Received: 20 April 2023 | Accepted: 19 July 2023

DOI: 10.1111/hiv.13529

ORIGINAL ARTICLE

Estimating the hospital costs of care for people living with HIV in England using routinely collected data

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Funding information
the National Institute for Health Research (NIHR), Grant/Award Number: RP-PG-1212-20006

Abstract

Background: Understanding the health care activity and associated hospital costs of caring for people living with HIV is an important component of assessing the cost effectiveness of new technologies and for budget planning.

Methods: Data collected between 2010 and 2017 from an English HIV treatment centre were combined with national reference costs to estimate the rate of hospital attendances and costs per quarter year, according to demographic and clinical factors. The final dataset included records for 1763 people living with HIV, which was analysed using negative binomial regression models and general estimating equations.

Results: People living with HIV experienced an unadjusted average of 0.028 (standard deviation [SD] 0.20) inpatient episodes per quarter, equivalent to one every 9 years, and 1.85 (SD 2.30) outpatient visits per quarter. The unadjusted mean quarterly cost per person with HIV (excluding antiretroviral drug costs) was £439 (SD 604). Outpatient appointments and inpatient episodes accounted for 88% and 6% of total costs, respectively. In adjusted models, low CD4 count was the strongest predictor of inpatient stays and outpatient visits. Low CD4 count and new patient status (having a first visit at the Trust in the last 6 months) were the factors that most increased estimated costs. Associations were weaker or less consistent for demographic factors (age, sex/sexual orientation/ethnicity). Sensitivity analyses suggest that the findings were generally robust to alternative parameter and modelling assumptions.

Conclusion: A number of factors predicted hospital activity and costs, but CD4 cell count and new patient status were the strongest. The study results can be incorporated into future economic evaluations and budget impact assessments of HIV-related technologies.

KEYWORDS

cost, cost-analysis, England, HIV, resource use

INTRODUCTION

Since the first cases of HIV/AIDS were described, a large number of health care interventions have been developed to help diagnose infection, treat people living with HIV, and prevent further transmissions [1]. However, funding decisions are becoming increasingly reliant on the outcomes of health technology assessments [2, 3]. In many countries, these assessments include an economic component in which evidence of clinical impact is combined with information on costs to produce cost-effectiveness and budget impact estimates [3, 4]. Randomized controlled studies are the gold standard method of establishing treatment effects, and observational studies are often used to measure resource use and costs, as they can be more reflective of routine clinical practices and patient populations [5, 6].

In the UK, Beck et al. and Mandalia et al. conducted a series of HIV costing studies based on routinely collected data [7–10]. They have been extensively used in the UK to evaluate the cost effectiveness of technologies such as rapid HIV testing in primary care [11] and pre-exposure prophylaxis with antiretroviral therapy (ART) [12]. However, the data on which the latest full publications were based (1996–2008) [13] are unlikely to reflect contemporary clinical guidelines and practice as they only include the early ART period, when treatment was less well tolerated and had lower efficacy [14]. Moreover, ART at this time was initiated at lower CD4 cell count levels, and individuals were typically diagnosed with later-stage infection, meaning outcomes were poorer by today's standards [15, 16].

In this study, we used a more recently collected routine clinical dataset (2010–2017) to estimate the clinic/hospital costs of care for people living with HIV in England according to factors such as viral load (VL) and immunological status.

MATERIALS AND METHODS

HIV clinic population

The analysis uses the HIV patient record system from North Middlesex University Hospital NHS Trust (NMUHT) [17], a large North London-based hospital in England, serving an ethnically diverse population with high deprivation. The clinic provides outpatient and inpatient care, ART treatment, specialist HIV advice, and multi-disciplinary care. All health care activity at the NMUHT is included in the database, covering HIV and non-HIV services. Health care activity at other Trusts is not included in the database, but referral to tertiary services is thought to be rare and limited to inpatient haemodialysis and level three haematology/oncology services.

The study sample uses data recorded between January 2010 and December 2017 for all individuals aged ≥18 years at the time of HIV diagnosis. Sociodemographic information included quarterly period of birth/death, date of HIV diagnosis, date first seen at the NMUHT HIV clinic, ethnicity (white; Black African; other ethnic background), sex (men/women), history of ART use, and likely HIV exposure route (men who have sex with men [MSM], heterosexual, intravenous drug use [IVDU], other). Information on sex, sexual orientation, and ethnicity was combined into a single categorical variable denoting Black African heterosexual men, other heterosexual men, Black African women, other women, and MSM. The dates and results of VL, CD4, and resistance testing were also obtained. A binary variable indicating history of virological failure was constructed by defining it as a VL measurement ≥200 copies/mL after having received ART for at least 6 months.

