person-years for COVID-19 and 4·09 per 100 000 person-years for influenza (aIRR 3·19, 95% CI 2·24–4·53). Differences were more pronounced in the first year versus the second year, during the summer season versus the winter season, and among people aged 65 years and older versus those younger than 65 years; however, there were no significant difference between males and females (table).

For the analysis of disease severity, we restricted the study population to individuals admitted to hospital in the winter season (COVID-19: n=11 264; influenza: n=8027) and excluded individuals admitted in the summer season (COVID-19: n=13 136; influenza: n=358; figure 1). Furthermore, five individuals were excluded due to missing information on region of residence. Characteristics of included and excluded patients are shown in the appendix (pp 8–9). The most notable difference was more vaccinations among the included versus excluded patients; the cutoff of vaccination within 6 months resulted in the winter season patients having being part of the mass vaccination from October to January more recently than the summer season patients.

The crude cumulative incidence curves for patients with COVID-19 or influenza showed a higher incidence of death among those with COVID-19 throughout the

	Admission (positive virus PCR test up to 14 days before or 2 days after admission date)						Mortality (death within 30 days of admission date)					
	n		Cases per 100 000 person-years		Adjusted IRR* (95% CI; COVID-19 *vs* influenza)	p value	n		Cases per 100 000 person-years		Adjusted IRR* (95% CI; COVID-19 *vs* influenza)	p value
	COVID-19	Influenza	COVID-19	Influenza			COVID-19	Influenza	COVID-19	Influenza		
Total	24 400	8385	204·64	70·23	2·04 (1·38–3·02)	..	2361	489	19·76	4·09	3·19 (2·24–4·53)	..
Year†	..	..	..	..	..	0·0096	..	..	..	..	..	0·0069
2022–23	16 046	3837	275·04	65·71	2·68 (1·74–4·12)	..	1496	197	25·61	3·37	5·93 (4·44–7·92)	..
2023–24	8354	4548	137·29	74·70	1·37 (0·90–2·10)	..	865	292	14·20	4·79	2·52 (1·90–3·33)	..
Season	..	..	..	..	..	<0·0001	..	..	..	..	..	<0·0001
Summer 2022	9195	158	289·23	4·97	42·91 (27·50–66·99)	..	793	7	24·93	0·22	110·11 (55·63–260·02)	..
Winter 2022–23‡	7118	3698	247·13	128·38	1·17 (0·77–1·77)	..	725	190	25·16	6·59	3·47 (2·79–4·33)	..
Summer 2023	4265	206	148·40	7·17	14·54 (9·39–22·53)	..	375	12	13·05	0·42	30·51 (17·58–58·37)	..
Winter 2023–24‡	3822	4323	129·14	146·04	0·67 (0·45–1·02)	..	468	280	15·80	9·45	1·58 (1·28–1·95)	..
Sex	..	..	..	..	..	0·71	..	..	..	..	..	0·95
Female	11 294	4252	188·17	70·74	1·90 (1·11–3·26)	..	1001	246	16·65	4·09	3·15 (1·90–5·23)	..
Male	13 106	4133	221·35	69·71	2·19 (1·27–3·79)	..	1360	243	22·92	4·10	3·22 (1·97–5·24)	..
Age at study start, years	..	..	..	..	..	<0·0001	..	..	..	..	..	<0·0001
0–39	1931	1970	34·99	35·73	0·98 (0·74–1·30)	..	8	11	0·14	0·21	0·67 (0·26–1·63)	..
40–64	4056	2081	110·64	56·71	1·95 (1·48–2·57)	..	164	59	4·54	1·70	2·67 (1·96–3·68)	..
≥65	18 413	4334	768·85	175·20	4·43 (3·37–5·82)	..	2189	419	91·73	17·32	5·24 (4·42–6·22)	..

