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ORIGINAL RESEARCH ARTICLE

Efficiency of the EmERGE Pathway of Care in Five European HIV Centres

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Abstract

Objective We aimed to calculate the efficiency of the EmERGE Pathway of Care in five European HIV clinics, developed and implemented for medically stable people living with HIV.

Methods Participants were followed up for 1 year before and after implementation of EmERGE, between April 2016 and October 2019. Micro-costing studies were performed in the outpatient services of the clinics. Unit costs for outpatient services were calculated in national currencies and converted to US$ 2018 OECD purchasing parity prices to enable between clinic comparisons in terms of outcomes and costs. Unit costs were linked to the mean use of services for medically stable people living with HIV, before and after implementation of EmERGE. Primary outcome measures were CD4 count and viral load; secondary outcomes were patient activation (PAM13) and quality of life (PROQOL-HIV). Out-of-pocket expenditure data were collected.

Results There were 2251 participants: 87–93% were male, mean age at entry was 41–47 years. Medically stable people living with HIV had outpatient visits in four sites which decreased by 9–31% and costs by 5–33%; visits and costs increased by 8% in one site, which had to revert back to face-to-face visits. Antiretroviral drugs comprised 83–91% of annual costs: the Portuguese site had the highest antiretroviral drug costs in US$ purchasing parity prices. Primary and secondary outcome measures of participants did not change during the study.

Conclusions EmERGE is acceptable and provided cost savings in different socio-economic settings. Antiretroviral drug costs remain the main cost drivers in medically stable people living with HIV. While antiretroviral drug prices in local currencies did not differ that much between countries, conversion to US$ purchasing parity prices revealed antiretroviral drugs were more expensive in the least wealthy countries. This needs to be taken into consideration when countries negotiate drug prices with pharmaceutical vendors. Greater efficiencies can be anticipated by extending the use of the EmERGE Pathway to people with complex HIV infection or other chronic diseases. Extending such use should be systematically monitored, implementation should be evaluated and funding should be provided to monitor and evaluate future changes in service provision.

1 Background

Mobile health (mHealth) is the use of digital health services and the transfer of information via mobile phones, tablet computers, smartphones or other monitoring devices [1–3]. Mobile health has become important in linking and integrating health services especially for people living with chronic diseases [4–6].

The Evaluating mHealth technology in HIV to improve Empowerment and healthcare utilisation: Research and innovation to Generate Evidence for personalised care (EmERGE) Study [7] investigated the use of a mHealth Clinical Pathway of Care in five HIV clinics in Belgium, Croatia, England, Portugal and Spain [8–12]. This included the production and implementation of a mobile health application (App) in these sites, which allowed personal health information to be exchanged between patients and their caregivers (Fig. 1).

Evaluating the impact of HIV health services in countries at both individual and health system levels has become a priority [13, 14]. The life expectancy of people living with HIV (PLHIV) now approximates that of those not living with HIV [15, 16], increasing the number of PLHIV, including those aged 50 years or older [17].

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Key Points for decision makers

Mobile health interventions can be developed across different healthcare settings in different countries and produce efficiencies in these countries. The efficiencies produced in this study were limited as the focus in this study was on medically stable people living with HIV.

Greater efficiencies can be anticipated if the EmERGE Pathway is extended to people with more complex HIV infection or other chronic conditions. Extending its use should be monitored systematically in terms of its use, cost, outcome and impact. Apart for funding to develop and monitor the extended use of pathways of care, health professionals and researchers should have access to contemporary and detailed routine information and when required, supplemented through micro-costing studies.

The cost of antiretroviral drugs provides a large proportion of the management cost for people living with HIV. National prices for antiretroviral drugs should be discussed and set taking into consideration the 'wealth' of that country, as reflected by indices such as the country's purchasing power parity index.

A recent review of mHealth highlighted nine functions that an 'ideal' App should fulfil [3]. In addition to these, the confidentiality and security of data collected, transmitted and stored at either end need to be protected (Table 1), and the tools used to ensure this need to be affordable and efficient [18].