Resource use

The resources included in the costing exercise were CD4 cell count and VL measurement, resistance testing, outpatient visits (information available: date, type [first visit, regular follow-up, telephone, nurse appointment, treatment support clinic, dietician, counselling, tuberculosis clinic, renal clinic, other]), admitted patient care (APC) episodes (information available: inpatient, day case, date of admission/discharge, elective or non-elective admission, and International Statistical Classification of Diseases and Related Health Problems, Tenth Revision [ICD10] codes).

Unit costs

Admitted patient care episodes (inpatient episodes and day-case visits)

The NHS 2018/19 reference costs were used to calculate all APC unit costs [18] by assigning each recorded APC to a health resource group (HRG) by primary ICD10 code, using the NHS Grouper software [19]. A unit cost was then assigned to each HRG from the NHS reference costs table [18]. Inpatient stays of <2 days were assigned a short stay unit cost, and stays of ≥2 days were assigned a long stay unit cost.

Around 28% of APCs could not be linked to an HRG, mostly because the primary ICD10 code was missing. In these instances, missing unit costs were estimated using a

generalized linear regression model, assuming a gamma distribution and identity link, based on the length of admission. A mean cost of £428 was used for missing day-case costs based on observed cases.

Outpatient appointments, CD4, VL, and resistance testing

The NHS 2018/19 reference costs [18] were also used to assign unit costs to outpatient appointments based on clinical speciality and HIV status (see Appendix A; Table A1). It was unclear as to which speciality code was most relevant for ~16% of all outpatient appointments. Where this was the case, it was assumed that each cost £274 (equivalent to a routine HIV follow-up appointment for a clinically stable person living with HIV).

The costs of treatment were estimated by multiplying the quantity of resources used, as recorded in the database, by the assigned unit costs. The costs of supplying ART were not included in the analysis because preferences for, and the costs of, specific ART regimens [20] have changed rapidly over time [14], due to therapeutic advances and the availability of generic formulations. Given these issues, when estimating costs it is typical to report the underlying health state costs only, to which the relevant drug costs can be added as necessary.

Data cleaning, transformations, and extrapolations

Duplicate hospital appointments were removed from the dataset if two or more were recorded for the same clinic type on the same day. Regular HIV outpatient appointments occurring on the same day as a nurse visit/blood test were counted as a single HIV outpatient appointment.

The data were arranged into quarterly annual periods over the 8-year period (Q1 2010 to Q4 2017), with each participant therefore contributing a maximum of 32 rows of data. Participants were then judged to be under the care of the clinic or not during each quarter. This step was important because one difficulty with costing studies is the importance of accounting for zero costs. That is, if a person does not use a resource within a time period, this could be because they did not require, and therefore receive, any care but could have done so if needed. For quarters where a person was deemed to be under clinic care, but no health care resources were used, a zero cost was recorded and it was retained in the dataset.

A person was considered to be under the care of the clinic, and therefore included in the dataset, from the date of an initial test result or initial hospital activity (APC or outpatient appointment), whichever occurred first. Periods in which a person was no longer considered to be receiving care from the clinic were omitted. Periods following death were also removed or if no engagement with the Trust was recorded for that specific individual (APC; outpatient appointment; CD4, VL, or resistance test result) over the preceding 12-month period. In the absence of a date of death or 12-month period without engagement with the Trust, the person was assumed to remain under follow-up, and associated costs (including zero costs) were counted. Individuals who were removed from the dataset for a period could be re-entered if later contacts with the Trust were subsequently recorded; see Figure 1 for an example.

Where two or more CD4 or VL tests had been recorded within a quarter, all were included in the calculation of costs, but a single value of CD4 or VL (the mean of the measurements) was assigned to the quarter. For quarters where test results were not available, linear interpolation was used to estimate CD4 count and VL values whenever the gap between test results was less than 12 months. When the gap was ≥12 months, or no further test results were available, the last recorded value was carried forward for a maximum of 12 months. After this time, CD4 count and VL values were assumed to be missing.

