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Home-based telerehabilitation in older patients with chronic obstructive pulmonary disease and heart failure: a randomised controlled trial

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Abstract

Background: chronic obstructive pulmonary disease (COPD) and chronic heart failure (CHF) frequently coexist in older people, reducing patients' quality of life (QoL) and increasing morbidity and mortality.
Objective: we studied the feasibility and efficacy of an integrated telerehabilitation home-based programme (Telereab-HBP), 4 months long, in patients with combined COPD and CHF. The primary outcome was exercise tolerance evaluated at the 6-min walk test (6MWT). Secondary outcomes were time-to-event (hospitalisation and death), dyspnoea (MRC), physical activity profile (PASE), disability (Barthel) and QoL (MLHFQ and CAT).
Study design: randomised, open, controlled, multicenter trial.
Methods: the Telereab-HBP included remote monitoring of cardiorespiratory parameters, weekly phone-calls by the nurse, and exercise programme, monitored weekly by the physiotherapist. All outcomes were studied again after 2 months of a no-intervention period.
Results: in total, 112 patients were randomised, 56 per group. Their mean (SD) age was 70 (9) years, and 92 (82.1%) were male. After 4 months, the IG were able to walk further than at baseline: mean (95% CI) Δ6MWT was 60 (22.2,97.8) m; the CG showed no significant improvement: −15 (−40.3,9.8) m; $P = 0.0040$ between groups. In IG, the media time to hospitalisation/death was 113.4 days compared with 104.7 in the CG ($P = 0.0484$, log-rank test). Other secondary outcomes: MRC ($P = 0.0500$), PASE ($P = 0.0015$), Barthel ($P = 0.0006$), MLHFQ ($P = 0.0007$) and CAT ($P = 0.0000$) were significantly improved in the IG compared with the CG at 4 months. IG maintained the benefits acquired at 6 months for outcomes.
Conclusions: this 4-month Telereab-HBP was feasible and effective in older patients with combined COPD and CHF.

Keywords: *chronic obstructive pulmonary disease, chronic heart failure, home rehabilitation, telemedicine services, older people*

Introduction

Aging is a growing issue—patients with chronic diseases such as chronic heart failure (CHF), chronic obstructive pulmonary disease (COPD), hypertension and diabetes are increasing in number and living longer [1, 2]. Diseases often coexist in the same patient; in particular, COPD and CHF, due to common risk factors, causing a significant added deterioration in patients' quality of life (QoL) and an increased morbidity and mortality [2–4]. The prevalence of COPD in CHF patients ranges from 20 to 32%, and that

of CHF in COPD is more than 20% [2, 4]. This prevalence seems to increase with age [5].

Patients with combined COPD and CHF are frail and characterised by a high risk of re-hospitalisations due to exacerbations, adding to the related burden of cost [2]. Each disease is an independent predictor of morbidity, mortality, impaired functional status and health service use [6, 7]. The combination of these two diseases presents diagnostic challenges [4] in that many symptoms such as dyspnoea, orthopnoea, exercise intolerance, fatigue and muscle weakness are common to both diseases [2]. Both COPD and CHF are chronic progressive diseases burdened by frequent exacerbations, with a course that fluctuates through a vicious cycle of dyspnoea, decreased activity, new exacerbations [8, 9], depression and social isolation, leading to death [10, 11]. Muscle atrophy contributes to muscle fatigue during exercise, obliging patients to stop exercising even if they have not yet exhausted their heart and lung capacity [12, 13].

The focus on COPD and CHF as a combined syndrome is increasing rapidly along with evidence highlighting the critical importance [14] of its effect on major health outcomes, including disability and QoL. In these single diseases, the multidisciplinary management approach with ICT seems to be a better solution to reduce re-hospitalisation [15, 16]. A few studies have reported rehabilitation in a home-based programme for COPD [17–19] or CHF [20, 21] patients, showing that the use of technology was safe and feasible, and it led to improvement of both physical and clinical parameters and QoL.

In patients where these two chronic diseases coexist, there is no evidence to date. Hence, the aim of this study was to investigate, after in-hospital rehabilitation, the feasibility and efficacy of a telerehabilitation home-based programme (Telereab-HBP) integrated with medical/nursing telesurveillance, compared to conventional care, in terms of: (i) exercise tolerance as the primary outcome, and (ii) time-to-event (hospitalisation for any reason, or death), dyspnoea, physical activity profile, disability and QoL, as the secondary outcomes.

