

Effectiveness of post-COVID-19 primary care attendance in improving survival in very old patients with multimorbidity: a territory-wide target trial emulation

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ABSTRACT

Objectives Older individuals with multimorbidity are at an elevated risk of infection and complications from COVID-19. Effectiveness of post-COVID-19 interventions or care models in reducing subsequent adverse outcomes in these individuals have rarely been examined. This study aims to examine the effectiveness of attending general outpatient within 30 days after discharge from COVID-19 on 1-year survival among older adults aged 85 years or above with multimorbidity.

Design Retrospective cohort study emulating a randomised target trial using electronic health records.

Setting We used data from the Hospital Authority and the Department of Health in Hong Kong, which provided comprehensive electronic health records, COVID-19 confirmed case data, population-based vaccination records and other individual characteristics for the study.

Participants Adults aged 85 years or above with multimorbidity who were discharged after hospitalisation for COVID-19 between January 2020 and August 2022.

Interventions Attending a general outpatient within 30 days of last COVID-19 discharge defined the exposure, compared to no outpatient visit.

Main outcome measures Primary outcome was all-cause mortality within one year. Secondary outcomes included mortality from respiratory, cardiovascular and cancer causes.

Results A total of 6183 eligible COVID-19 survivors were included in the analysis. The all-cause mortality rate following COVID-19 hospitalisation was lower in the general outpatient visit group (17.1 deaths per 100 person-year) compared with non-visit group (42.8 deaths per 100 person-year). After adjustment, primary care consultations within 30 days after discharge were associated with a significantly greater 1-year survival (difference in 1-year survival: 11.2%, 95% CI 8.1% to 14.4%). We also observed significantly better survival from respiratory diseases in the general outpatient visit group (difference in 1-year survival: 6.3%, 95% CI 3.5% to 8.9%). In a sensitivity analysis for different grace period lengths,

KEY POINTS

- ⇒ Question: Does visiting a general outpatient clinic within 30 days after discharge from last hospitalisation for COVID-19 improve 1-year survival among Chinese older adults aged 85 years or above with multimorbidity?
- ⇒ Finding: using a territory-wide linked healthcare database in Hong Kong and target trial emulation approach, we found that general outpatient attendance within 30 days after discharge was associated with an improved 1-year survival compared to no attendance within 30 days.
- ⇒ Meaning: timely primary care follow-up after COVID-19 hospitalisation through general outpatient attendance can effectively reduce mortality for high-risk older adults with multimorbidity. Healthcare systems should implement mechanisms to ensure and facilitate primary care follow-up for this population.

we found that the earlier participants had a general outpatient visit after COVID-19 discharge, the better the survival.

Conclusions Timely primary care consultations after COVID-19 hospitalisation may improve survival following COVID-19 hospitalisation among older adults aged 85 or above with multimorbidity. Expanding primary care services and implementing follow-up mechanisms are crucial to support this vulnerable population's recovery and well-being.

INTRODUCTION

Accumulated epidemiologic evidence consistently suggests that older people living with multimorbidity, referred to as the co-occurrence of two or more chronic conditions, are disproportionately burdened by the COVID-19 pandemic.^{1 2} It is shown that

multimorbidity is associated with an elevated risk of infection as well as serious complications once infected.^{3,4} Since the WHO declared the end to the global public health emergency alert in early May 2023,⁵ many countries have essentially entered the exit phase of the pandemic.^{6,7} The focus of clinical research is now shifted to the epidemiology and management of the clinical sequelae of COVID-19 as an endemic^{8,9} as well as potential interactions with preexisting chronic conditions.

The pandemic has revealed the heightened vulnerability of patients with multimorbidity, thereby reinforcing the necessity for postinfection care models that can offer comprehensive and coordinated healthcare services. Multimorbidity is predominantly driven by old age¹⁰ and is known to be associated with significantly poorer quality of life¹¹ and greater risk of mortality¹² even in the absence of the pandemic. Post-SARS-CoV-2-infection interventions or care models in reducing subsequent adverse health outcomes in these people have rarely, if at all, been examined. While previous research has suggested that regular and timely primary care consultations may improve a range of outcomes after a severe respiratory infection,¹³ there is no data for such consultations shortly after a hospitalised COVID-19 episode. Of particular concern, the oldest-olds, typically aged 85 or older, living with multimorbidity are at much heightened risk of mortality following an acute respiratory infection.³ In the fifth wave of COVID-19 pandemics in Hong Kong from 1 December 2021 to 29 January 2023, the case fatality rate (CFR) among people over 80 years old was the highest among all age groups at 7.03%, while the CFR for those who had never been vaccinated against COVID-19 was 14.56%.¹⁴

In a real-world clinical setting, it is inappropriate to conduct a randomised controlled trial (RCT) to experiment with the potential effect of primary care consultations following a COVID-19 episode due to obvious ethical concerns. To address this, target trial emulation has emerged as a powerful methodology to mimic the design and analysis of a hypothetical RCT to estimate causal effects when an actual trial is infeasible.¹⁵ In this study, we aimed to conduct a target trial emulation study with a territory-wide public healthcare database in Hong Kong to examine the effectiveness of such consultations using longitudinal observational data. We hypothesised that a primary care consultation shortly after a COVID-19 episode would reduce the risk of mortality in Chinese older people aged 85 years or above.

METHODS

We followed the framework proposed by Hernan and Robins¹⁶ and Maringe *et al*¹⁷ (the latter being one of the authors of this work) to emulate a target trial on the effectiveness of attending general out-patient clinics (GOPC) on the outcome of all-cause mortality after discharge from last COVID-19 episode. The key components of

the target trial and emulated trial are specified in online supplemental eTable 1.

