

A RETROSPECTIVE DATABASE STUDY OF A CHRONIC THROMBOEMBOLIC PULMONARY HYPERTENSION PATIENT COHORT TO EVALUATE THE PATIENT CHARACTERISTICS AND ECONOMIC BURDEN OF ILLNESS IN ENGLAND

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Introduction

- Chronic thromboembolic pulmonary hypertension (CTEPH) is a rare disease mostly occurring as a complication of pulmonary embolism (PE) (1). According to a recent meta-analysis (2), this complication develops in 3.4% of patients who survive an acute PE.
- The estimated incidence of CTEPH in Europe is at least 5 cases per million person-years (3).
- CTEPH results from an obstruction of pulmonary vessels with organized blood clots, hence increasing pulmonary blood pressure. It manifests as dyspnoea, fatigue, palpitations, and chest pain and, if left untreated, will progress to right ventricular failure. Pulmonary endarterectomy (PEA) represents the treatment of choice for CTEPH and leads in most patients to substantial haemodynamic improvement, which is in turn associated with improvements in functional status and in long-term survival. However, surgery is not possible in 30% to 50% of patients due to either distal pulmonary vascular obstruction or significant comorbidities thought to be associated with unacceptably high risk (4).
- There is currently only one licensed treatment option available for CTEPH (riociguat, a soluble guanylate cyclase stimulator) (5) but CTEPH patients often use off-label prescriptions of drugs initially intended for pulmonary arterial hypertension (PAH) patients as well. There has also been the recent development of balloon pulmonary angioplasty (BPA), a complex procedure to be repeated 3 to 10 times, and that can be combined with targeted medical therapy (6).
- Given that a high proportion of patients are ineligible for potentially curative treatment (PEA), the economic burden of CTEPH patients in England is expected to be high but is currently unknown.

Objectives

To define and characterise a CTEPH cohort of patients, and to calculate its economic burden from the Hospital Episode Statistics (HES) database

Methods

Study design

This is a descriptive, non-interventional, retrospective cohort study of CTEPH patients with a study period from 1 October 2012 to March 2018.

Data source

HES is an administrative database, which captures all inpatient admissions, all outpatient appointments, and all emergency attendances at National Health Service (NHS) hospitals in England but does not collect data on clinical characteristics.

Study cohort

As no single parameter is sufficient to confirm a CTEPH diagnosis in HES, a combination of different diagnosis codes was applied, defined from a previous feasibility study:

Inclusion criteria	Exclusion criteria
> 1 record with ICD-10 diagnostic code for PH (I27.0 or I27.2) <i>and</i> > 1 record with ICD-10 diagnostic code for PE (I26: Pulmonary Thromboembolism)	- Patients < 18 years old at index date or - Missing age or gender at index

ICD-10: International Classification of Diseases, Tenth Revision

To protect patient confidentiality, data were anonymised and results with patient counts <6 were masked (i.e. not reported) in accordance with the low patient number suppression rule defined by NHS Digital.

Index date

The index date was defined as the earliest of:

- the date of first PH related ICD-10 code
- the date of first prescription of PAH or CTEPH specific drug (i.e. PDE-5 inhibitors, endothelin receptor antagonists, soluble guanylate cyclase stimulators, and drugs acting on the prostacyclin pathway)

Study outcomes measurements

Point prevalence. The number of CTEPH patients alive and living in England on 31st of December was extracted from HES for each year within the study period. The denominator was derived from estimates of the total population in England obtained from the UK Office for National Statistics.

Economic burden of hospitalisation. In England, commissioners pay healthcare providers for each patient seen or treated considering the complexity of the patient's healthcare needs. These costs can be calculated from the HES database and are based on healthcare resource groups (HRG), i.e. groups of diagnoses and interventions that consume similar levels of NHS resources, and on associated tariffs. To generate the appropriate HRG code, secondary care events are grouped into spells, which include the different diagnoses made, the events that occurred during an admission (specialist visits, procedures, and investigations), and the duration of care in different settings. To perform our analysis, we stratified these costs into "CTEPH related costs" for episodes with a PH ICD-10 code and "non-CTEPH related costs" for episodes with no PH ICD-10 code as an inpatient admission, outpatient visit and emergency attendance.