N=5·9 million with 11·9 million person-years of follow-up. Summer season refers to June 1–Nov 30, and winter season refers to Dec 1–May 31 (appendix p 7). The p values are derived from the tests for heterogeneity between the IRRs. IRR=incidence rate ratio. *IRR adjusted for sex and age (0–39 years, 40–64 years, and ≥65 years). †2022–23 refers to May 16, 2022, to May 16, 2023; 2023–24 refers to May 16, 2023, to study end. ‡The cumulative number of cases assigned to the winter seasons (n=18 961) differs slightly from the numbers included in the analysis of disease severity (n=19 291) as detailed in the appendix (p 7).

Table: **Absolute numbers, crude incidence rates, and adjusted IRRs of admissions and 30-day mortality for patients with COVID-19 or influenza among the Danish population**

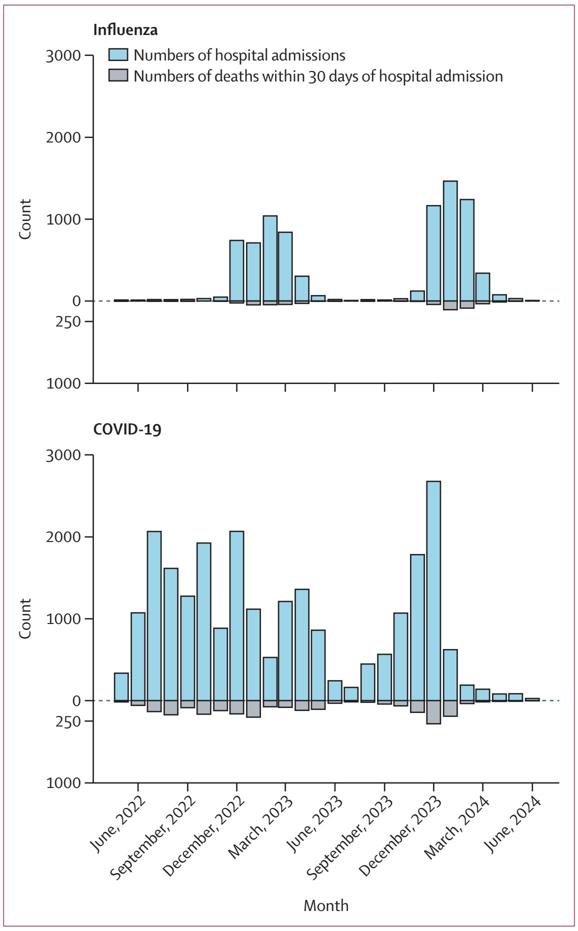

Figure 2: **Number of COVID-19 and influenza hospital admissions and deaths in Denmark by month from May, 2022, to June, 2024**

30 days following admission (day 30: 10·8% [95% CI 10·2–11·4] for COVID-19 *vs* 5·8% [5·3–6·3] for influenza; figure 3). However, in the weighted analysis, cumulative incidences were more similar during the first 10–12 days, after which the cumulative incidence of death for patients with COVID-19 continued to increase from day 12 to 30, whereas it started to level off for patients with influenza, resulting in non-overlapping CIs after 23 days (day 30: 10·8% [10·2–11·4] for COVID-19 *vs* 8·8% [7·9–9·7] for influenza; figure 3). There was a higher risk of death within 30 days of admission among patients with COVID-19 compared with those with influenza (aRD 1·99 [95% CI 0·89–3·08]) after adjusting for differences in patient characteristics between the groups. This finding translates to an estimated 20 (95% CI 9–31) additional deaths per 1000 patients admitted to hospital with COVID-19 compared with those hospitalised with influenza.

The relative risk of mortality at 30 days following admission was slightly higher for patients with COVID-19 than for patients with influenza (aRR 1·23 [95% CI 1·08–1·37]; figure 4). In stratified analyses, an increased relative risk of mortality 30 days after admission for patients with COVID-19 versus those with influenza was seen for patients aged 65 years and older but not those younger than 65 years, for males but not females, for patients with comorbidities but not those without, and for patients unvaccinated against both COVID-19 and influenza but not those vaccinated against both or either. Cumulative incidence curves for all strata can be found in the appendix (pp 10–13).