Materials and methods

Design overview

The study design has recently published [22]. Consenting eligible patients with combined COPD and CHF undergoing in-hospital rehabilitation were randomised (1:1) to either the intervention group (IG) or control group (CG). The institutional review board of the Salvatore Maugeri Foundation (CEC deliberation No. 916, 3 June 2013) approved the study, which was registered on 17/10/2014 at http://www.clinicaltrials.gov (NCT02269618) and conducted according to the recommendations for Interventional Trials, SPIRIT and CONSORT guidelines, the principles of the Helsinki Declaration and good clinical practice.

The confirmed diagnosis of CHF (NYHA class II-IV) and COPD (B, C and D GOLD class) had to be documented by an echocardiogram (CHF) [7] and by a spirometry examination (COPD) [6] performed within the previous 12 months. Patients were excluded if they did not return to home after hospitalisation, they had physical activity limitations due to non-cardiac/pulmonary conditions, limited life expectancy (<6 months), or severe cognitive impairments (Mini Mental Test Examination <16).

Control group

Patients in CG received the standard care programme including medications and oxygen prescription, visits from the general practitioner, and in-hospital check-ups on demand. At enrolment in the study, patients were instructed in an educational session about the desirability of maintaining a healthy lifestyle and were invited to practice daily physical activity as preferred.

Intervention group

Patients in IG received an educational intervention from a Nurse Tutor (NT) and a Physiotherapist Tutor (PT) and were followed by both during the Telereab-HBP, which lasted 4 months [22]. The NT made a weekly structured phone call to each patient, collecting information about the disease status and symptoms, offering advice regarding diet, lifestyle and medications, previously defined with the cardiologist and pulmonologist supervising the programme. Patients were provided with a pulse oximeter (GIMA, Milan, Italy), and a portable one-lead electrocardiograph (Card Guard Scientific Survival Ltd., Rehovot, Israel) for real time telemonitoring of vital signs. Patients could call in the case of urgent need or emergency 24 h/day 365 days/year.

PT designed a personalised exercise programme for each patient who were provided with mini-ergometer, pedometer and diary. PT instructed patients and their caregivers on how to perform the exercises correctly, focusing on the rehabilitation goals. The number/intensity of training sessions according to patients' progress were adjusted during 4 months or in the case of problems [22]. The 'basic level' of programme consisted of 15–25 min of exercise with mini-ergometer without load and 30 min of callisthenic exercises, performed three times/week and free walking twice a week. The 'high level' consisted of 30–45 min of mini-ergometer with incremental load (from 0 to 60 W), 30–40 min of muscle reinforcement exercises using 0.5 kg weights and pedometer-based walking, performed from 3 to 7 days/week.

The programme was targeted to reach a moderate or high level of dyspnoea and/or muscle fatigue according to the Borg scale [23]. Based on this assessment, the PT could decide to increase or maintain the workload [22]. The PT made a weekly phone call to each patient, verified the training level of physical activity performed and planned the rehabilitation targets for the following week and gave extra reinforcement on the value of lifestyle changes and the importance of exercise.

Outcomes and follow-up

All enroled patients were visited at hospital discharge (T0), after 4 months (T1) and 2 months later (T2), during which no intervention was made.

The feasibility was assessed in terms of side effects related to Telereab-HBP, the number of patients who completed the programme, the percentage of the prescribed training sessions that were actually performed. Satisfaction about the assistance was measured by the patient at T1. The six items, with a score from 0 (not at all satisfied) to 4 (very satisfied), enquired about the service as a whole, the use of the devices, the healthcare professionals' willingness to respond to the patient's needs, clarity of the indications and suggestions made by the nurse and physiotherapist, the feeling of support, and if the service was felt to be a real help or not [22].

The primary outcome was exercise tolerance improvement measured by the difference (Δ) between T1 and T0 in the metres walked at the 6-min walk test (6MWT) [24].