Data source

The Hospital Authority (HA), the sole provider of public inpatient services and a major provider of outpatient services in Hong Kong, together with the Department of Health (DH), which oversees public health affairs in the city, provided all the data for this study. HA manages all publicly funded hospital and the majority of public outpatient clinics [including its specialist out-patient clinics (SOPCs) services and GOPCs]. GOPCs are responsible for delivering high-quality primary care services that are accessible to financially vulnerable individuals, the elderly and patients with chronic illnesses.¹⁸ These services include general medical consultations, chronic disease management, preventive care, health education and follow-up care for patients discharged from hospitals. There are a total of 77 general outpatient clinics located throughout the territories of Hong Kong, 23 of which also provide services during evenings and holidays.¹⁹ Given the small total area of Hong Kong where 7.5 million people reside, the GOPCs serve as a highly accessible first contact point with the healthcare system for patients. Electronic health records maintained by the HA were linked anonymously with the COVID-19 confirmed case database and population-based vaccination records kept by the DH, which is responsible for the mass roll-out of the vaccines and enforcing the mandatory self-reporting of SARS-CoV-2-positive test results by Hong Kong residents. The linked database covers a wide variety of longitudinal individual characteristics including chronic conditions, medication history, healthcare utilisation, COVID-19 history, vaccination records, etc. The database covers more than 80% of all health service users in Hong Kong before the pandemic and essentially covers all residents in Hong Kong for major acute care services. The database's detailed and longitudinal nature allows for thorough tracking of patient health trajectories and outcomes, thereby supporting the validity of our study. Numerous pharmacovigilance studies, including those focused on multimorbidity, have been conducted using this linked database.^{20,21}

The target trial

A trial investigating the effect of primary care consultant on post-COVID-19-infection mortality among older patients aged 85 or above with multimorbidity served as the target trial of this emulation study. The trial would enrol participants who were 85 years or older on the discharge date of hospitalisation for the last COVID-19 episode before 1 February 2023. Participants would be excluded if they were diagnosed with only one chronic disease before discharge.

The trial would have started on 1 January 2020 and ended on 1 February 2023. Eligible participants were randomly assigned to one of the two designed arms on their date of discharge. Within 30 days after discharge,

treatment arm attended GOPC and control arm did not attend GOPC. Each participant was followed until death, loss to follow-up or end of the study (1 February 2023).

The primary outcome was all-cause mortality and the secondary outcomes included respiratory, cardiovascular and cancer mortality.

The emulated trial

The emulated trial was designed largely in line with the target trial above. Specifically, eligible participants had a date of last discharge between 1 January 2020 and 1 August 2022, allowing a minimum potential observation period of 6 months until the end of data availability (1 February 2023). Using the diagnosis records from public health services, we identified participants with multimorbidity, co-occurrence of two or more chronic conditions, utilising a widely used list of 30 chronic conditions with the corresponding International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) codes provided in online supplemental eTable 2. Those who had only one or none of the listed chronic conditions before the discharge from last COVID-19 episode were excluded.

The date of discharge from the last hospitalisation for COVID-19 was defined as the index date, that is, time zero to mimic the time of randomisation. Considering the actual practice of discharged patients not immediately sent to GOPC, we set a grace period of 30 days to initiate 'treatment'. Because of the uncertainty of treatment assignment at time zero in the emulated trial with a grace period,²² we cloned every eligible participant and assigned one clone to each treatment strategy. Individuals were assigned as GOPC group if they attended GOPC within the grace period we defined. The control group did not attend GOPC within the grace period or only attend GOPC after the grace period. When the subject's actual treatment violated the assigned treatment strategy, the duplicate would be artificially censored as presented in online supplemental eFigure 1.

After treatment assignment, participants were observed until the occurrence of death or the end of data availability (1 February 2023). The primary outcome was all-cause death. Secondary outcomes included death from respiratory diseases (ICD-10-CM: J00-J99), cardiovascular diseases (ICD-10-CM: I00-I99) and cancer (ICD-10-CM: C00-C97). The causal contrast of interest in this study was per-protocol effect, which was the comparative effect of following the treatment strategies specified in the study protocol. In the emulated trial using observational data, participants who violated the treatment assignment were censored at their time of deviation.

Statistical analysis

To adjust the potential bias from artificial censoring, we used a Cox regression model to predict the probability of being uncensored at each time point of event occurrence and assigned the inverse of these probability as weights. Baseline confounders include demographic

characteristics, number of COVID-19 vaccines, inpatient information, baseline chronic conditions and medication history. We calculated the total number of doses of COVID-19 vaccine administered to participants before their last hospitalisation from the vaccination data provided by the DH. Inpatient information included the duration of the last COVID-19-episode hospitalisation and whether the patient was admitted to intensive care unit (ICU). To identify the medication history of patients within 90 days prior to the index date, we used a list of British National Formulary codes to categorise the medicines, as shown in online supplemental eTable 3. Particularly, we identified the use of three designated COVID-19 antivirals during the last COVID-19 episode, nirmatrelvir/ritonavir, remdesivir and molnupiravir, respectively. Since we did not specify any time-varying variable in our study, baseline covariates were entered in the weighting model to eliminate the imbalance.

After adjusting for immortal time bias and confounding bias using clone-censor-weight approach, we used weighted Kaplan-Meier estimator to obtain the survival curves of each group. Since the all-cause mortality is substantial after discharge from respiratory infection, we adopted 1-year survival as our estimand.²³ Accounting for the inflation of the sample size and the uncertainty in weight estimation, the 95% CI for difference in 1-year survival was obtained using non-parametric bootstrap with 1000 replicates.

We conducted a series of sensitivity analyses to test the robustness of the results. First, we varied the length of the grace period between 10 days and 120 days. Second, we adopted pooled logistic regression instead of Cox regression model after clone-censor-weight to generate the OR.²⁴ Third, we identified regular outpatient attendees before COVID-19 pandemic by visiting GOPC three or more times in 2019 to see if the results were robust. Last, we used a leave-one-out approach for multimorbidity operationalisation to examine the robustness of results across different multimorbidity compositions.

All analyses were carried out using SAS V.9.4 and R software V.4.0.5. A two-sided p value <0.05 was taken as indicative of statistical significance.

RESULTS

Subject characteristics

We identified a total of 6183 COVID-19 survivors who met the study eligibility criteria. The flowchart of cohort selection is shown in figure 1. There were 488 subjects that attended GOPC within 30 days after discharge from the last COVID-19 episode while there were 5695 subjects who did not attend GOPC within 30 days after discharge from the last COVID-19 episode. Table 1 presents the baseline characteristics of the subjects. The mean age of GOPC group was 89.72 (SD: 3.94) and that of non-GOPC group was 90.58 (SD: 4.18). There were 270 (55.33%) female subjects among GOPC group and 3331 (58.49%) of that among non-GOPC group. Notably, more than half