In a sensitivity analysis investigating immortal time bias, results for disease severity were similar to the main finding (aRR 1·22 [95% CI 1·07–1·36]). In a sensitivity analysis also of disease severity, we calculated the aHR for 30-day mortality (aHR 1·23 [1·09–1·40]) and found that this concealed a time-dependent effect (ie, we detected a proportional hazards assumption violation). Specifically, the increased relative risk was observed only 12–30 days after admission (0–11 days, aHR 1·10 [0·95–1·28]; 12–30 days, aHR 1·51 [1·21–1·88]).

Discussion

COVID-19 has continued to cause a more serious winter burden of hospital admissions and mortality than influenza in Denmark, even after May, 2022. The burden of hospital admissions and mortality from COVID-19 has been larger than for influenza, particularly during 2022–23, in the summer (when influenza is rare), and among older populations. In the winter season, admission numbers were more similar to those for influenza, but there were still more COVID-19 deaths, and the COVID-19 admissions were more serious, primarily among non-vaccinated patients, those with comorbidities, and male patients.

We found that the burden of hospital admissions for COVID-19 was more than 2 times that of influenza, which is compatible with the crude ratio we calculated based on dashboard surveillance data on cumulative rates over time from the CDC.[4,27,28] A key question is whether the COVID-19 burden will decrease as the pandemic subsides and SARS-CoV-2 gradually becomes endemic. However, with only 2 years of data, this is currently difficult to establish. In the second year, from May, 2023, to June, 2024, we observed a decrease in the number of admissions and deaths with COVID-19 compared with the previous year, although they were still higher than for influenza. Crude surveillance data from other countries (eg, the USA, Ireland, and New Zealand) also showed a decrease in COVID-19 admissions from May, 2022, to June, 2024,[29–31] whereas wastewater signals of infection levels (copies of DNA per person per day) showed no consistent decrease and even suggested near pandemic-high levels.[32–35] One straightforward explanation for the decrease in admissions is that individuals at higher risk (eg, aged >65 years) of severe clinical outcomes of COVID-19 are offered protection through the annual COVID-19 vaccination programme, thus boosting and improving their immunity and protection against COVID-19. However, we are inclined to mention two observations not consistent with this hypothesis: first, COVID-19 vaccination coverage in older populations in Denmark decreased from 95% in the first year (ie, 2022–23) to 78% in the second year (ie, 2023–24), when the speed of roll-out of vaccinations was also slower;[36] and second, we observed a slightly lower vaccine effectiveness against admission with new SARS-CoV-2 variants that emerged during the second year (the hypermutated BA.2.86 and subvariant JN.1) relative to previous variants that year.[17] However, two observations should be considered: vaccination coverage in Denmark was the highest in Europe in 2023–24, and the rolled out vaccination was shown to have offered effective protection throughout all the winter months of 2023–24.[37] Repeating our analysis in the coming years might address whether the burden of COVID-19 is decreasing.

With regard to our observations on disease severity, previous studies, also using 30-day mortality as an indicator for severe disease, have suggested that COVID-19 admissions are more severe than those for influenza. Among older male patients in the US veterans' cohort, 30-day mortality was 61% higher for COVID-19 than for influenza in 2022–23 (aHR 1·61 [95% CI 1·29–2·02], n=11 399), and 35% higher in 2023–24 (1·35 [1·10–1·66] n=11 272).[3,4] In our larger study in the general population in Denmark in the same period (n=33 369), the difference was more modest, with only a 23% higher 30-day mortality for COVID-19 than for influenza admissions (aHR 1·23); this corresponds to approximately 20 more deaths per 1000 admissions with COVID-19 relative to influenza. Interestingly, sensitivity analyses suggested these deaths were at risk of occurring weeks and not days after admission (day 12–30 and not day 1–11). A potential reason for the higher mortality could be that COVID-19, compared with influenza, is characterised by more persistent respiratory symptoms and more systemic effects (eg, gastrointestinal symptoms and different body dysfunctions [olfactory, cardiac, hepatobiliary, renal]), probably as a result of viral or indirect injury to tissue cells, although the pathophysiological mechanisms are not fully understood.[38,39]