Results: Patients characteristics

- The study cohort comprised a total of 2,932 CTEPH patients for the whole study period (from 2013 to 2017). For the year 2017 only, point prevalence was estimated at 36.6 patients per million inhabitants, with a total of 2,152 prevalent patients identified. This compares well to the 2,058 prevalent patients reported for the 31st March 2017 in the 8th National PH Audit, a prospective audit of processes and outcomes covering all 8 centers designated to diagnose and treat PH patients in England and Scotland (7).
- Gender distribution for the CTEPH population captured in HES over the 5-year period (2013-2017) was reported to be 55.2% female and 44.8% male. 18.5% of the population studied were under 50 years of age at index date whilst 45.0% were 70 years or older (Table 1). Both the gender and the age at index date were comparable to literature values (7) (8), and remained constant over 5 years.

Table 1: Main characteristics of study participants (N=2,932)

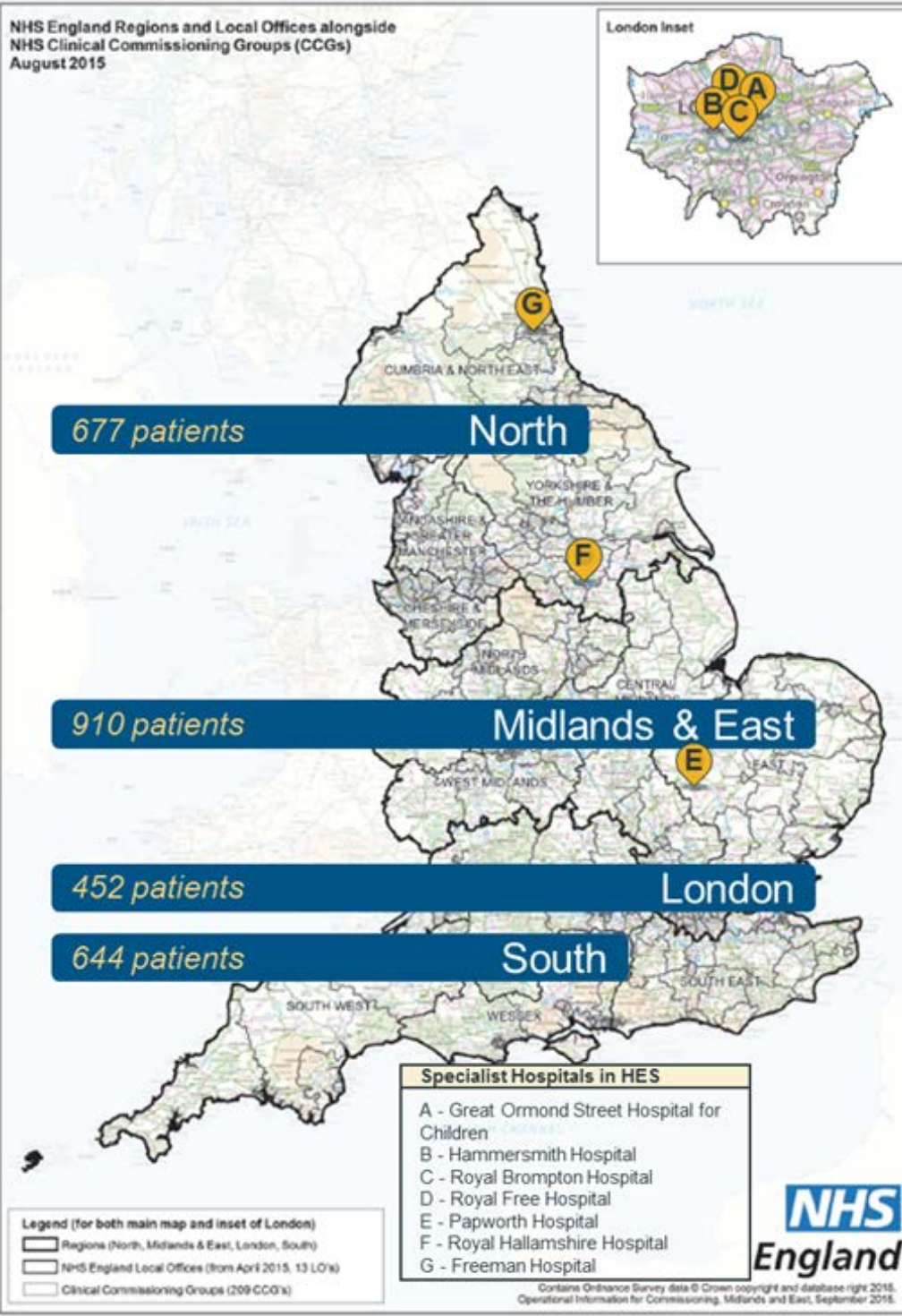
	N	%
Gender		
Female	1,619	55.2
Male	1,313	44.8
Age at index date*, in years		
18-19	9	0.3
20-29	84	2.9
30-39	151	5.2
40-49	296	10.1
50-59	405	13.8
60-69	667	22.7
more than 70	1,320	45.0