The secondary outcomes were the reduction of time-to event (hospitalisation for any reason, or death) during the 4-month study period and the Δ(T1 − T0) in: (i) dyspnoea by Medical Research Council (MRC), (ii) physical activity profile (PASE), (iii) impairment/disability (BARTHEL) and (iv) QoL by Minnesota Living with Heart Failure Questionnaire (MLHFQ) and COPD Assessment Test (CAT).

In addition, we analysed the Δ(T2 − T1) and between groups from baseline to follow-up, to verify the patients' empowerment and ability to maintain the objectives achieved.

Sample size and statistical analysis

A priori sample-size for independent groups t-test was calculated based on previously published RCT data on COPD and CHF rehabilitation [25, 26] on primary outcome estimating an improvement at T1 with respect to T0 in the IG of 30 ± 50 m on 6MWT and no change expected in the CG (0 ± 50 m), at 80% of power and a significance level of $P < 0.05$, our RCT would need a sample size consisting of at least 44 participants in each group. By taking the probability of drop-outs into account (20–25% of enroled patients), we decided to include at least 55–60 patients in each group.

Data are presented as mean (standard deviation, SD), mean (95% confidence Interval, CI) and by percentage for categorical and binary variables.

Statistical analysis was carried out by a certified health professional using STATA 13.0 software (StataCorp, College Station, TX, USA). Distribution and normality of variables were tested by the Kolmogorov–Smirnov test. To compare groups at T0 and clinical variables in the groups at T0, T1 and T2, Student's *t*-test for continuous variables and the chi-squared test for categorical variables were used. Survival probability was measured by means of Kaplan–Meier survival analysis, while survival difference between groups was evaluated with the log-rank test. Additional statistical evaluation to test the differences between groups from baseline to follow-up were done by two-way analysis of variance (ANOVA) for repeated measures (time and group). Significant differences across time or between groups were reported at the alpha level of 0.05. All reported *P* values were two-sided.

Results

Enrolment of patients started in July 2013 and ended in October 2014. Follow-up ended in April 2015. In total, 112 patients were randomised (56 per group). Table 1 shows demographic and clinical characteristics of patients at T0. A study flow chart is presented in Supplementary data, Figure 1S, available in *Age and Ageing* online). Overall, 11 (20%) patients in IG were lost to follow-up, and 21 (37.5%) in CG ($P = 0.0365$).

In IG no major side effects were recorded. Overall, 48 (86%) patients ended the 4-month Telereab-HBP performing evaluations at T1. And 52 (93%) patients performed the prescribed exercises: 19% performed 2.3 (0.5) activity sessions/week, 65% performed 4 (0.5) activity sessions/week and 16% performed 6 (0.6) activity sessions/week (Supplementary data, Table 1S, available in *Age and Ageing* online).

All IG patients started the physical activity at the basic level; only the 25% advanced to a higher activity level.

The patient's satisfaction with the programme was very high in all 48 evaluated patients, with an overall mean score of 22.3 (2.25).

Figure 1 shows results for 6MWT. After 4 months, the IG were able to walk further than at baseline: Δ6MWT was 60 (22.2,97.8) m; the CG showed no significant improvement: −15 (−40.3,9.8) m; and there was a significant difference in Δ6MWT between the groups $P = 0.0040$.

Figure 2 shows Kaplan–Meier survival analysis of time-to-event. In IG, the media time to hospitalisation/death was 113.4 days compared with 104.7 in the CG—the groups were significantly different ($P = 0.0484$, log-rank test); it further increased in the next two months of follow-up (Supplementary data, Figure 2S, available in Age and Ageing online, log-rank test $P = 0.0387$). Hospitalisations were 21 in IG (11 for cardiovascular diseases, 6 for respiratory diseases and 5 for other causes) and 37 in CG (25 for cardiovascular diseases, 11 for respiratory diseases and 1 for other causes).

As shown in Supplementary data, Table 2S, available in *Age and Ageing* online, the other secondary outcomes were significantly improved in the IG compared with the CG at 4 months, The ΔMRC was −0.17 (−0.3,−0.02) in IG and 0.07 (−0.1,0.3) in CG, $P = 0.0500$. ΔPASE was 18.1 (−0.6,36.9) in IG and −21.3 (−35.7,−7.0) in CG, $P = 0.0015$. ΔBARTHEL was 5.4 (3.6,7.2) in IG and 1.3 (−0.2,2.8) in CG, $P = 0.0006$. ΔMLHFQ was −10.5 (−14.2,−6.8) in IG and −0.44 (−4.9,4.0) in CG, $P = 0.0007$. ΔCAT was −5.3 (−6.9, −3.7) in IG and 1.6 (−0.4,3.5) in CG, $P = 0.0000$.