Statistical analysis

We report unadjusted and adjusted quarterly mean counts of inpatient episodes (model 1) and outpatient appointments (model 2). The adjusted analyses used negative binomial regression models and are reported as incidence rate ratios (IRRs). Model 3 contains an adjusted analysis of costs, performed using generalized estimating equations with an exchangeable correlation structure. A gamma distribution was used to allow for the skewness of the data and because costs cannot be negative. An identity link was used for providing additive covariate effects on the mean costs. The results are reported as mean costs per quarter.

All three statistical models included the following covariates: age (18–30 [base], 31–50, 51–70, ≥71 years); sex, sexual orientation, and ethnicity (MSM [base], Black African heterosexual men, other heterosexual men, Black African women, other women); IVDU as the HIV transmission route (yes; no [base]); quarterly period as a continuous variable from Q1 2010 to Q4 2017 (values of 0–31, respectively); whether a new patient (defined as the period within the first 6 months of either having an initial HIV diagnosis or initial contact with the HIV centre, whichever occurred first [yes; no]); CD4 count (≤50, 51–200, 201–500, ≥501 [base] cells/μL); and history of

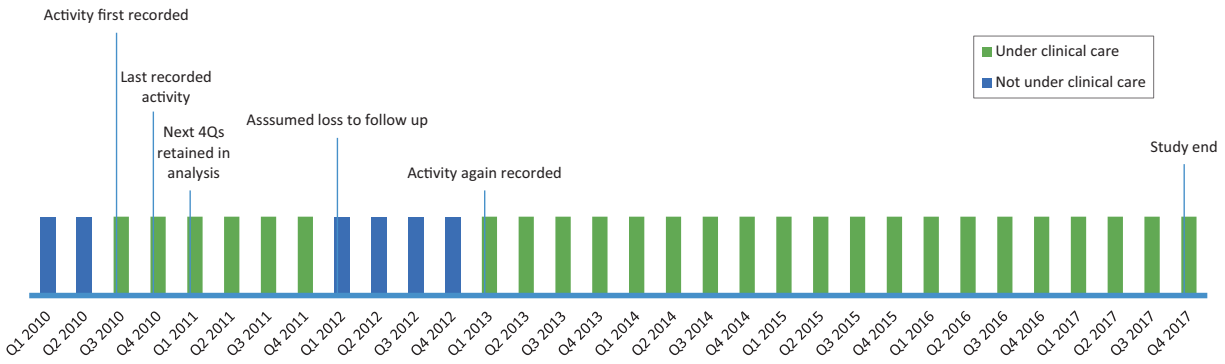

FIGURE 1 Example participant timeline. The timeline represents a hypothetical person living with HIV who was first treated at the Trust in July 2010 (Q3 2010) with further evidence of contact during the next quarter (Q4 2010). No further activity was reported until Q1 2013, and then in all subsequent quarters.

virological failure and current VL (previous VL failure and current VL ≤200 copies/mL, current VL ≥200 copies/mL irrespective of VL failure history, no known previous VL failure and current VL <200 copies/mL [base]). The sex, sexual orientation, and ethnicity variable, and the variable denoting whether IVDU was the likely HIV transmission route were fixed throughout follow-up; all the other variables (CD4, current VL/history or VL failure, new patient status, age, and calendar period) were time updated at each quarter.

As a sensitivity analysis, the three models were each re-run to test for potentially important interactions between CD4 count and time from initial Trust contact, VL/history of virological failure and time from initial Trust contact, and CD4 count and VL/history of virological failure. In further univariate sensitivity analyses, the three models were reanalysed assuming that quarterly periods were defined as inactive after 6 or 18 months of no recorded activity (instead of 12 months) and missing CD4/VL test results were only extrapolated for 6 or 18 months rather than 12 months. In a final sensitivity analysis, the cost of each outpatient appointment where the clinical speciality was unclear was reduced from £274 per visit by 50%. Analyses were done with STATA (Version 16.0) (27)

RESULTS

The final dataset included details of 1763 people living with HIV with a median duration of follow up of 6 years (interquartile range [IQR] 2.5–8). The majority of people were Black African heterosexual women or men (59%) (Table 1). The overall mean age was 37.3 (standard deviation [SD] 10.7) years, and over 90% of individuals had received ART before the end of the study period.