In stratified analyses, we found that the higher risk of mortality by day 30 for patients with COVID-19 compared with patients with influenza was even greater among patients who were unvaccinated against COVID-19 and influenza. This finding not only stresses the important role of the seasonal booster vaccination programme for those aged 65 years and older, but also the role of inadequate COVID-19 immunity in younger age groups, constituting more than half of this unvaccinated group. Another important observation was that among patients without comorbidities (eg, patients without cardiac disease, chronic obstructive pulmonary disease, or diabetes), the risk of mortality was similar for COVID-19 and influenza, whereas patients with COVID-19 who had comorbidities still had more serious admissions than those with influenza who had comorbidities. Finally, we observed that male but not female patients with COVID-19 had a higher risk of mortality when compared to patients with influenza of the same sex. A higher

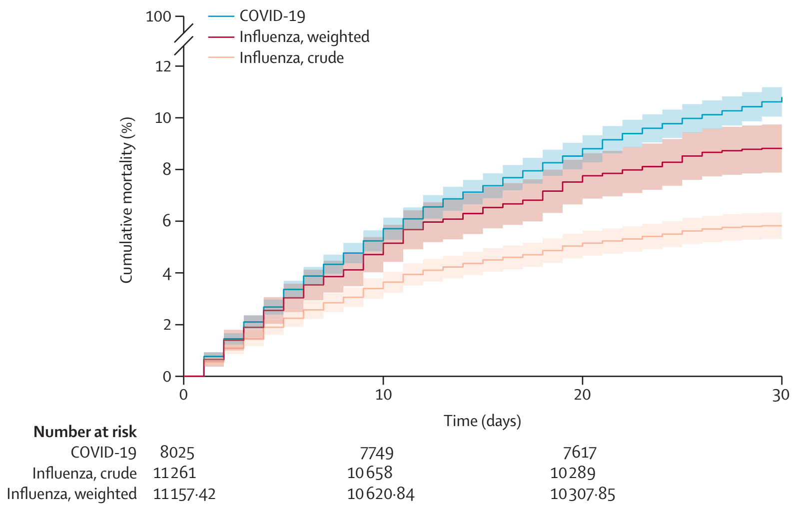

Figure 3: **Cumulative incidence of death among hospitalised patients**
The patient population is restricted to those admitted to hospital with COVID-19 (n=11 261) or influenza (n=8025) during the 2022–23 and 2023–24 winter seasons in Denmark. Summer season refers to June 1–Nov 30, and winter season refers to Dec 1–May 31 (appendix p 7). Both crude and weighted estimates are presented for influenza, with weighted estimates adjusted for differences in sex, age at test (10-year intervals), season, country of origin, region of residence, vaccination status, and a range of comorbidities between the groups using inverse probability weighting.

	N	Number of deaths, n (%)	aRR* (95% CI)
Main analysis			
Overall	19 286	1700 (8·8%)	1·23 (1·08–1·37)
Stratified analysis			
Sex			
Male	9969	942 (9·4%)	1·36 (1·14–1·59)
Female	9317	758 (8·1%)	1·08 (0·90–1·26)
Age			
<65 years	6503	158 (2·4%)	1·33 (0·86–1·80)
≥65 years	12 783	1542 (12·1%)	1·22 (1·07–1·37)
Comorbidity			
Any	14 565	1476 (10·1%)	1·27 (1·11–1·43)
None	4721	224 (4·7%)	1·06 (0·73–1·39)
Vaccination in the past 180 days			
Vaccinated against both	8847	877 (9·9%)	1·14 (0·97–1·30)
Not vaccinated	8509	657 (7·7%)	1·36 (1·05–1·67)
Vaccinated against either	9397	941 (10·0%)	1·11 (0·95–1·28)