IG maintained the benefits acquired at 6 months for all outcomes. The effects of the intervention from baseline to follow-up, analysed by ANOVA for repeated measures (times and groups), confirmed the significant improvement for 6MWT ($P = 0.0001$), MRC ($P = 0.0190$), PASE ($P = 0.0001$), BARTHEL index ($P = 0.0000$), MLHFQ ($P = 0.0001$), CAT ($P = 0.0001$) (Supplementary data, Table 2S, available in *Age and Ageing* online).

Supplementary data, Table 3S, available in *Age and Ageing* online shows the number of PT/NT and telemonitoring interventions carried out during the study.

Table 1. Baseline patient characteristics

	Intervention group (n = 56)	Control group (n = 56)	P
Male, n (%)	50 (88%)	42 (75%)	0.05
Age (years)	71 (9)	70 (9.5)	0.667
BMI (kg/m^2)	28.5 (5.8)	27.7 (5.4)	0.437
GOLD class, n (%), (new GOLD B, C, D)			0.763
IB	19 (33.9%)	15 (26.7%)	
IC	1 (1.8%)	0	
IIB	20 (35.7%)	26 (46.4%)	
IIC	2 (3.6%)	0	
IIIC	2 (3.6%)	0	
IIID	2 (3.6%)	5 (9.0%)	
IVB	1 (1.8%)	1 (1.8%)	
IVD	9 (16.0%)	9 (16.1%)	
NYHA class, n (%)			0.690
II	25 (45%)	29 (52%)	
III	22 (39%)	19 (34%)	
IV	9 (16%)	8 (14%)	
EF% pred	44.5 (12.4)	43.3 (13.2)	0.628
FEV1% pred	66.6 (18.6)	66.1 (16.4)	0.897
FVC% pred	80.9 (18.3)	78.8 (17.6)	0.534
FEV1/FVC	60 (10.2)	62 (8.9)	0.280
LTOT yes, n (%)	27 (48.3%)	26 (46.2%)	1.000
MRC dyspnoea scale	2.8 (0.98)	2.7 (0.98)	0.576
$PaCO_2$ (mmHg)	38.2 (9.6)	38.6 (6.7)	0.795
FiO_2	21.6 (2.7)	22.1 (3.4)	0.461
PaO_2/FiO_2	365 (69)	341 (69)	0.077
pH	7.44 (0.05)	7.44 (0.03)	0.423
SpO_2 %	95.7 (2.4)	94.9 (2.0)	0.063
MLHFQ score	34.4 (17.3)	35.6 (17.4)	0.707
CAT score	15.7 (6.2)	15.4 (6.4)	0.787
Barthel score	89.9 (12.9)	91.9 (8.2)	0.337
6MWT (m)	329 (115)	308 (105)	0.313
PASE score	95.8 (65.7)	78.2 (42.3)	0.097
Pharmacotherapy, n (%)			
SABA	6 (10.3%)	4 (7.7%)	0.740
LAMA	15 (27.6%)	13 (23.1%)	0.827
LABA + LAMA	4 (6.9%)	7 (11.5%)	0.525
LABA + ICS	8 (13.8%)	13 (23.1%)	0.333
LAMA + LABA + ICS	23 (41.4%)	19 (34.6%)	0.558
Digitalis	4 (6.9%)	11 (19.2%)	0.096
Beta-blocker	37 (65.5%)	30 (53.9%)	0.248
ACE inhibitors/ARBs	25 (44.8%)	28 (50.0%)	0.705
Diuretics	42 (75.9%)	47 (80.8%)	0.350
Aldosterone antagonists	27 (48.3%)	32 (57.7%)	0.449