The dataset comprised 36 781 quarterly periods between 2010 and 2017. It included 69 241 clinic/hospital visits, 98% of which were outpatient appointments (Table 2). The unadjusted analysis showed that people living with HIV recorded an average of 1.85 (SD 2.30) outpatient appointments per quarter. Regular HIV follow-up and first visits to the HIV clinic were the most frequent type of outpatient appointment (53%), followed by blood tests with a nurse (19%). There were 1048 inpatient episodes, equivalent to an average of 0.028 (SD 0.2) inpatient episodes per quarter (or one episode every 9 years). The mean length of inpatient stay was 0.31 (SD 3.11) days per quarter. The overall unadjusted mean cost per person with HIV per quarter was £439 (SD £604). Outpatient appointments were the major cost component, accounting for 88% of total costs, followed by inpatient appointments (6%) and tests (5%). The proportion of total costs attributable to 'routine HIV care' was estimated to be 71% (£310/£439), calculated by summing the costs of HIV-specific outpatient appointments (first visits, regular visits, and blood tests with a nurse) together with the costs for the HIV tests (CD4, VL, and resistance).

Table 3 shows the quarterly rates and adjusted IRRs for inpatient and outpatient episodes according to the levels of the covariates. Lower CD4 counts were strongly associated with higher rates of inpatient episodes (model 1, $p < 0.001$) and outpatient appointments (model 2, $p < 0.001$). For example, the quarterly rate of inpatient episodes was almost 10 times higher (IRR 9.98; 95% confidence interval [CI] 6.95–14.31) for people with a CD4 ≤50 cells/μL compared with those with a CD4 ≥501 cells/μL. Inpatient episode rates (IRR 2.72; 95% CI 2.13–3.46) and outpatient appointment rates (IRR 2.12; 95% CI 2.01–2.22) were two to three times higher for people newly registered with HIV than for those already in care.

TABLE 1 Cohort demographics.

Characteristic	*N* (%)	Mean (SD)
Total	1763	-
Age at first attendance	-	37.3 (10.7)
Sex, sexual orientation, and ethnicity[b]		
MSM	264 (15)	-
Black African heterosexual men	349 (20)	-
Other heterosexual men	258 (15)	-
Black African women	687 (39)	-
Other women	205 (12)	-
IVDU	34 (2)	
First ever recorded CD4 cells/μL[a]	-	323 (278)[c]
First ever recorded log VL[a]	-	3.80 (1.45)
First recorded CD4 during study period	-	440 (276)[d]
First recorded log VL during study period	-	2.73 (1.59)
Ever received ART[a]		
Yes	1596 (91)	-
No	167 (9)	-
Year first diagnosed with HIV[a]		
1985–1989	5 (<1)	-
1990–1994	55 (3)	-
1995–1999	180 (10)	-
2000–2004	434 (25)	-
2005–2009	428 (24)	-
2010–2014	492 (28)	-
2015–2017	169 (10)	-

Abbreviations: ART = antiretroviral therapy; IQR = interquartile range; IVDU = intravenous drug use; MSM = men who have sex with men; SD = standard deviation; VL = viral load.
[a]These values could have been recorded before 2010.
[b]139/871 (16%) of men were assumed to be heterosexual where the likely exposure route was not categorized as either sex between men or heterosexual sex, and 14/1763 (<1%) people were assumed to not be of Black African origin.
[c]Median 274 cells/μL (IQR 115–460).
[d]Median 410 cells/μL (IQR 240–610).

History of virological failure combined with VL measurement significantly predicted the rate of inpatient episodes ($p < 0.001$) and, to a lesser extent, outpatient appointments ($p < 0.001$). For example, compared with individuals with VL <200 copies/mL and no history of virological failure, inpatient admission rates were 1.87 (95% CI 1.51–2.32) times higher for people with a current VL ≥200 copies/mL, irrespective of virological failure history, and 1.39 (95% CI 1.08–1.80) times higher for those with current VL <200 and history of virological failure.

TABLE 2 Unadjusted resource use and cost per 3-month (quarter) period.