To date, most mHealth studies have not included the cost for developing, implementing and supporting these Pathways, let alone assess their cost effectiveness or cost savings that implementation potentially provides. The need for such efficiency studies has been recognised in the past [19, 20], but to date few efficiency studies have been performed [3, 4, 21].

Few studies since have compared the use of mHealth in different healthcare systems and countries, and it was for this reason that this comparative analysis was performed in five European countries. Before-and-after studies were performed to assess the efficiency of implementing the EmERGE Pathway in five European HIV clinics [22]. Details of the HIV clinics participating and the clinic-specific results are described in a number of publications that have published to date [8–12]. To enable both outcomes and costs to be compared between sites in the different countries, national monetary units were converted to OECD US 2018 purchasing power parities (US$PPP) [23]. This transformation enabled between-clinic comparative analyses to be produced.

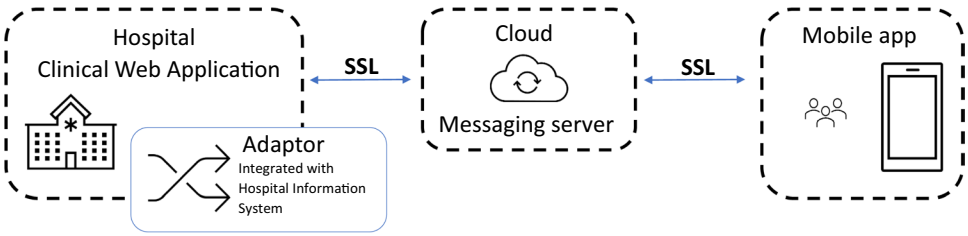

Fig. 1 Conceptual framework of the EmERGE Pathway of Care. *App* application, *SSL* secure sockets layer [7]

Table 1 Eleven requirements of a tele-medicine system [3*, 18**]

1. Patient-provider and peer communication*
2. Medication and appointment reminders*
3. A medication checklist, pill identification function and list of current and discontinued medicines*
4. Laboratory reports (CD4 count, viral load, sexually transmitted infections, glucose and complete blood count)*
5. Pharmacy information*
6. Nutrition and fitness trackers*
7. Resources, links to social services, substance abuse support, video testimonials, case management*
8. Settings (profile picture, password and alerts)*
9. A search function*
10. Protecting the confidentiality and security of personal information at rest and in-transit**
11. Affordability and efficiency of the technology**

The specific objectives of this study were: (1) to calculate and compare the use of outpatient services of each clinic by EmERGE participants 1 year before and 1 year after the implementation of the EmERGE Pathway; (2) to calculate and compare unit costs of HIV outpatient services for EmERGE participants between clinics; (3) to calculate and compare the change in annual outpatient costs between clinics, pre- and post-implementation of EmERGE; and (4) to calculate and compare the efficiency, cost effectiveness or cost minimisation, of the implementation of the EmERGE Pathway between clinics.

2 Methods

2.1 Context

Participating clinics were teaching hospitals that provide local, regional or national HIV services: Institute of Tropical Medicine (ITM) Antwerp, Belgium; University Hospital for Infectious Diseases (UHID), Zagreb, Croatia; Hospital Clinic-IDIBAPS (HC-IDIBAPS), Barcelona, Spain; Hospital Capuchos, (HC-CHLC). Lisbon, Portugal and the Brighton and Sussex University Hospitals NHS Trust (BSUHT), Brighton, UK. The day that EmERGE participants were recruited was their baseline and they were followed up for 12 months in their respective HIV unit between April 2016 and October 2019. Recruitment criteria for participants included that they were medically stable PLHIV and virally suppressed (MS-PLHIV; Table 2) [24]. Recruitment procedures, which were similar across all five sites, have been described elsewhere [8–12]. As participants in each of the sites were medically stable, they predominantly used HIV outpatient services, which were the foci of the micro-costing exercises in each site.