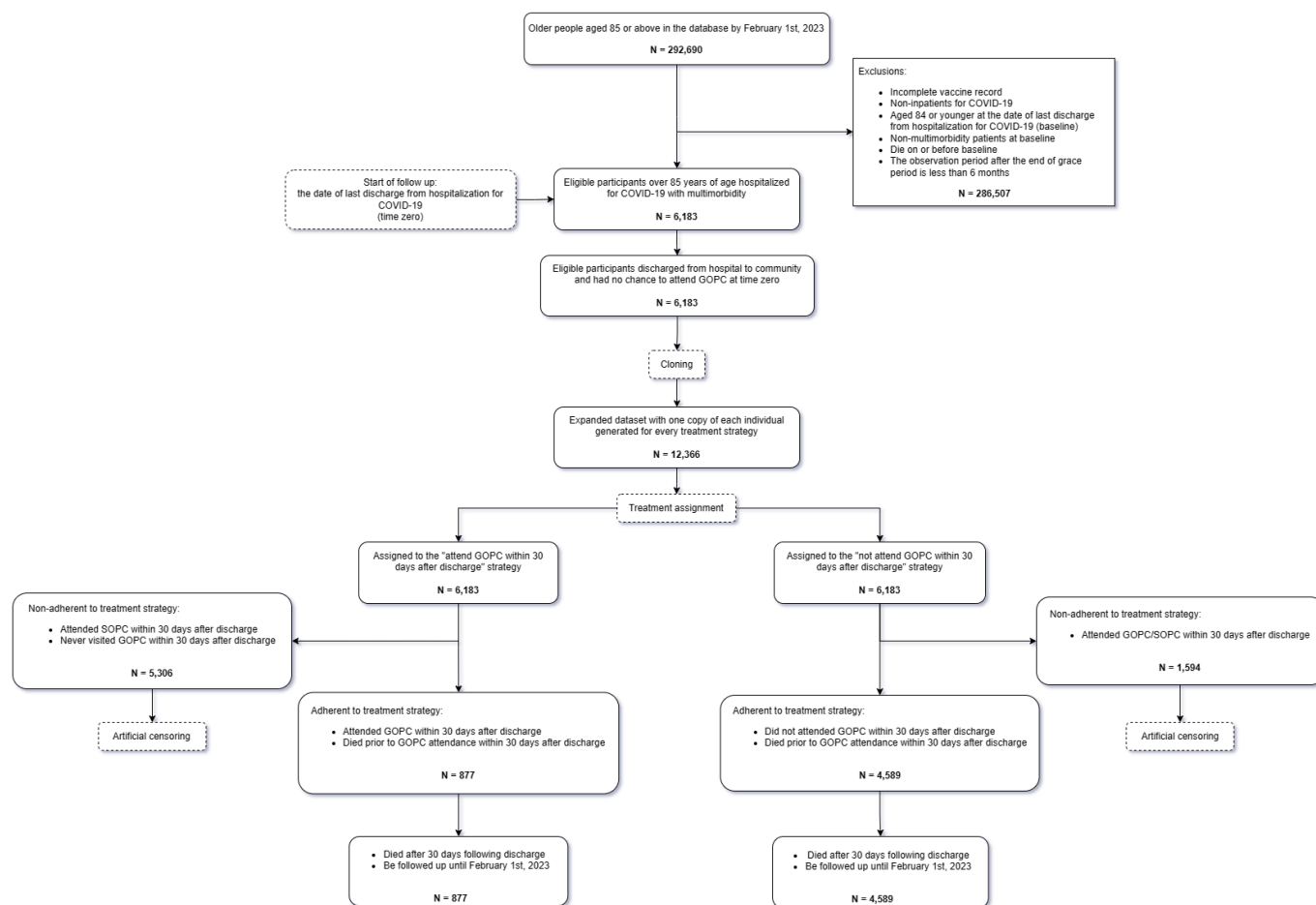


Figure 1 Cohort selection flowchart. GOPC, general out-patient clinics; SOPC, specialist out-patient clinics.

of the subjects in both groups had never received the COVID-19 vaccines (GOPC group: 51.02%, non-GOPC group: 55.66%). The most common chronic conditions in GOPC group were hypertension (93.65%), diabetes (55.53%), severe constipation (23.77%) and chronic kidney disease (23.16%), while the chronic conditions with a higher proportion within non-GOPC group were hypertension (83.14%), diabetes (42.56%), chronic kidney disease (25.72%) and chronic pain (24.83%). As for specific COVID-19 antiviral medicines during their last COVID-19 episode, only a small proportion of subjects were treated with Molnupiravir (GOPC group: 16.80%, non-GOPC group: 16.87%), Remdesivir (GOPC group: 17.42%, non-GOPC group: 11.61%) and Nirmatrelvir/ritonavir (GOPC group: 7.79%, non-GOPC group: 5.25%). As shown in online supplemental eFigure 2, the characteristics of the two groups were fairly balanced after cloning and weighting, as they showed a slight difference greater than 0.15.

Main findings

During the follow-up, there were 66 deaths in the GOPC group while there were 1684 deaths in the non-GOPC group in the first year after the last hospitalisation for COVID-19. The all-cause mortality rate 1 year following

COVID-19 hospitalisation were 17.1 and 42.8 deaths per 100 person-years for GOPC group and non-GOPC group. In the original cohort before cloning and confounding adjustment, the 1-year survival after the last discharge from COVID-19 was 86.0% (95% CI 82.9% to 89.2%) and 68.5% (95% CI 67.0% to 69.9%), respectively, for GOPC group and non-GOPC group. The survival curve showed obvious differences of survival between the two groups in both original cohort and weighted emulated cohort in figure 2.

Figure 3 shows the results of the main analysis. After clone-censor-weight adjustment, subjects who attended GOPC within 30 days after discharge from last COVID-19 episode were shown to have a significantly higher 1-year survival than those who did not (difference in 1-year survival: 11.2%, 95% CI 8.1% to 14.4%). The results of the adjusted subgroup analyses were consistent with the main results. The significant higher 1-year survival was observed for both sexes, with women showing a slightly higher improvement (difference in 1-year survival: 13.3%, 95% CI 9.4% to 17.2%) compared with men (difference in 1-year survival: 9.6%, 95% CI 5.0% to 14.7%). Besides, subjects with a higher number of baseline chronic diseases had a greater survival benefit from the GOPC attendance,