Resource	Total no. (%)	Mean no. (SD)[a]	Mean cost £ (SD)[a]
Hospital appointments/visits			
All outpatient appointments	68 058 (98)	1.85 (2.30)	388 (485)
Only first or regular HIV outpatient appointments	36 166	0.98 (1.09)	281 (312)
Only blood tests with a nurse	12 860	0.35 (0.69)	7 (12)
Day-case visits	135 (<1)	0.004 (0.08)	2 (32)
Inpatient episodes	1048 (2)	0.028 (0.20)	26 (233)
Tests			
CD4 tests	12 569	0.34 (0.56)	7 (13)
VL tests	24 757	0.67 (0.84)	13 (17)
Resistance tests	1564	0.04 (0.25)	2 (13)
Overall cost	-	-	439 (604)

Abbreviations: SD = standard deviation; VL = viral load.
[a]Including participants who did not receive the listed health care element.

Older age was associated with higher rates of inpatient episodes ($p < 0.001$) but, compared with those aged 18–30 years, the risk was significantly higher only in the group aged ≥71 years (IRR 3.20; 95% CI 1.68–6.10). Age was not associated with the rate of outpatient appointments ($p = 0.73$). The variable representing sex, sexual orientation, and ethnicity was also significantly associated with rates of inpatient episodes and outpatient appointments ($p < 0.001$ in both instances). The analysis showed the rate of inpatient stays was highest for other heterosexual men, followed by MSM, then other women, with Black African women and Black African men having the lowest rates. On the other hand, the rate of outpatient appointments was highest for Black African and other women, followed by MSM, and was lowest for heterosexual men. IVDU status was not significantly associated with inpatient or outpatient episodes.

The quarterly rate of inpatient stays and outpatient appointments reduced, albeit modestly, with increasing calendar time (IRR per quarter for inpatient stays 0.98 [95% CI 0.97–0.99], and IRR outpatient visits 0.99 [95% CI 0.99–0.99]), equivalent to yearly decreases of ∼8% and 4%, respectively.

All factors apart from IVDU status were significantly associated with costs (Table 4). The adjusted mean cost of caring for people with HIV in the base group of all categories (i.e., for an MSM aged 18–30 years, non IVDU, not a new patient, with the most favourable CD4 and VL

TABLE 3 Unadjusted quarterly rates and adjusted IRRs per quarter estimated using negative binomial models.

	Inpatient episodes (model 1)				All outpatient visits (model 2)			
Category	**Quarterly no.[b]**	**IRR**	**95% CIs**	***p*-value**	**Quarterly no.[b]**	**IRR**	**95% CIs**	***p*-value**
Age in years	-	-	-	<0.001	-	-	-	0.73
18–30 (base)	0.03	-	-	-	2.30	-	-	
31–50	0.024	0.89	0.64; 1.23	-	1.86	1.01	0.95; 1.07	-
51–70	0.032	1.26	0.88; 1.80	-	1.72	1.03	0.96; 1.11	-
≥71	0.10	3.20	1.68; 6.10	-	1.69	1.01	0.88; 1.64	-
Sex, sexual orientation, and ethnicity	-	-	-	<0.001	-	-	-	<0.001
MSM (base)	0.031	-	-	-	1.91	-	-	-
Black African heterosexual men	0.023	0.58	0.41; 0.82	-	1.71	0.91	0.84; 0.98	-
Other heterosexual men	0.047	1.08	0.75; 1.55	-	1.74	0.88	0.80; 0.95	-
Black African women	0.021	0.70	0.52; 0.96	-	1.85	1.04	0.97; 1.11	-
Other women	0.042	0.90	0.61; 1.31	-	2.14	1.02	0.94; 1.11	-
IVDU	-	-	-	-	-	-	-	-
No (base)	0.028	-	-	-	1.85	-	-	-
Yes	0.049	0.98	0.48; 2.02	0.96	1.78	1.03	0.87; 1.23	0.72
Quarterly period[a]	-	0.98	0.97; 0.99	<0.001	-	0.99	0.99; 0.99	<0.001
New patient	-	-	-	-	-	-	-	-
No (base)	0.023	-	-	-	1.76	-	-	
Yes	0.19	2.72	2.13; 3.46	<0.001	4.76	2.12	2.01; 2.22	<0.001
CD4 count (cells/μL)	-	-	-	<0.001	-	-	-	<0.001
≤50	0.35	9.98	6.95; 14.31	-	5.09	1.62	1.47; 1.78	-
51–200	0.10	5.20	3.98; 6.72	-	3.34	1.48	1.40; 1.55	-
201–500	0.026	1.85	1.50; 2.28	-	2.02	1.14	1.11; 1.18	-
≥501 (base)	0.013	-	-	-	1.67	-	-	-
History of virological failure and current VL (copies/mL)	-	-	-	<0.001	-	-	-	<0.001
No virological failure history and VL <200 (base)	0.018	-	-	-	1.61	-	-	-
Virological failure history and VL <200	0.024	1.39	1.08, 1.80	-	2.20	1.14	1.09; 1.19	-
Current VL ≥200 irrespective of virological failure history	0.077	1.87	1.51; 2.32	-	3.12	1.18	1.13; 1.22	-