Outpatient services were supported by clinical and overhead departments. The detailed service pathway of EmERGE participants within each clinic have been described elsewhere [8–12, 25]. Four of the sites operated one HIV clinic: as per EmERGE protocol, one visit per year was an electronic 'visit'; after reviewing the test results, these were sent via the EmERGE App to participants with recommendations for future treatment. The other annual visit was a routine face-to-face (F2F) visit, or virtual visit (V-visit) for the participants seen in the virtual clinic of the HC-IDIBAPS during their first year of the study.

The Barcelona site initially operated three separate HIV outpatient clinics: two F2F clinics while the third offered a video-consultation appointment system since 2005 [26]. However, the videoconferencing and sound system in use was inadequate for the Study and could not be upgraded in a timely manner to continue to provide services; this clinic was closed during the second year of the study. Participants who attended the virtual clinic during the first year of the study were transferred to the two F2F clinics during the second year [8].

2.2 Data Collected

Information on the annual use, cost and outcome of HIV services by EmERGE participants before and after the implementation of EmERGE Pathway was required to estimate its efficiency. This required process information on the use of

Table 2 Inclusion and exclusion criteria for EmERGE participants [24*]

Inclusion criteria: patients who meet all of the following criteria were eligible for this study	Documented HIV infection
	Aged at least 18 years
	Able to give informed consent
	In possession of a smartphone, tablet or similar technology supporting the mobile health platform
	Clinically stable on anti-retroviral therapy. This was defined as receiving anti-retroviral therapy for at least 1 year and an unchanged regime for at least 3 months, 2 consecutive undetectable viral load measures (< 50 copies/mL), no current pregnancy and without any new World Health Organization clinical stage 2, 3 or 4 events within the previous 12 months*
Exclusion criteria: patients who met one or more of the following criteria were excluded from the study	Aged less than 18 years
	Pregnant
	Participating in a clinical trial or receiving an investigational medication
	Unable to comprehend the patient information sheet
	Unable to comprehend the instructions for using the mobile health platform
	Considered for any other reason by their regular physician to be unsuitable for study participation

services by individual EmERGE participants, unit costs of services used and outcome measures.

2.3 Costing Health Facilities

The "top-down" or "bottom-up/ingredient-based" methods are the main methods for micro-costing a service [27, 28]. The method used depended on the available granularity of the data: an ingredient-based approach could be used, *mutatis mutandis*, in four clinics, while the 'top-down' method had to be applied in one site, the BSUHT [25]. Having reviewed some of the underlying data, a top-down overall unit cost per outpatient visit, incorporating SCOPE expenditures of this clinic, was agreed with the Head of Income and Costing at the BSUH based on HIV outpatient expenditure provided by the BSUH to the UK Department of Health in 2019 [11].

2.4 Process Data

Process data consisted of the use of services by individual participants pre-EmERGE and post-EmERGE and were obtained from electronic medical records. Participants predominantly used HIV outpatient services in each site, which were the foci of the micro-costing studies for the sites.

2.5 Unit Costs Data

The micro-costing studies were based on UNAIDS guidance documents [27, 28]. To estimate unit costs, departmental process and financial data were collected from relevant departments. Individual process data identified services used by individual EmERGE participants. Departmental financial data collected included *staff, consumables, overheads, procedures* and *equipment costs* (SCOPE) [25]. These data were combined with the departmental workload generated by EmERGE participants to estimate departmental unit costs. Unit costs and outpatient resource use were combined to calculate annual costs of outpatient services for EmERGE participants [25].

The unit and annual costs were initially estimated in national currencies [25]. To allow for comparisons between the five sites, located within different healthcare systems and economies, cost estimates were converted to OECD US$PPP (Table 3) [23]. Based on the 2018 OECD US$PPP, the conversion factor for Belgium was 0.770, Croatia 3.331, Spain 0.635, UK 0.687 and Portugal 0.579 [30].

The country's gross domestic product was used as a proxy indicator of a country's wealth, based on the value of all final goods and services produced within a nation, within a given year. The 2017 gross domestic product PPP estimates were used to make comparisons between the size or 'wealth' of the national economies of the countries with participating clinics [23, 30].