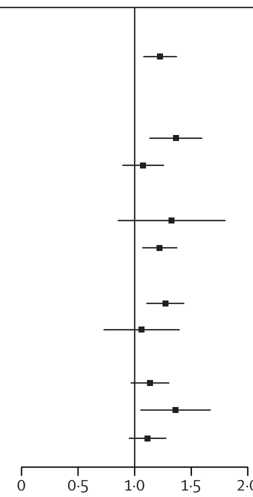

Figure 4: **Risk of mortality at 30 days following admission with COVID-19 versus influenza, overall and with stratifications on baseline characteristics**
The patient population is restricted to those admitted to hospital with COVID-19 (n=11 261) or influenza (n=8025) during the 2022–23 and 2023–24 winter seasons in Denmark. Summer season refers to June 1–Nov 30, and winter season refers to Dec 1–May 31 (appendix p 7). Data shown are aRRs and 95% CIs. aRR=adjusted risk ratio.
*Differences in sex, age at test (10-year intervals), season, country of origin, region of residence, vaccination status, and a range of comorbidities between the groups were adjusted for using inverse probability weighting.

severity for males compared with females with COVID-19 has previously been reported (eg, in an international study of 10 259 patients in intensive care units from 2020 to 2022),[40] with psychosocial and biological mechanisms as possible explanations.

Limitations of this study include that our findings are less generalisable to countries with lower vaccination rates or with large disparities in health-care access. In Denmark, all citizens have access to free health care and services (including tests), regardless of race, ethnicity, or social status. To account for potential minor disparities in demographics of those who choose to access free health care, we accounted for country of origin. The study was also limited by only using PCR test samples to define COVID-19 and influenza admissions and deaths. An alternative would have been to use diagnoses and cause-of-death registrations. However, since none are equally defined (eg, how often the virus is registered as identified as part of the defining ICD-10 diagnosis), complete, or validated for COVID-19 and influenza, such a comparison would risk bias. At least for COVID-19, we know from surveillance data from May, 2022, to March, 2023 that more than 70% of the test-defined COVID-19 hospital admissions were due to (50%) or possibly due to (20%) COVID-19 when evaluated against diagnoses.[41] An advantage of using tests only was that the test guidelines for COVID-19 and influenza in the health-care sector had similar clinical indications in common (ie, symptoms and risk of a severe disease). Of course, initial symptoms indicating the need for a test might also be similar between COVID-19 and influenza (eg, fever, sore throat, muscle pain, and cough). These circumstances could explain why we observed that more than 80% of patients were tested simultaneously (on the same date) for COVID-19 and influenza. Dissimilar test guidelines for COVID-19 and influenza also posed a potential study limitation. For example, in 2022, the guideline outlined decreased but still focused screening for COVID-19 in the health sector, consistent with our observation that more COVID-19 tests than influenza tests were performed in 2022, which, together with the omicron variants' capability of higher infectivity and spread, might bias study findings by adding coincidental COVID-19 admissions in 2022. However, we observed that the weekly test-positive rate in the 2 years was generally higher for COVID-19 than for influenza, supporting that tests were more often indicated on symptoms, and coincidental admissions were therefore less likely to bias the overall conclusion that COVID-19 is a more serious burden than influenza. Nevertheless, we cannot entirely rule out coincidental COVID-19 admissions.