Abbreviation: CI, confidence interval; IRR, incidence rate ratio adjusted for all model parameters; IVDU, intravenous drug use; MSM, men who have sex with men; VL, viral load.

[a]Fitted as a continuous variable where Q1 2010 = 0 and Q4 2017 = 31.

[b]Unadjusted rates per 3-month period.

category) was £518 (95% CI 450–587) per quarter. The largest additional cost was for new patients (£654 per quarter), then for CD4 category (£618, £295, and £62 for CD4 categories ≤50, 51–200, and 201–500 cells/μL, respectively) and for VL ≥200 copies/mL irrespective of virological failure history (£165), or VL <200 copies/mL virological failure with a history of virological failure (£90).

Age was predictive of costs ($p = 0.008$), but there was some evidence to suggest the relationship was non-linear. For example, compared with individuals aged 18–30 years (base), the quarterly care costs for people with HIV aged 31–50 years were £77 (95% CI 26–129) lower. However, compared with individuals aged 18–30 years, the quarterly costs for people aged ≥71 years was only £18 (95% CI −65 to 101) lower. The variable representing sex, sexual orientation, and ethnicity was also significantly associated with cost ($p < 0.001$), with the lowest costs for Black African and other heterosexual men and the highest cost for other women. However, this

TABLE 4 Estimated costs per quarter using generalized estimating equations.

Category	Model 3		
	Coefficient (£)[b]	95% CI (£)	*p*-value
Constant	518	450; 587	<0.001
Age in years	-	-	0.008
18–30 (base)	-	-	-
31–50	−77	−129; −26	-
51–70	−72	−127; −17	-
≥71	−18	−101; 65	-
Sex, sexual orientation, and ethnicity	-	-	<0.001
MSM (base)	-	-	-
Black African heterosexual men	−74	−120; −29	-
Other heterosexual men	−48	−97; 2	-
Black African women	−19	−61; 22	-
Other women	39	−19; 96	-
IVDU	-	-	-
No (base)	-	-	-
Yes	26	−57; 109	0.54
Quarterly period[a]	−5	−6; −4	<0.001
New patient	-	-	<0.001
No (base)	-	-	-
Yes	654	578; 730	<0.001
CD4 count (cells/μL)	-	-	<0.001
≤50	618	348; 887	-
51–200	295	235; 355	-
201–500	62	45; 78	-
≥501 (base)	-	-	-
History of virological failure and current VL (copies/mL)	-	-	<0.001
No virological failure history and VL <200 (base)	-	-	-
Virological failure history and VL <200	90	61; 119	-
Current VL ≥200 irrespective of virological failure history	165	126; 204	-

Abbreviations: CI, confidence interval; IVDU, intravenous drug use; MSM, men who have sex with men; VL, viral load.

[a]Fitted as a continuous variable where Q1 2010 = 0 and Q4 2017 = 31.

[b]Adjusted for all model parameters.

variable, age, and calendar year had less of an impact than other factors.

Sensitivity analysis

None of three tests for interaction were statistically significant when predicting rates of inpatient episodes ($p \geq 0.25$ in all instances). While all tests for interaction were statistically significant when predicting outpatient appointment rates ($p < 0.001$ in all instances) and costs ($p \leq 0.013$ in all instances), qualitatively different effects of one variable according to levels of another were not seen.

Restricting the definition of an active period or extrapolating CD4/VL measurements to orover 6 months rather than 12 months had a negligible impact on the results of all three models. The results also did not materially change when the definition of an active period was increased to 18 months and CD4/VL measurements were additionally extrapolated over this duration, except to reduce the coefficient associated with CD4 ≤ 50 cells/μL to £499 (95% CI 236–761). Reducing the cost of each outpatient appointment where the clinical speciality was unclear by 50% from £274 reduced the quarterly cost of treatment in the first 6 months following HIV diagnosis to £578 (95% CI 513–643), having a CD4 ≤50 cells/μL to £542 (95% CI 316–769) and the constant to £475 (95% CI 414–536), but had negligible impact on the remaining coefficients.