Table 1 Subject characteristics

	Attend GOPC within 30 days	Not attend GOPC within 30 days	SMD*
Participants, N	488	5695	
Age, mean (SD)	89.72 (3.94)	90.58 (4.18)	0.21
Sex, n (%)			
Female	270 (55.33)	3331 (58.49)	0.03
Male	218 (44.67)	2364 (41.51)	0.03
COVID-19 vaccine doses, n (%)			
0	249 (51.02)	3170 (55.66)	0.05
1	130 (26.64)	1437 (25.23)	0.01
2	100 (20.49)	972 (17.07)	0.03
3	9 (1.84)	116 (2.04)	<0.01
Hospitalisation duration for last COVID-19 episode, mean (SD)	15.48 (14.43)	17.69 (15.81)	0.15
ICU admission for last COVID-19 episode, n (%)	5 (1.02)	26 (0.46)	0.01
Baseline chronic disease, n (%)			
Hypertension	457 (93.65)	4735 (83.14)	0.11
Diabetes	271 (55.53)	2424 (42.56)	0.13
Chronic kidney disease	113 (23.16)	1465 (25.72)	0.03
Chronic pain	112 (22.95)	1414 (24.83)	0.02
Chronic heart failure	83 (17.01)	1338 (23.49)	0.06
Atrial fibrillation	81 (16.60)	1323 (23.23)	0.07
Severe constipation	116 (23.77)	1281 (22.49)	0.01
Stroke or transient ischaemic attack	94 (19.26)	1089 (19.12)	<0.01
Dementia	51 (10.45)	983 (17.26)	0.07
Chronic pulmonary disease	58 (11.89)	914 (16.05)	0.04
Myocardial infarction	19 (3.89)	527 (9.25)	0.05
Depression	14 (2.87)	291 (5.11)	0.02
Hypothyroidism	20 (4.10)	253 (4.44)	<0.01
Asthma	25 (5.12)	246 (4.32)	0.01
Cancer, non-metastatic (breast, cervical, colorectal, lung, prostate)	24 (4.92)	232 (4.07)	0.01
Peptic ulcer disease	22 (4.51)	221 (3.88)	0.01
Parkinson's disease	7 (1.43)	177 (3.11)	0.02
Epilepsy	4 (0.82)	101 (1.77)	0.01
Cancer, metastatic	7 (1.43)	97 (1.70)	<0.01
Cirrhosis	4 (0.82)	53 (0.93)	<0.01
Rheumatoid arthritis	4 (0.82)	53 (0.93)	<0.01
Peripheral vascular disease	5 (1.02)	49 (0.86)	<0.01
Schizophrenia	1 (0.20)	52 (0.91)	0.01
Chronic viral hepatitis B	4 (0.82)	36 (0.63)	<0.01
Cancer, lymphoma	3 (0.61)	36 (0.63)	<0.01
Psoriasis	5 (1.02)	25 (0.44)	0.01
Alcohol misuse	2 (0.41)	22 (0.39)	<0.01
Irritable bowel syndrome	2 (0.41)	7 (0.12)	<0.01
Inflammatory bowel disease	0	3 (0.05)	0.05
Multiple sclerosis	0	2 (0.04)	0.04

Continued

Table 1 Continued

	Attend GOPC within 30 days	Not attend GOPC within 30 days	SMD*
Specific COVID-19 antiviral drugs, n (%)			
Molnupiravir	82 (16.80)	961 (16.87)	<0.01
Remdesivir	85 (17.42)	661 (11.61)	0.06
Nirmatrelvir/ritonavir	38 (7.79)	299 (5.25)	0.03
Medication history, n (%)			
Antibacterial drugs	385 (78.89)	5021 (88.17)	0.09
Calcium channel blockers	360 (73.77)	3688 (64.76)	0.09
Lipid-lowering agents	298 (61.07)	3004 (52.75)	0.08
Steroid	203 (41.60)	2744 (48.18)	0.07
Antiplatelets	237 (48.57)	2634 (46.25)	0.02
Renin-angiotensin system agents	237 (48.57)	2608 (45.79)	0.03
Antiviral drugs	249 (51.02)	2314 (40.63)	0.10
Diuretics	138 (28.28)	1979 (34.75)	0.06
Beta-blockers	157 (32.17)	1875 (32.92)	0.01
Antidiabetic drugs	166 (34.02)	1533 (26.92)	0.07
Insulins	100 (20.49)	1124 (19.74)	0.01
Nitrates	73 (14.96)	1017 (17.86)	0.03
Antidepressants	41 (8.40)	860 (15.10)	0.07
Oral anticoagulants	36 (7.38)	779 (13.68)	0.06
Immunosuppressants	31 (6.35)	298 (5.23)	0.01
Antiarrhythmic drugs	17 (3.48)	251 (4.41)	0.01

*For categorical variables, we calculated the raw difference between proportion.
GOPC, general out-patient clinics; ICU, intensive care unit; SMD, standard mean difference.

with those having four or more chronic conditions showing a significant increase in 1-year survival (difference in 1-year survival: 16.4%, 95% CI 10.4% to 22.7%). Notably, for subjects in the 95+ age group, post-COVID-19 GOPC visit improved the survival in 1 year by 21.8%, compared with the non-GOPC group (95% CI 13.9% to 29.6%). For older adults with multimorbidity who were not fully vaccinated, the 1-year survival was significantly increased by GOPC visit within 30 days after survival from acute COVID-19 (difference in 1-year survival: 13.5%, 95% CI 9.8% to 17.1%).

Results of secondary outcomes are shown in online supplemental eFigure 3. In addition to all-cause mortality, we also observed a significant increase in the 1-year survival from respiratory mortality in the GOPC group (difference in 1-year survival: 6.3%, 95% CI: 3.5% to 8.9%). However, there was no significant difference between the two groups in the two outcomes of cardiovascular death (difference in 1-year survival: 0.6%, 95% CI -0.9% to 2%) and cancer death (difference in 1-year survival: 1.1%, 95% CI -0.3% to 2.6%).

Sensitivity analyses results

First, we analysed the effect of different grace period durations on mortality, as presented in figure 4. The results showed that when COVID-19 older survivors with

multimorbidity visited GOPCs within 20–120 days after hospitalisation, there was a significant improvement of 9.0% or above in 1-year survival, suggesting that our findings were consistent across a range of reasonable follow-up windows. From this analysis, we observed that the earlier the GOPC attendance within 20–60 days after the COVID-19 discharge, the more likely the older people would survive in 1 year.

Second, no notable deviations from the main findings were observed in the sensitivity analyses using pooled logistics regression to calculate OR. Older people of the GOPC group were shown to have a significantly lower mortality than those of non-GOPC group (OR: 0.65, 95% CI 0.55 to 0.73). No significant difference of cardiovascular and cancer death was estimated between the GOPC group and non-GOPC group. These results supported the robustness of our findings across different statistical methods for estimating survival rates.

Third, there are a higher survival in 1 year after discharge in GOPC group among pre-COVID-19 regular GOPC attendees (difference in 1-year survival: 11.2%, 95% CI 7.9% to 14.7%), as presented in online supplemental eFigure 4.