Although beyond the scope of our study, it is important to acknowledge the burden of infections not requiring hospital admission and the burden of post-infection sequelae from COVID-19. The societal burden might include more frequent use of primary care services or consequences of absence from work.[42–44]

In conclusion, during the first 2 years after the COVID-19 pandemic began to subside, COVID-19 still represented a greater disease burden than influenza in Denmark, with more hospital admissions and deaths, and slightly more severe disease, primarily among non-vaccinated people, those with comorbidities, and male patients. These results highlight the need for continued attention, public health efforts, and resources to mitigate the ongoing impact of COVID-19.

Contributors

All authors contributed to study conception and design and interpretation of the data. IBS did the statistical analyses. PB and IBS had access to and verified the underlying data and drafted the manuscript. All authors provided critical revisions and final approval for the decision to submit for publication. PB confirms that all authors have seen and approved the final text.

Declaration of interests

We declare no competing interests.

Data sharing

Aggregated admission and mortality data are available for download from dashboards at Statens Serum Institut (www.ssi.dk). De-identified individual-level data are available for research upon reasonable request to Statens Serum Institut and the Danish Health Data Authority and within the framework of the Danish data protection legislation and any required permission from relevant authorities. Applications should be submitted to Forskerservice (https://sundhedsdatastyrelsen.dk/da/forskerservice) where they will be reviewed on the basis of relevance and scientific merit. Data are available now, with no defined end date.

Acknowledgments

This study was conducted as part of the Danish COVID-19 surveillance with governmental financial support.

References

1 Mølbak K, Widgren K, Jensen KS, et al. Burden of illness of the 2009 pandemic of influenza A (H1N1) in Denmark. *Vaccine* 2011; **29** (suppl 2): B63–69.
2 UN. WHO chief declares end to COVID-19 as a global health emergency. 2023. https://news.un.org/en/story/2023/05/1136367 (accessed Jan 21, 2025).
3 Xie Y, Choi T, Al-Aly Z. Risk of death in patients hospitalized for COVID-19 vs seasonal influenza in fall–winter 2022–2023. *JAMA* 2023; **329:** 1697–99.
4 Xie Y, Choi T, Al-Aly Z. Mortality in patients hospitalized for COVID-19 vs influenza in fall–winter 2023–2024. *JAMA* 2024; **331:** 1963–65.
5 European Centre for Disease Prevention and Control. Facts/factsheet about seasonal influenza. 2024. https://www.ecdc.europa.eu/en/seasonal-influenza/facts/factsheet2024 (accessed Jan 21, 2025).
6 Centers for Disease Control and Prevention. Influenza/about flu/when is flu season. 2024. https://www.cdc.gov/fluview/overview/ (accessed Jan 21, 2025).
7 Pedersen CB. The Danish civil registration system. *Scand J Public Health* 2011; **39** (suppl): 22–25.
8 Grove Krause T, Jakobsen S, Haarh M, Mølbak K. The Danish vaccination register. *Euro Surveill* 2012; **17:** 20155.
9 Schmidt M, Schmidt SA, Sandegaard JL, Ehrenstein V, Pedersen L, Sørensen HT. The Danish National Patient Registry: a review of content, data quality, and research potential. *Clin Epidemiol* 2015; **7:** 449–90.
10 The Danish Health Data Authority. Register of selected chronic diseases and severe mental disorders. 2018. https://www.esundhed.dk/Dokumentation/DocumentationExtended?id=29 (accessed July 5, 2024).
11 The Danish Health Data Authority. Nursing homes and nursing home residents. 2019. https://sundhedsdatastyrelsen.dk/media/16012/Plejehjemsadresser_plejehjemsbeboere.pdf (accessed July 5, 2024).

12 Heidari S, Babor TF, De Castro P, Tort S, Curno M. Sex and gender equity in research: rationale for the SAGER guidelines and recommended use. *Gac Sanit* 2019; **33:** 203–10.

13 Voldstedlund M, Haarh M, Molbak K. The Danish Microbiology Database (MiBa) 2010 to 2013. *Euro Surveill* 2014; **19:** 20667.