* defined as the earliest of the date of first PH related ICD-10 code and the date of first prescription of PAH or CTEPH specific drug within the study period

The greatest proportion of CTEPH patients in England were shown to live in the Midlands and East (910 patients, 33.7%), based on the location of the General Practice (GP) they were registered with (Figure 1).

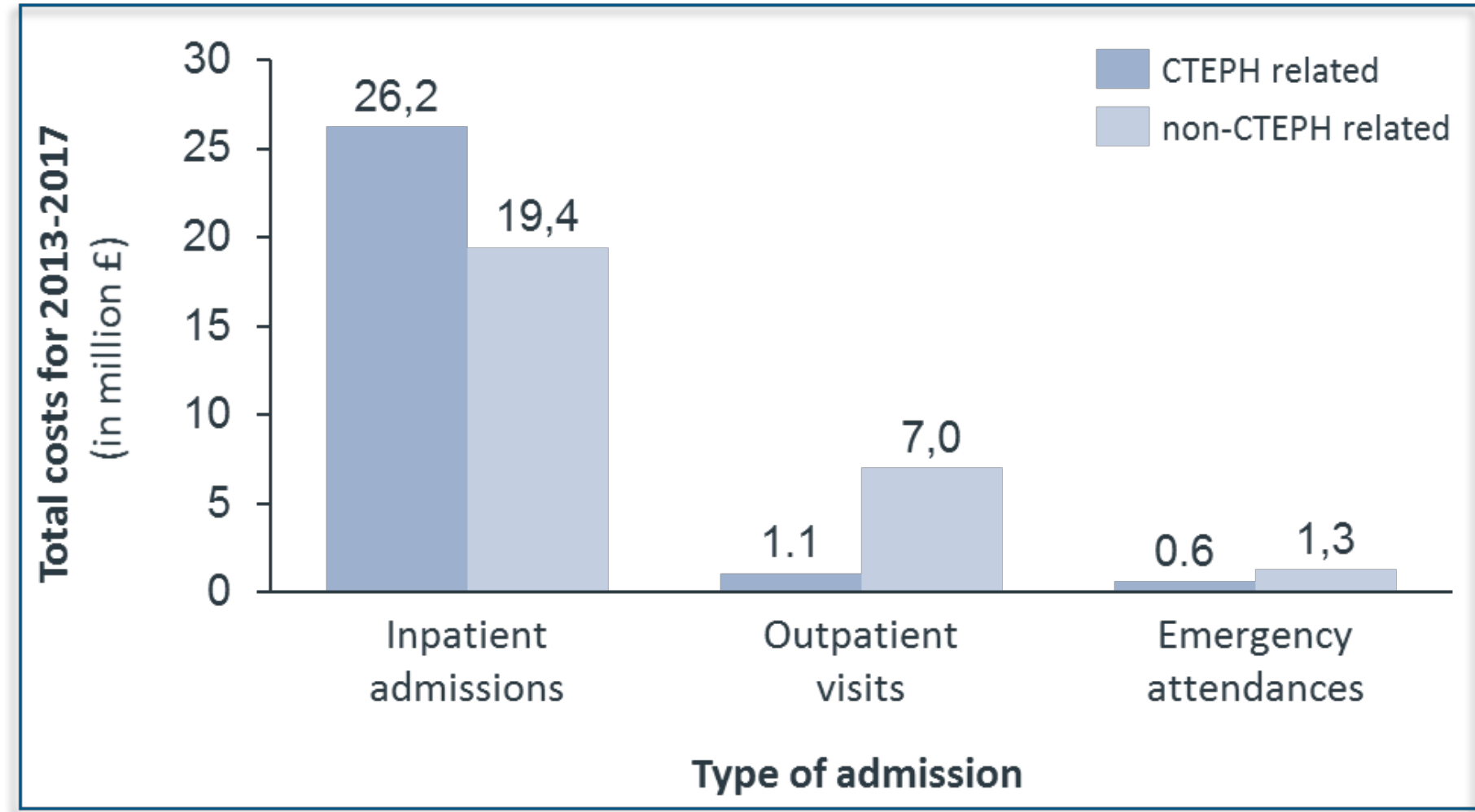
Note: The total number of patients in Figure 1 is 2,683 as patients with treatment costs covered by NHS but who do not reside in England are not represented