Finally, as shown in table 2, the results of sensitivity analyses by leave-one-out approach indicated the main

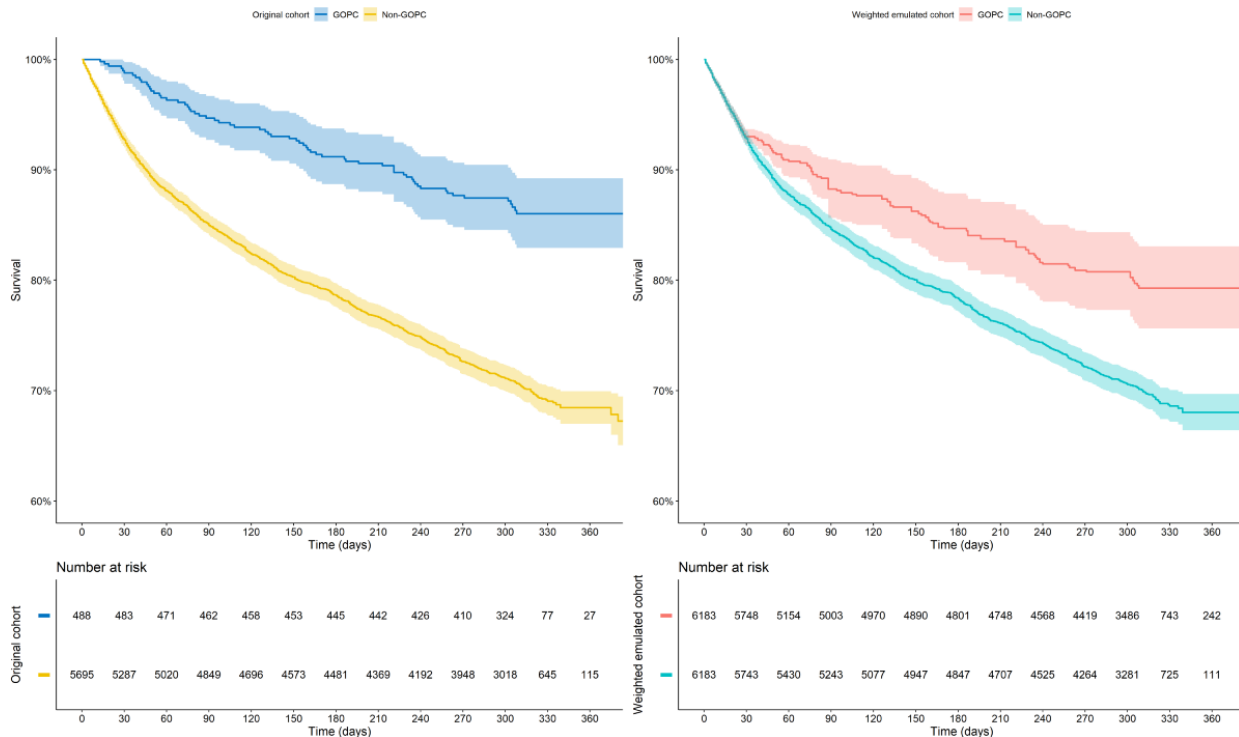
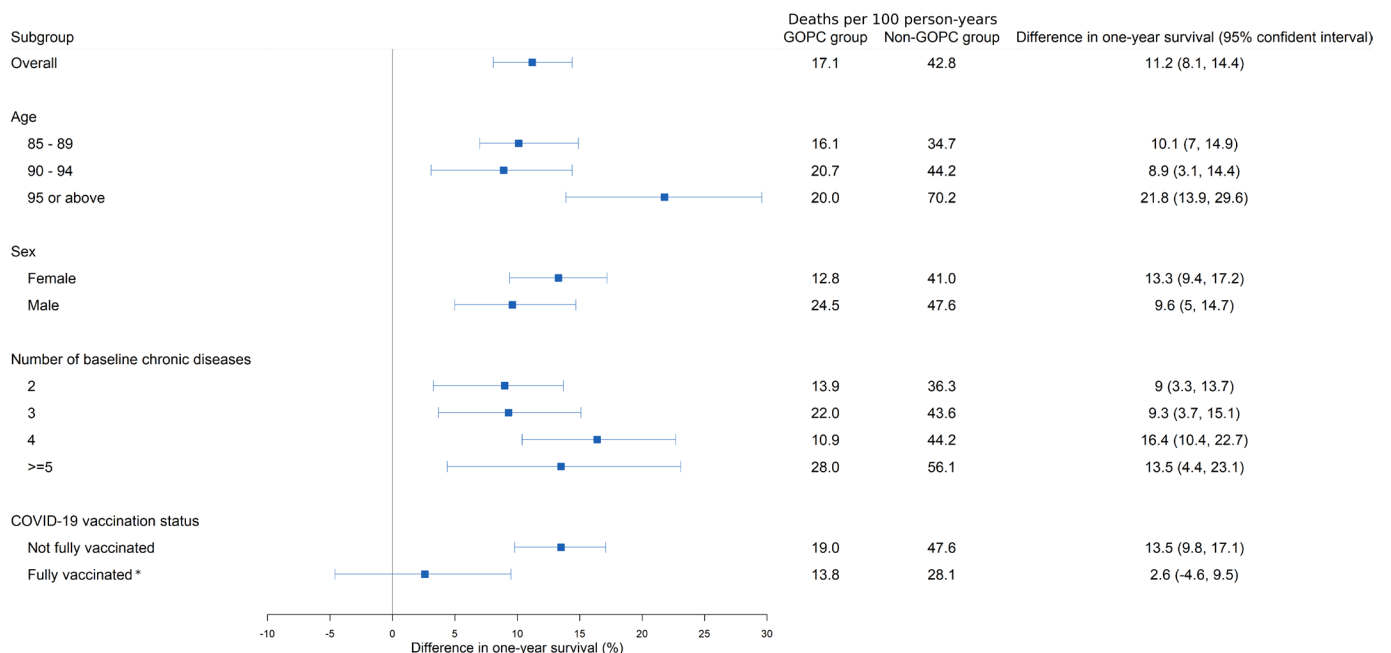


Figure 2 Comparison of 1 year survival curve between the original cohort and the weighted emulated cohort. GOPC, general out-patient clinics.

findings were consistent across different operationalisations of multimorbidity, which demonstrated that our results were not dependent on any single chronic disease and different definition of multimorbidity.