Data are presented as number, percentage or mean (standard deviation, SD). BMI, body mass index; GOLD, global initiative for chronic obstructive lung disease; NYHA, New York Heart Association; EF, ejection fraction; FEV1, forced expiratory volume at 1 s; LTOT, long-term oxygen therapy; FVC, forced vital capacity; MRC, Medical Research Council; $PaCO_2$, carbon dioxide arterial tension; FiO_2, inspiratory fraction of oxygen; PaO_2, arterial oxygen tension; SPO_2, oxygen saturation; MLHFQ, Minnesota Living with Heart Failure Questionnaire; CAT, chronic obstructive pulmonary disease assessment test; 6MWT, 6-min walk test; PASE, physical activity scale for the elderly; SABA, short-acting beta2-agonist; LAMA, long-acting muscarinic antagonist; LABA, long-acting beta2-agonist; ICS, Inhaled CorticoSteroid; ACE, angiotensin-converting enzyme; ARB, angiotensin receptor blockers.

During Telereab-HBP, 1,234 NT-calls and 864 PT-calls were made: the mean duration was 15.3 (7.2) min (each call ranged from 5 to 25 min) for NT-calls and 30 (12) min (each call ranged from 20 to 45 min) for PT-calls for intervention. The mean duration of any single complete intervention carried out together from NT and PT was 45 min per patient per week.

Discussion

Previous studies demonstrated the efficacy of tele-health or tele-rehabilitation in COPD [16, 27] and in CHF [15, 28] considered separately, but this is the first study to provide evidence that a Telereab-HBP is feasible, safety, effective and able to maintain the results for 6 months, in older population with middle-severe combined chronic pulmonary and cardiac diseases enroled in a stable clinical condition after an in-hospital rehabilitation period.

The feasibility and safety of the programme was testified by no major side effects recorded and the effectiveness by the significant improvement in exercise tolerance (6MWT): in the IG, at the end of 4 months, the patients walked a mean of 60 m more with respect to baseline, while in the

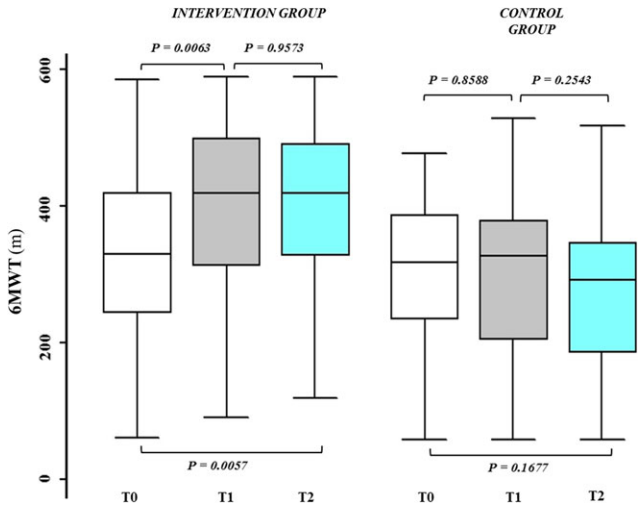

Figure 1. Box-plot of 6-min walk test (6MWT) results at T0, T1 and T2 in intervention and control groups.

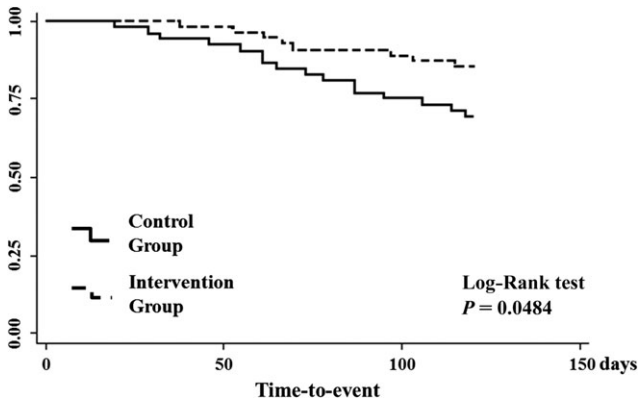

Figure 2. Kaplan–Meier survival analysis of time-to-event (re-hospitalisation for all causes, death). Survival difference between groups was evaluated with the log-rank test. The solid line represents the control group and dotted line represents the intervention group.

CG the patients reduced a mean of 15 m in 6MWT. Similarly, the patients in the IG reduced dyspnoea and maintained a better physical activity profile with a decreasing impairment/disability, a better QoL and more time free from new events (re-hospitalisations for all causes and death).