Figure 1: Geographic distribution of prevalent CTEPH patients in England (2013-2017)



Results: Healthcare Resource Utilisation

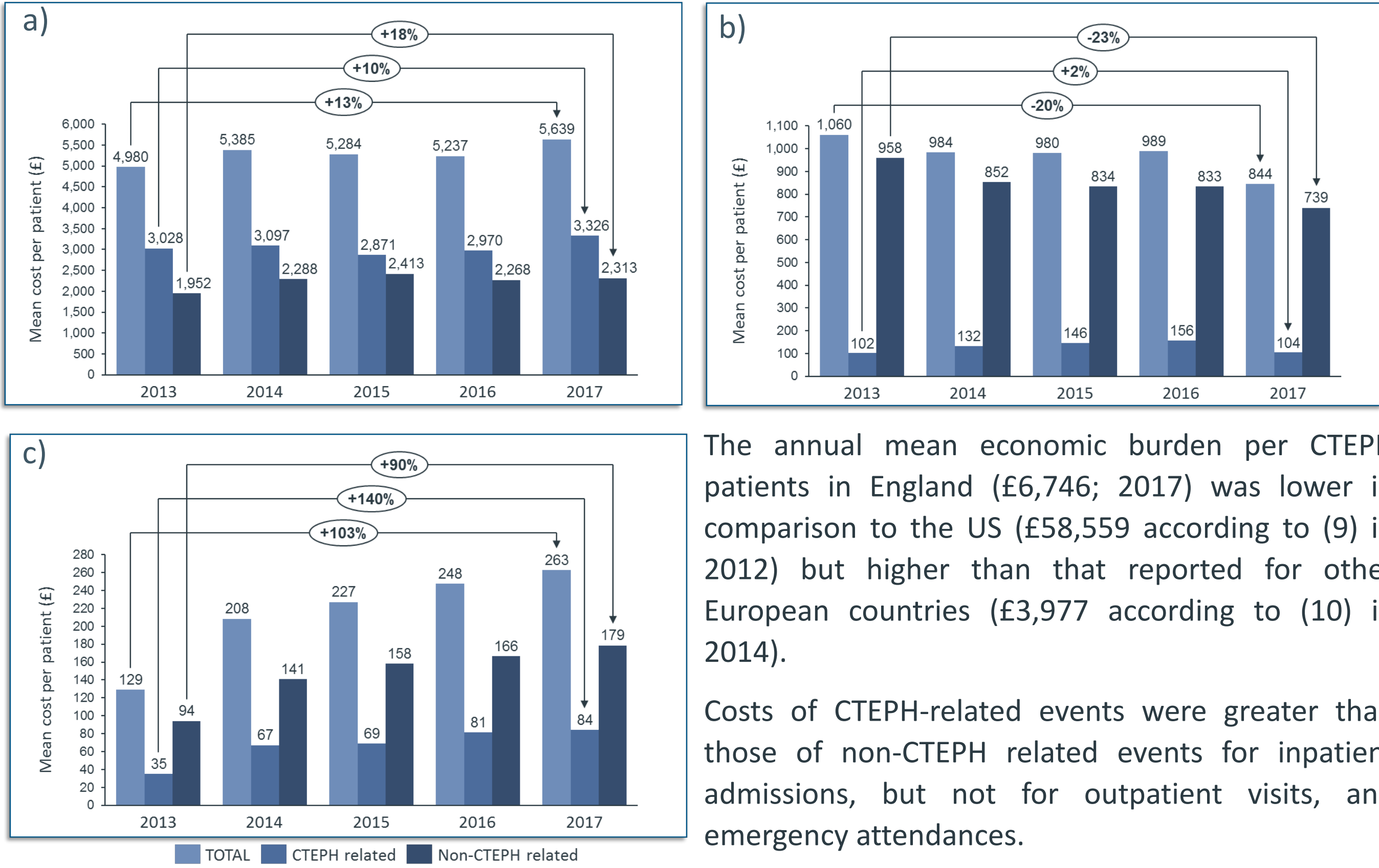
Figure 2: Total economic burden of prevalent CTEPH patients in HES in million £ for the period 2013-2017



Overall, for the 2013-2017 period, the total costs for prevalent CTEPH patients seeking hospital care for all causes (CTEPH-related and non-CTEPH related) were £55.6 million (Figure 2). Among those, £45.6 million accounted for inpatient admissions (82.0%), £8.1 million accounted for outpatient visits (14.6%), and £1.9 million accounted for emergency attendances (3.4%).