DISCUSSION

Using the target trial emulation framework, we observed that attending GOPC within 30 days after discharge from a COVID-19 episode is associated with a better survival in 1 year among older adults with multimorbidity. Moreover, the results of our sensitivity analysis demonstrate that the sooner the visit to the GOPC within 20–60 days after discharge, the more likely the patient survives within the



*Being fully vaccinated for COVID-19 entails the receipt of the recommended number of doses, typically two or more, of COVID-19 vaccines.

Figure 3 Forest plot of main analysis and subgroup analysis. GOPC, general out-patient clinics.

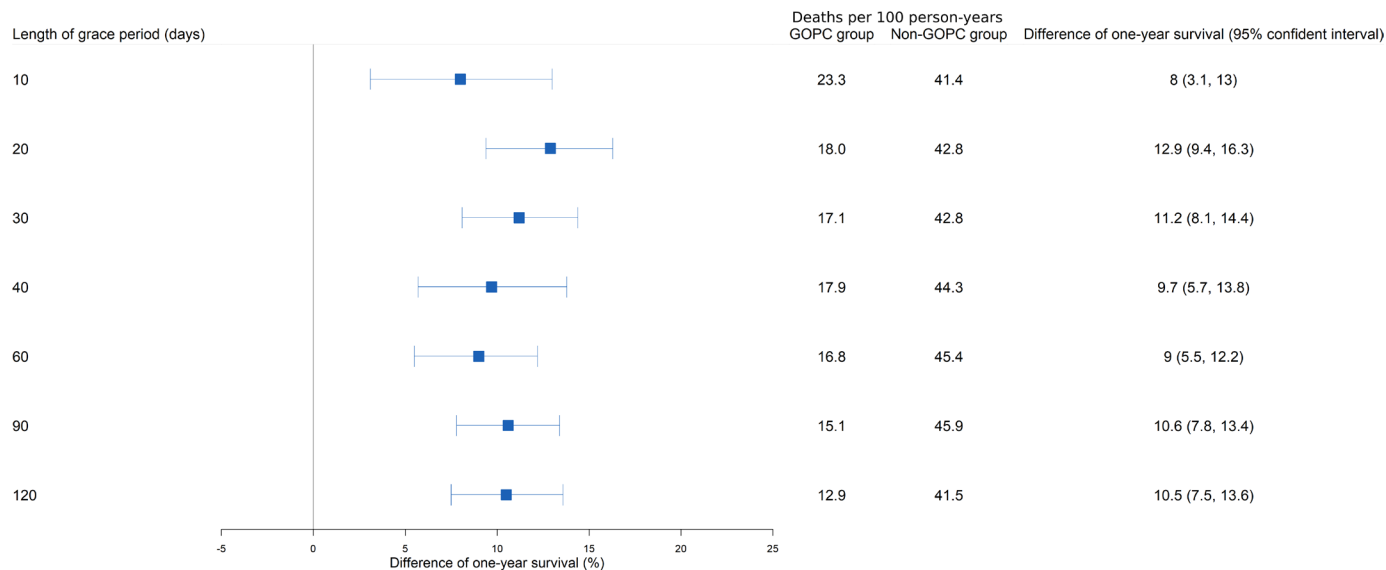


Figure 4 Differences in 1-year survival for grace period from 10 to 120 days. GOPC, general out-patient clinics.

observation period. This range of grace period was identified as optimal because it balanced the need for timely follow-up with the practical considerations of scheduling and patient recovery.^{25 26} The findings are robust across various subgroups and different operationalisations of multimorbidity. Subgroup analysis showed that the benefits of timely follow-up care were widely applicable to patients with different characteristics, especially high-risk groups with characteristics such as having four or more baseline chronic diseases, being over 95 years old or not fully vaccinated. For regular GOPC attendees before the pandemics, resuming to visit GOPC for health management shortly after discharge from the COVID-19 hospitalisation significantly improves the survival in 1 year. Our findings provide novel real-world evidence that a primary care consultation shortly after a COVID-19 episode might increase the survival in Chinese older people aged 85 years or above.

The majority of preceding studies have primarily focused on investigating the effect of specialised rehabilitation interventions of particular post-COVID-19 symptoms on COVID-19 patients.²⁷ For example, Lesley *et al* conducted a literature review indicating that pulmonary rehabilitation intervention can alleviate post-COVID-19 symptoms among elder people over 60 years old.²⁸ Most of these studies are case reports or clinical randomised trials with a limited sample size of less than 100 participants. Furthermore, the outcomes they explored were mainly the relief of post-COVID-19 symptoms, and there was a lack of observation of long-term, more severe outcomes. Additionally, previous investigations have predominantly concentrated on assessing the effectiveness of specific rehabilitation interventions, most of which are not commonly practised in primary care settings. Our study, in contrast, is the first territory-wide evaluation of real-world primary care on severe outcome, that is, mortality, among older people who are most at risk after discharge from COVID-19. Adapting the target trial emulation

design, we have mitigated the issue of immortal time bias that frequently arises in this type of real-world research and have accounted for a wide range of covariates, considering the multimorbidity of the elderly population.

In spite of the clear strengths of this study, there are several limitations to note while interpreting the results. First, indication bias has been reduced using the clone-censor-weight approach but has not been entirely eliminated. There is a possibility that individuals who were able to access GOPC services were inherently characterised by a better overall health status and a better health awareness. However, our sensitivity analysis, which focused exclusively on individual who had records of regular GOPC visits before COVID-19 pandemic, yielded highly comparable results. Second, the presence of unobserved confounders poses another limitation. Factors such as disease severity, lifestyle choices, disability status, socioeconomic circumstances and the accessibility of care in different locations may affect the outcomes. Also, it is worth mentioning that while those who are older and more multimorbid prefer to visit the public sector for primary care,²⁹ the attendance of patients in the private sector could introduce confounding factors that were not accounted for in this study. Our study population predominantly represents older adults using the Hong Kong public healthcare system, which acts as a safety net for uninsured or financially disadvantaged individuals. Despite this, many people with chronic conditions stay in the public system due to its affordability and high-quality services.³⁰ Thus, our cohort is socioeconomically diverse and representative of the general older population in Hong Kong. Moreover, while our study predominantly focused on a Chinese population, the principles of primary care management and the benefits of timely follow-up visits are universally applicable. However, healthcare systems, cultural contexts and patient behaviours vary significantly across different regions. For example, the centralised and publicly funded healthcare system in

Table 2 Difference in 1-year survival between GOPC group and non-GOPC group in the sensitivity analysis using leave-one-out method