In the 2 months after the end of the Telereab-HBP, the benefits acquired were maintained in term of primary and secondary outcomes only for IG, while in the CG the 6MWT decreased of further of 43 m. The same result was obtained for 'time-to-event' in the IG evaluated at 6 months.

Patients with complicated and combined chronic conditions, such as COPD and CHF, and often more comorbidities, should follow personalised rehabilitation programmes at home forever: the benefits reached in in-hospital rehabilitation decrease already just a few weeks after the end of a programme [29, 30].

This finding further highlights the need for continuous motivational and educational input, which, in our programme, was provided by the NT and PT directly in the phone calls and in the remote reinforcement. In fact, the patient needs, on the one hand, to be continually encouraged to carry out physical activity to maintain an adequate level of independence in activities of daily living and, on the other, to be sensitised and equipped to recognise early signs and symptoms of a possible worsening.

The results of this integrated NT and PT activity determined a very high response by the patients: 81% of them performed more than three weekly sessions of rehabilitation activity and 69% of them obtained an increase in exercise tolerance.

It would be important to increasingly perceived 'physical activity drug' as such, both by doctors and patients, following the main guidelines [6, 7]. Similarly results had been seen in the older people with CHF [28].

The older population studied represent a highly selected sample in which the multidisciplinary disease management approach, that is the best outcome in terms of prolonged survival and reduced hospital-readmission rates [6, 7], has been shifted to a more personalised one.

Limitations

Due to the nature of the trial, it was not possible to blind patients and healthcare personnel to intervention. However, outcome assessors and data analysts were blinded to the allocation. We tried to standardise as much as possible the nursing and physiotherapy approach in the three hospitals involved in the enrolment of patients, conducting joint training of staff, organisational meetings and planning before commencing patient enrolment.

The exercise programme carried out was more a programme of physical activity maintenance than exercise training in the true sense. Only in a subgroup of patients, in fact, did we measure the incremental load (watts) performed by the patients during the 4 months of the Telereab-HBP.

This exercise programme is not suitable for patients with limited physical activity caused by orthopaedic problems. We must think of something suitable for them.

The studied patients after 2 months of the end of the home programme in the control group were fewer than the minimum number calculated for sample size. Further randomised studies will be needed to confirm our results.

Conclusions

A new model of nurse/therapist telerehabilitation programme is feasible, safe, and, effective in improving exercise capacity and maintain better general condition of dyspnoea, physical activity profile, disability and QoL in complex patients with both COPD and CHF. Time to

event seems to be slightly longer than the control group. This programme could be a successful opportunity to follow complex chronic patients at home.

Key points

- Chronic obstructive pulmonary disease (COPD) and chronic heart failure (CHF) frequently coexist in older people.
- This study aimed to demonstrate that a telerehabilitation home-based programme was feasible and effective in these patients.
- Our programme improved all studied parameters (6-min walk test (6MWT), quality of life (QoL), dyspnoea, physical activity profile, disability and time-to-event).

Supplementary data

Supplementary data are available at *Age and Ageing* online.

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Authors' contributions

P.B., S.S., M.P., Ma.Vo., Mi.Vi., M.T.L.R.: developed the design and study protocol; T.G., D.B., G.C., B.S.: collected data; P.B., M.P.; S.S.; Ma.Vo., Mi.Vi., M.T.L.R.: monitored data collection; P.B., M.P.: drafted the article; S.S., M.V.: critically revised the article. All authors read and approved the final version.

Conflict of interest

None declared.

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Associations of acetylcholinesterase inhibitor treatment with reduced mortality in Alzheimer's disease: a retrospective survival analysis

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Abstract

Background: dementia is increasingly recognised as life-limiting condition. Although the benefits of acetylcholinesterase inhibitors (AChEIs) on cognition and function are well established, their effect on survival is less clear.
Objective: to investigate associations between AChEI prescription and mortality in patients with Alzheimer's dementia (AD) in a naturalistic setting, using detailed baseline data on cognition, functioning, and mental and physical wellbeing.
Methods: we used a large mental healthcare database in South London, linked to Hospital Episode Statistics and Office for National Statistics mortality data, to assemble a retrospective cohort. We conducted a survival analysis adjusting for a wide range of potential confounders using propensity scores to reduce the impact of confounding by indication.