The total costs for prevalent CTEPH patients were £14.5 million in 2017, corresponding to a mean cost per patient of £6,746: £5,639 for inpatient admissions, £844 for outpatient visits, and £263 for emergency attendances. Compared to the total mean cost in 2013 (£6,169), this corresponds to an overall increase of 9% (+13% for inpatient admissions, -20% for outpatient visits, and +103% for emergency attendances, see Figure 3).

Figure 3: Mean cost per prevalent CTEPH patients for a) inpatient admissions b) outpatient visits c) emergency attendances



The annual mean economic burden per CTEPH patients in England (£6,746; 2017) was lower in comparison to the US (£58,559 according to (9) in 2012) but higher than that reported for other European countries (£3,977 according to (10) in 2014).

Costs of CTEPH-related events were greater than those of non-CTEPH related events for inpatient admissions, but not for outpatient visits, and emergency attendances.

Limitations

- The prevalence and incidence rates reported in this study using HES are likely to vary given the difficulty in diagnosing CTEPH, due to the lack of an identifiable causative event and/or the lack of early definitive symptoms of CTEPH. Also, patients with no documented history of acute PE, likely to represent up to 25% of CTEPH patients (8), are expected to be missing from the present cohort.
- Given the identification of patients was based on HES, we cannot exclude that patients whose PEA has led to significant improvements in functional status have not been hospitalised over the study period and hence have not been identified as prevalent patients.
- As HES does not capture retail pharmacy activity where PDE-5 inhibitors are mainly dispensed, there is an under-reporting of PAH/CTEPH drugs used by CTEPH patients. Hence, this may lead to missing some patients or under-reporting of costs.

Conclusions

The algorithm identified a CTEPH population of a size comparable with literature values and for the first time an economic burden for CTEPH patients in England has been calculated.

The high costs associated with inpatient admissions, specifically the cost of managing CTEPH related events, are higher than outpatient visits and emergency attendances.

REFERENCES

- Kim NH, Delcroix M, Jais X, et al. Chronic thromboembolic pulmonary hypertension. *Eur Respir J*. 2019; Vol. 53, 1.
- Simonneau G, Torbicki A, Dorfmüller P, and Kim N. The pathophysiology of chronic thromboembolic pulmonary hypertension. *Eur Respir Rev*. 2017; Vol. 26, 143.
- Delcroix M, Kerr K, and Fedullo P. Chronic Thromboembolic Pulmonary Hypertension. Epidemiology and Risk Factors. *Ann Am Thorac Soc*. 2016; Vol. 3.
- Kim NH, Delcroix M, Jais X, et al. Chronic thromboembolic pulmonary hypertension. *Eur Respir Rev*. 2018; in press [https://doi.org/10.1183/13993003.01915-2018].
- Sitbon O, Gombert-Maitland M, Granton J, et al. Clinical trial design and new therapies for pulmonary arterial hypertension. *Eur Respir J*. 2019; Vol. 53, 1801908 [https://doi.org/10.1183/13993003.01908-2018].
- Lang I, Meyer BC, Ogo T, et al. Balloon pulmonary angioplasty in chronic thromboembolic pulmonary hypertension. *Eur Respir Rev*. 2017; Vol. 26, 143.
- National Audit of Pulmonary Hypertension 8th Annual Report. NHS Digital. [Online]. https://digital.nhs.uk/data-and-information/publications/statistical/hypertension-audit/national-audit-of-pulmonary-hypertension-8th-annual-report.
- Pepke-Zaba J, Delcroix M, Lang I, et al. Chronic thromboembolic pulmonary hypertension (CTEPH): results from an international prospective registry. *Circulation*. 2011; Vol. 124, 18.
- Said Q, Martin BC, Joish VN, Kret al. The cost to managed care of managing pulmonary hypertension. *J Med Econ*. 2012; Vol. 15, 3.
- Schweikert B, Pittrow D, Vizza CD, et al. Demographics, clinical characteristics, health resource utilization and cost of chronic thromboembolic pulmonary hypertension patients: retrospective results from six European countries. *BMC Health Serv Res*. 2014; Vol. 14, 246.
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