Chronic disease left out	Difference in 1-year survival (%)	95% CI
Hypertension	11.7	(7.8 to 15.7)
Diabetes	11.8	(8.1 to 15.1)
Chronic kidney disease	11.1	(7.6 to 14.3)
Chronic pain	11.3	(7.9 to 14.7)
Chronic heart failure	11.1	(7.8 to 14.4)
Atrial fibrillation	11.1	(7.6 to 14.5)
Severe constipation	11.3	(7.7 to 14.6)
Stroke or transient ischaemic attack	11.1	(7.6 to 14.5)
Dementia	11.5	(8.1 to 14.5)
Chronic pulmonary disease	11.2	(7.6 to 14.8)
Myocardial infarction	11.0	(7.4 to 14.4)
Depression	11.3	(7.9 to 14.6)
Hypothyroidism	11.1	(7.6 to 14.4)
Asthma	11.3	(7.8 to 14.6)
Cancer, non-metastatic (breast, cervical, colorectal, lung, prostate)	11.5	(8.0 to 14.6)
Peptic ulcer disease	11.4	(7.9 to 14.8)
Parkinson's disease	11.1	(7.7 to 14.3)
Epilepsy	11.4	(8.2 to 14.5)
Cancer, metastatic	11.3	(7.7 to 14.7)
Cirrhosis	11.2	(7.9 to 14.6)
Rheumatoid arthritis	11.3	(7.8 to 14.6)
Peripheral vascular disease	11.2	(7.6 to 14.3)
Schizophrenia	11.3	(7.9 to 14.5)
Chronic viral hepatitis B	11.2	(7.8 to 14.4)
Cancer, lymphoma	11.2	(7.9 to 14.3)
Psoriasis	11.3	(7.8 to 14.6)
Alcohol misuse	11.3	(7.8 to 14.5)
Irritable bowel syndrome	11.2	(8.1 to 14.4)
Inflammatory bowel disease	11.2	(8.1 to 14.4)
Multiple sclerosis	11.2	(7.7 to 14.7)

GOPC, general out-patient clinics.

Hong Kong ensures relatively uniform access to primary care services like GOPCs. In contrast, countries with less integrated healthcare systems might experience different outcomes due to disparities in access to care.³¹ Therefore, caution should be exercised when generalising the results to other populations. To enhance the external validity of the findings, it is necessary to conduct further replications of similar analyses in other populations and settings.

Consistent with previous research, we observed a significant association between receiving follow-up care at the primary care level shortly after respiratory infection hospitalisation and improved health outcomes.³² This association can plausibly be attributed to several important pathways. First, timely primary care follow-up facilitates the monitoring and management of symptoms after

respiratory infection hospitalisation, leading to symptoms alleviation and reducing the risk of further development of complications.³³ Second, early identification of potential problems allows healthcare providers to address any emerging conditions promptly, preventing serious adverse events and promoting optimal recovery.^{34 35} Third, according to the National Institute for Health and Care Excellence (NICE) guideline, general practice assesses patients' baseline multimorbidity during their first follow-up visit and then develops patient-centred, multidisciplinary rehabilitation support.³⁶ For example, respiratory rehabilitation therapy is recommended for patients with previous neurological and muscular comorbidity.³⁷ Finally, the enhancement of self-management specific to the current diseases or symptoms through

primary care follow-up empowers patients to actively participate in their own healthcare and achieve improved outcomes.^{38 39}

According to our findings, the current evidence is in favour of recommendations that healthcare systems implement timely primary care follow-up mechanisms specifically for older individuals following a COVID-19 hospitalisation. This targeted approach aims to reduce the risk of death in this most vulnerable population. One potential strategy is to develop protocols for healthcare providers involved in the care of patients with COVID-19 to ensure that primary care services/follow-up care is provided within a specified time interval after discharge. By prioritising and facilitating primary care follow-up, healthcare systems can effectively support the recovery and well-being of older adults with multimorbidity, and likely extend the life expectancy despite having experienced a severe episode of COVID-19.

Additionally, it is crucial to extend primary care services to support older people in the community as far as possible. Expanding primary care in community settings allows for a patient-centred approach to healthcare delivery. For example, implementing various forms of home care to ensure accessibility and convenience of older patients,⁴⁰ which can enhance the continuity of healthcare and facilitate early intervention should any health problem arise.

In conclusion, our study demonstrated that receiving follow-up care at the primary care level shortly after COVID-19 hospitalisation significantly improve survival and achieve better health outcome. Future research should focus on assessing the effectiveness of expanding the primary care services to support community-based older populations.