14 Schønning K, Dessau RB, Jensen TG, et al. Electronic reporting of diagnostic laboratory test results from all healthcare sectors is a cornerstone of national preparedness and control of COVID-19 in Denmark. *APMIS* 2021; **129:** 438–51.

15 WHO, European Centre for Disease Prevention and Control. Operational considerations for respiratory virus surveillance in Europe. 2022. https://www.ecdc.europa.eu/en/seasonal-influenza/surveillance-and-disease-data/facts-sentinel-surveillance (accessed Jan 21, 2025).

16 Fogh K, Graakjær Larsen T, Martel CJ, et al. Surveillance of SARS-CoV-2 infection based on self-administered swabs, Denmark, May to July 2022: evaluation of a pilot study. *Euro Surveill* 2023; **28:** 2200907.

17 Moustsen-Helms IR, Bager P, Larsen TG, et al. Relative vaccine protection, disease severity, and symptoms associated with the SARS-CoV-2 omicron subvariant BA.2.86 and descendant JN.1 in Denmark: a nationwide observational study. *Lancet Infect Dis* 2024; **24:** 964–73.

18 Statens Serum Institut. Denmark. Dashboard for COVID-19, influenza, and RSV surveillance. 2024. https://experience.arcgis.com/experience/220fef27d07d438889d651cc2e00076c/page/Covid-19-Regionalt/2024 (accessed Jan 21, 2025).

19 Statens Serum Institut. Timeline for COVID-19 in Denmark. 2024. https://www.ssi.dk/-/media/arkiv/subsites/covid19/presse/tidslinje-over-covid-19/covid-19-tidslinje-for-2020-2022-lang-version---version-1---april-2022.pdf2024 (accessed Jan 21, 2025).

20 The Danish Health Authority. Recommendations, (and history of versions of the recommendations), about prevention of respiratory infections including COVID-19 in care facilities. 2023. https://www.sst.dk/da/udgivelser/2023/Vejledning-om-forebyggelse-af-smitte-med-ny-coronavirus-paa-plejehjem-mv-og-i-hjemmeplejen (accessed Dec 13, 2023).

21 The Danish Society for Clinical Microbiology. Guideline for handling of influenza, including diagnostics, antimicrobial treatment and prevention. 2022. https://dskm.dk/guidelines/luftvejsinfektioner/ (accessed Jan 21, 2025).

22 The Danish Health Authority. Guideline, and history of guideline versions, for handling of COVID-19 in the health system. https://www.sst.dk/da/udgivelser/2023/Retningslinjer-for-haandtering-af-covid-19 (accessed Jan 21, 2025)

23 The Danish Health Authority. Udrulning af sæsonvaccinationer. 2020–2024. https://www.sst.dk/da/Fagperson/Forebyggelse-og-tvaergaaende-indsatser/Vaccination/Udrulning-af-saesonvaccinationer (accessed Jan 21, 2025).

24 Statens Serum Institut. COVID-19 vaccine dashboard until 23 March 2023. 2024. https://experience.arcgis.com/experience/9824b03b114244348ef0b10f69f490b4/page/page_3/ (accessed Jan 21, 2025).

25 Danish COVID-19 Genome Consortium. Genomic overview of SARS-CoV-2 in Denmark. 2020–2024. https://www.covid19genomics.dk/statistics (accessed Jan 21, 2025).

26 Chesnaye NC, Stel VS, Tripepi G, et al. An introduction to inverse probability of treatment weighting in observational research. *Clin Kidney J* 2021; **15:** 14–20.

27 Centers for Disease Control and Prevention. The Coronavirus Disease 2019 (COVID-19) Hospitalization Surveillance Network (COVID-NET). 2024. https://www.cdc.gov/covid/php/covid-net/ (accessed Jan 21, 2025).