DISCUSSION

We assessed the costs of caring for people with diagnosed HIV infection using routinely collected data (2010–2017) from a large HIV treatment centre in a country with universal access to health care, in combination with information on national unit costs. The mean adjusted cost of caring for people with HIV was £518 per quarter in the base group of all categories, excluding the cost of ART. Outpatient visits accounted for 98% of hospital activity and 88% of total costs. Inpatient stays were infrequent (once every 9 years on average) and accounted for only 6% of total costs. Multivariable analysis showed that the factors most strongly associated with increased costs were being a new patient to the Trust and having a low CD4 count category, followed by current viral non-suppression or previous virological failure. Demographic factors had a lesser impact on costs. The sensitivity analyses suggest that the findings were generally robust to alternative assumptions.

Directly comparing our cost estimates with those in the existing literature is difficult because of differences in study design and levels of reporting [21]. However, the most recent UK study that has been published in full used routine data from 14 hospitals to estimate annual costs for two cohorts: people who were first diagnosed with HIV with CD4 ≤200 cells/μL or those with CD4 >200 cells/μL, who had not previously received ART [13]. Inflating the reported 2008 costs to 2018/19 values produces annual clinic/hospital costs of about £8035 and £5085 (excluding the costs of ART provision) for the two groups, respectively, which are considerably higher than our unadjusted estimate of about £1756 per year (£439 × 4). While it is difficult to be precise about the cause of this variation, assuming our definition of mean unadjusted outpatient plus test costs (£1640) is equivalent to the definition of outpatient test plus procedures costs (£1529–£1871) in Beck et al., the two analyses produce qualitatively similar results. The main differences appear to be in the inpatient costs, which, depending on the chosen cohort from Beck et al., are ∼£727–£1666 per year lower in our study. Moreover, Beck et al. also include a 'non-ART drugs' category, which represents an additional £2324–£3790 per person per year. However, as the drugs and/or their purpose are not specifically listed, it is difficult to know whether they represent costs that are still relevant in a contemporary sense but have been excluded from our analysis or whether they are subsumed within the national reference costs that we have applied.

In a similar study to ours in a different north London-based hospital, Rein et al. reported a mean unadjusted rate of hospitalization of about once every 17 years, over a similar calendar period [22]. The rate we report is approximately double this amount, once every 9 years. Given that CD4 count has been shown to be the strongest predictor of care usage, one plausible explanation for this difference is that the Rein sample, which was recruited from an HIV outpatient clinic, recorded a median CD4 count of 621 cells/μL (IQR 441-820) at the study start. The equivalent value in our study, which enrolled a broader sample in that it included all adults with HIV registered at the NMUHT, was 410 cells/μL (IQR 240-610). Thus, our study may contain proportionately more periods in which people with HIV were experiencing lower levels of immunological functioning and were therefore more likely to be hospitalized.

Unlike previous analyses such the UK's REACH study [23], we did not find that increasing age was associated with increased levels of outpatient activity. A number of factors could explain these different findings. First, REACH defined 'contact' using a combination of test results and ART usage rather than outpatient visits per se. Second, REACH included data from an earlier time period, when clinical practices could have been different (2000–2012). Last, it is possible that the care requirements of people with HIV change as they aged. For example, it is possible that the need for routine HIV outpatient visits has reduced but the total number of visits is maintained because of factors related to ageing. Further analysis disaggregating the clinic types could help address this issue.

The strength of this analysis is that it is based on a large cohort of individuals diagnosed with HIV, but a limitation is that the sample is from a single UK Trust. A second limitation is that we were not able to adjust the predictions for the impact of lifestyle factors such as smoking and history of recreational drug use, which are known to be prevalent in HIV-diagnosed populations [24], and also for socioeconomic factors, which are strongly linked to health outcomes [25]. Thus, the independent impact of these factors in terms of their contribution to total hospital costs is unknown. Third, the SARS-CoV-2 pandemic has unquestionably changed how most HIV and non-HIV services are currently being delivered in the UK. However, the extent to which these changes will remain permanent is unknown, meaning the relevance of our results for use in future studies is difficult to judge. Fourth, while cost estimates are an essential component of any economic assessment, on their own they have an ambiguous interpretation. For example, a relatively 'low' cost could be indicative of better health, and therefore less need, or could partly reflect difficulties accessing appropriate care. Last, the costs are stated in 2018/19 UK prices [26] and should be inflated to current prices if used any subsequent analysis–for 2021/22, this would be by ∼7.5% (https://kar.kent.ac.uk/100519/).