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REFERENCES

- 1 Richardson SJ, Carroll CB, Close J, *et al.* Research with older people in a world with COVID-19: identification of current and future priorities, challenges and opportunities. *Age Ageing* 2020;49:901–6.
- 2 Wong SYS, Zhang D, Sit RWS, *et al.* Impact of COVID-19 on loneliness, mental health, and health service utilisation: a prospective cohort study of older adults with multimorbidity in primary care. *Br J Gen Pract* 2020;70:e817–24.
- 3 Russell CD, Lone NI, Baillie JK. Comorbidities, multimorbidity and COVID-19. *Nat Med* 2023;29:334–43.
- 4 Sompawong AW, Harun H, Mimika RA, *et al.* Neurological manifestations of COVID-19 in Indonesia: assessment of the role of sex and age. *Narra J* 2023;3:e277.
- 5 Lenharo M. WHO declares end to COVID-19's emergency phase. *Nature* 2023;882.
- 6 Associated Press. Spain calls an end to COVID-19 health crisis and obligatory use of masks in hospitals, pharmacies. 2023. Available: <https://www.usnews.com/news/health-news/articles/2023-07-04/spain-calls-an-end-to-covid-19-health-crisis-and-obligatory-use-of-masks-in-hospitals-pharmacies> [Accessed 18 Jul 2023].
- 7 Shingler B, Miller A. What the end of the COVID emergency means for Canada. CBCnews; 2023. Available: <https://www.cbc.ca/news/health/canada-who-pandemic-no-longer-emergency-1.6833775> [Accessed 18 Jul 2023].
- 8 Zeng N, Zhao Y-M, Yan W, *et al.* A systematic review and meta-analysis of long term physical and mental sequelae of COVID-19 pandemic: call for research priority and action. *Mol Psychiatry* 2023;28:423–33.
- 9 The Lancet Regional Health – Europe. Long COVID: an opportunity to focus on post-acute infection syndromes. *Lancet Reg Health Eur* 2022;22:100540.
- 10 Barnett K, Mercer SW, Norbury M, *et al.* Epidemiology of multimorbidity and implications for health care, research, and medical education: a cross-sectional study. *Lancet* 2012;380:37–43.
- 11 Makovski TT, Schmitz S, Zeegers MP, *et al.* Multimorbidity and quality of life: systematic literature review and meta-analysis. *Ageing Res Rev* 2019;53:100903.
- 12 Nunes BP, Flores TR, Mielke GI, *et al.* Multimorbidity and mortality in older adults: a systematic review and meta-analysis. *Arch Gerontol Geriatr* 2016;67:130–8.
- 13 Smith SM, Wallace E, O'Dowd T, *et al.* Interventions for improving outcomes in patients with multimorbidity in primary care and community settings. *Cochrane Database Syst Rev* 2021;1:CD006560.
- 14 Covid-19 thematic Website, together, we fight the virus, Archive of Statistics on provisional analysis on reported death cases. COVID-19 Thematic Website - Together, We Fight the Virus; 2023. Available: https://www.coronavirus.gov.hk/eng/death_analysis.html [Accessed 21 Sep 2023].
- 15 Hernán MA, Wang W, Leaf DE. Target trial emulation: a framework for causal inference from observational data. *JAMA* 2022;328:2446–7.
- 16 Hernán MA, Robins JM. Using big data to emulate a target trial when a randomized trial is not available. *Am J Epidemiol* 2016;183:758–64.
- 17 Maringe C, Benitez Majano S, Exarchakou A, *et al.* Reflection on modern methods: trial emulation in the presence of immortal-time bias. assessing the benefit of major surgery for elderly lung cancer patients using observational data. *Int J Epidemiol* 2020;49:1719–29.
- 18 Wong SYS, Kung K, Griffiths SM, *et al.* Comparison of primary care experiences among adults in general outpatient clinics and private general practice clinics in Hong Kong. *BMC Public Health* 2010;10:397.
- 19 Introduction of general out-patient clinic services. Hospital authority; 2024. Available: https://www.ha.org.hk/visitor/ha_visitor_index.asp?Content_ID=10052&Lang=ENG&Dimension=100&Parent_ID=10042&Ver=HTML
- 20 Lai FTT, Yan VKC, Ye X, *et al.* Booster vaccination with inactivated whole-virus or mRNA vaccines and COVID-19-related deaths among people with multimorbidity: a cohort study. *CMAJ* 2023;195:E143–52.
- 21 Lai FTT, Huang L, Chui CSL, *et al.* Multimorbidity and adverse events of special interest associated with COVID-19 vaccines in Hong Kong. *Nat Commun* 2022;13:411.
- 22 Petito LC, Garcia-Albéniz X, Logan RW, *et al.* Estimates of overall survival in patients with cancer receiving different treatment regimens: emulating hypothetical target trials in the surveillance, epidemiology, and end results (SEER)–Medicare linked database. *JAMA Netw Open* 2020;3:e200452.
- 23 Averin A, Shaff M, Weycker D, *et al.* Mortality and readmission in the year following hospitalization for pneumonia among US adults. *Respir Med* 2021;185:106476.
- 24 D'Agostino RB, Lee ML, Belanger AJ, *et al.* Relation of pooled logistic regression to time dependent Cox regression analysis: the framingham heart study. *Stat Med* 1990;9:1501–15.
- 25 Venturelli S, Benatti SV, Casati M, *et al.* Surviving COVID-19 in Bergamo province: a post-acute outpatient re-evaluation. *Epidemiol Infect* 2021;149:e32.
- 26 Yan Z, Yang M, Lai C-L. Long COVID-19 syndrome: a comprehensive review of its effect on various organ systems and recommendation on rehabilitation plans. *Biomed* 2021;9:966.
- 27 Polastri M, Ciasca A, Nava S, *et al.* Two years of COVID-19: trends in rehabilitation. *Pulmonol* 2024;30:1–3.
- 28 Soril LJJ, Damant RW, Lam GY, *et al.* The effectiveness of pulmonary rehabilitation for post-COVID symptoms: a rapid review of the literature. *Respir Med* 2022;195:106782.
- 29 Chung RYN, Chan D, Chau NNS, *et al.* Poverty affects access to regular source of primary care among the general population in Hong Kong. *Soc Policy Adm* 2019;53:854–71.
- 30 Wong ELY, Coulter A, Cheung AWL, *et al.* Patient experiences with public hospital care: first benchmark survey in Hong Kong. *Hong Kong Med J* 2012;18:371–80.
- 31 Riley WJ. Health disparities: gaps in access, quality and affordability of medical care. *Trans Am Clin Climatol Assoc* 2012;123:167–72.
- 32 Woodcock T, Greenfield G, Lalvani A, *et al.* Patient outcomes following emergency admission to hospital for COVID-19 compared with influenza: retrospective cohort study. *Thorax* 2023;78:706–12.
- 33 Greenhalgh T, Knight M, A'Court C, *et al.* Management of post-acute COVID-19 in primary care. *BMJ* 2020;370:m3026.
- 34 Spruit MA, Holland AE, Singh SJ, *et al.* COVID-19: interim guidance on rehabilitation in the hospital and post-hospital phase from a European respiratory society-and American thoracic society-coordinated International task force. *Eur Respir J* 2020;56:2002197.
- 35 Bhaskaran K, Rentsch CT, Hickman G, *et al.* Overall and cause-specific hospitalisation and death after COVID-19 hospitalisation in England: a cohort study using linked primary care, secondary care, and death registration data in the opensafely platform. *PLoS Med* 2022;19:e1003871.
- 36 Shah W, Hillman T, Playford ED, *et al.* Managing the long term effects of COVID-19: summary of NICE, SIGN, and RCGP rapid guideline. *BMJ* 2021;372:136.
- 37 Seo J-W, Kim SE, Kim Y, *et al.* Updated clinical practice guidelines for the diagnosis and management of long COVID. *Infect Chemother* 2024;56:122–57.
- 38 Ansari S, Hosseinzadeh H, Dennis S, *et al.* Activating primary care COPD patients with multi-morbidity through tailored self-management support. *NPJ Prim Care Respir Med* 2020;30:12.
- 39 Rochfort A, Beirne S, Doran G, *et al.* Does patient self-management education of primary care professionals improve patient outcomes: a systematic review. *BMC Fam Pract* 2018;19:163.
- 40 Lai FTT, Wong EL, Tam ZP, *et al.* Association of volunteer-administered home care with reduced emergency room visits and hospitalization among older adults with chronic conditions: a propensity-score-matched cohort study. *Int J Nurs Stud* 2022;127:104158.