28 Centers for Disease Control and Prevention. Laboratory-confirmed influenza hospitalizations. 2024. https://gis.cdc.gov/GRASP/Fluview/FluHospRates.html (accessed Jan 21, 2025).

29 Health New Zealand. COVID-19 trends and insights. https://tewhatuora.shinyapps.io/covid19/ (accessed Jan 21, 2025).

30 Health Protection Surveillance Centre. Epidemiology of COVID-19 in Ireland. https://respiratorydisease-hpscireland.hub.arcgis.com/pages/covid-19 (accessed Jan 21, 2025).

31 Centers for Disease Control and Prevention. COVID data tracker. https://covid.cdc.gov/covid-data-tracker/#datatracker-home (accessed Jan 21, 2025).

32 Centers for Disease Control and Prevention. National wastewater surveillance system. National and regional trends 2022–2024. https://www.cdc.gov/nwss/rv/COVID19-nationaltrend.html (accessed Jan 21, 2025).

33 Health Protection Surveillance Centre. Wastewater surveillance reports. https://www.hpsc.ie/a-z/nationalwastewatersurveillanceprogramme/2024wastewatersurveillanceprogrammereports/ (accessed Jan 21, 2025).

34 Institute of Environmental Science and Research. Wastewater dashboard. https://www.esr.cri.nz/ (accessed Jan 21, 2025).

35 Statens Serum Institut. National surveillance of SARS-CoV-2 in wastewater, 2022–2024. 2024. https://en.ssi.dk/surveillance-and-preparedness/surveillance-in-denmark/covid-19/national-surveillance-of-sars-cov-2-in-wastewater (accessed Jan 21, 2025).

36 The Danish Health Authority. Erfaringsopsamling. 2024. https://www.sst.dk/-/media/Nyheder/2024/Vaccination/Erfaringsopsamling.ashx?sc_lang=da&hash=2D310410A769D59018459F3721070192 (accessed Jan 21, 2025).

37 Andersson NW, Thiesson EM, Pihlström N, et al. Comparative effectiveness of monovalent XBB.1.5 containing COVID-19 mRNA vaccines in Denmark, Finland, and Sweden: target trial emulation based on registry data. *BMJ Med* 2024; **3:** e001074.

38 Merad M, Blish CA, Sallusto F, Iwasaki A. The immunology and immunopathology of COVID-19. *Science* 2022; **375:** 1122–27.

39 Piroth L, Cottenet J, Mariet AS, et al. Comparison of the characteristics, morbidity, and mortality of COVID-19 and seasonal influenza: a nationwide, population-based retrospective cohort study. *Lancet Respir Med* 2021; **9:** 251–59.

40 Premraj L, Weaver NA, Ahmad SA, et al. Sex differences in the outcome of critically Ill patients with COVID-19—an international multicenter critical care consortium study. *Heart Lung* 2024; **68:** 373–80.

41 Statens Serum Institut. COVID-19 og andre luftvejsinfektioner. https://files.ssi.dk/covid19/overvagning/rapport/ugentlige-tendenser-covid19-andre-luftvejs-uge13-2023-a4rp (accessed Jan 21, 2025).

42 Løkke FB, Hansen KS, Dalgaard LS, Öbrink-Hansen K, Schiøttz-Christensen B, Leth S. Long-term complications after infection with SARS-CoV-1, influenza and MERS-CoV—lessons to learn in long COVID? *Infect Dis Now* 2023; **53:** 104779.

43 O'Regan E, Svalgaard IB, Sørensen AIV, et al. A hybrid register and questionnaire study of COVID-19 and post-acute sick leave in Denmark. *Nat Commun* 2023; **14:** 6266.

44 Spiliopoulos L, Sørensen AIV, Bager P, et al. Postacute symptoms 4 months after SARS-CoV-2 infection during the omicron period: a nationwide Danish questionnaire study. *Am J Epidemiol* 2024; **193:** 1106–14.