In summary, we assessed the frequency of inpatient and outpatient hospital visits by people with HIV and the associated costs, at an English health care Trust. The results indicated that the majority of costs were attributable to outpatient appointments and that the strongest predictors of cost were being a new Trust patient and having a very low CD4 count. Future studies should assess the impact of the SARS-CoV-2 pandemic on these findings.

AUTHOR CONTRIBUTIONS

Alec Miners, Fiona C. Lampe, Valentina Cambiano, Achim Schwenk, Alison Rodger, Valerie Delpech, and Andrew N. Phillips conceived and planned the project. Achim Schwenk provided the data, and Alec Miners and Zia Sadique processed the data and conducted the analyses. Alec Miners drafted the manuscript. All authors contributed to data interpretation and writing and revision of the manuscript. Alec Miners had full access to the

data in the study and takes responsibility for the integrity of the data and accuracy of the data analysis.

ACKNOWLEDGEMENTS

The authors thank Sheila Miller at the North Middlesex University Hospital NHS Trust for compiling the data extract.

FUNDING INFORMATION

This paper summarizes independent research supported by the National Institute for Health Research (NIHR) under its Programme Grants for Applied Research Programme (grant reference number RP-PG-1212-20006). The views expressed are those of the authors and not necessarily those of the NHS, the NIHR, or the Department of Health. This research is being conducted as part of a NIHR-funded programme grant called PANTHEON; a collaborative project between University College London, the London School of Hygiene and Tropical Medicine, the Medical Research Council, and others. The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript.

CONFLICT OF INTEREST STATEMENT

Valentina Cambiano has received consulting fees from the World Health Organization. Alison Rodger has received speaker's fees from Gilead. Alec Miners is currently an employee of Source Economics. The other authors declare no conflicts.

DATA AVAILABILITY STATEMENT

The dataset contains individual treatment records of people living with HIV and cannot be shared.

ETHICS STATEMENT

The study received UK Health Research Approval to proceed, reference 17/HRA/0013; individual patient consent was not required.

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How to cite this article: Miners A, Lampe FC, Cambiano V, et al. Estimating the hospital costs of care for people living with HIV in England using routinely collected data. *HIV Med*. 2023;1-11. doi:10.1111/hiv.13529

APPENDIX A

TABLE A1 Types of outpatient appointment and associated unit cost.

Type	Unit cost (£)	Source and outpatient service code
First HIV visit	283	NHS national reference costs 2018/19, HIV1[c]
Regular HIV follow-up	274/284[a]	NHS national reference costs 2018/19, HIV2/HIV3[c],[a]
Nurse appointment	19.73	Curtis et al.[d] and assumptions[b]
Counselling	199	NHS national reference costs 2018/19, 656[c]
Dietician	85	NHS national reference costs 2018/19, 655[c]
Phone call	7	NHS national reference costs 2018/19, ASC1[c]
Midwifery	99	NHS national reference costs 2018/19, 560[c]
Renal clinic	196	NHS national reference costs 2018/19, 306[c]
Tuberculosis clinic	291	NHS national reference costs 2018/19, 350[c]
Other	274	Assumption
CD4 test	22	Assumption
Viral load test	20	Assumption
Resistance test	50	Assumption

Note: [a] Stable/complex people with HIV defined as CD4 >200 and ≤200 cells/mm^3, respectively. [b] Based on 20% of visits with a band 7 nurse at £103 per hour^2 for 20 minutes and 80% of visits with a band 6 nurse at £74 per hour^2 for 10 minutes, all with an extra £3 for clinical chemistry tests. [c] NHS Improvement. *National schedule of reference costs 2018/19*. [Available from: https://www.england.nhs.uk/national-cost-collection/#ncc1819. [d] Curtis L, Burns A. *Unit costs of health and social care 2018*. [cited 18/12/2018]; Available from: https://kar.kent.ac.uk/70995/1/Unit%20Costs%202018%20-%20FINAL%20with%20bookmarks%20and%20covers%20%282%29.pdf.