2.6 Statistical Methods

Data analyses were based on all participants with baseline visits. CD4 count and viral load data were collected longitudinally at the participating sites. We used mixed models to derive 3-monthly time-weighted changes since the baseline visit in CD4 counts and viral load measurements [31]. We assessed the time period up to 1 year prior to and 1 year post-entry into the EmERGE Study. All statistical analyses were carried out using SAS statistical software 9.4 [32]. A MIXED procedure was used by fitting CD4 results as a dependent variable. Independent variables included the fixed effects of study visit timepoints grouped into 3 months. A covariance matrix was used to model the within-patient errors. Estimates of effects are based on MIXED models and assume any missing data were missing at random. Trends over time are presented as point estimates derived from the models. Similarly, viral load data were analysed using this method after log transformation in order to stabilise their variance.

The mean number of services used per patient year (MPPY) was calculated using methods employed previously [33–35], based on the following formula:

$$M = \frac{\sum_{i=1}^{n}\sum_{j=1}^{k} S_{ij}}{\sum_{i=1}^{n}\sum_{j=1}^{k}(t_{ij} - t_{i(j-1)})} \times 365, \quad (1)$$

where n is the total number of individuals, k is the day of censoring, S_{ij} is the use of service by individual i on jth day, t_{ij} is the number of days of follow-up for individual I, and M is the mean of services S per patient-year.

The denominator comprised the total follow-up for all participants 1-year pre-entry and 1-year post-entry into EmERGE. The data were left censored at the 1-year pre-baseline visit. Post-1-year follow-up data were right censored at either 1 year since the baseline visit if participants were still under follow-up at 1 year, or if they had died during the 1-year follow-up then their date of death, or if they were lost to follow-up, which ever came first. Numerators were calculated by summing the use of outpatient services (Eq. 1). Exact Poisson 95% confidence intervals were estimated for MPPY based on the distribution of the observed number of outpatient visits divided by the total duration of follow-up for all patients during a calendar year. Average annual costs per patient-year of HIV outpatient service provision were produced by multiplying the MPPY outpatient visits by their respective unit costs. The total annual costs for providing services were obtained by adding the annual costs for outpatient visits, with the annual cost of tests, drugs and procedures performed at each of the sites [25, 29].

Table 3 Unit costs of tests and ARVs for EmERGE clinics in OECD US$ 2018 PPP [23]

Institute of Tropical Medicine, Antwerp	Cost/unit cost, US$PPP
Unit cost per EmERGE patient outpatient clinic visit	210.4
Unit cost per EmERGE patient central laboratory test	18.2
Unit costs per EmERGE patient viral load test	32.5
Unit costs per EmERGE patient CD4 test	2.60
Annual cost of ARVs for EmERGE patients	11,477
University Hospital for Infectious Diseases, Zagreb	**Cost/unit cost**
Unit cost per EmERGE outpatient clinic visit	101.8
Pharmacy department costs	
Annual pharmacy costs excluding drugs per EmERGE patient	95.2
Annual pharmacy cost of ARVs per EmERGE patient	10,670.7
Total annual pharmacy costs per EmERGE patient	10,765.8
Unit cost per EmERGE patient biochemistry laboratory test	2.70
Unit cost per EmERGE patient haematology laboratory test	13.8
Unit costs per EmERGE patient viral load test	163.0
Unit cost per EmERGE patient CD4 test	156.7
Unit cost per EmERGE patient radiology investigation	0.90
Infectious Diseases Department, Hospital Clínic, IDIBAPS, Barcelona	**Cost/unit cost**
Unit cost per EmERGE dispensario clinic outpatient visit	270.1
Unit cost per EmERGE ICMiD office virtual outpatient visit	70.9
Unit cost per EmERGE ICMiD office anal canal day ward procedure	626.13
Unit cost per EmERGE day-care hospital Outpatient visit	185.29
Unit cost per EmERGE day-care hospital Fibro scan day ward procedure	100.7
Unit cost per EmERGE day-care hospital DEXA scan day ward procedure	100.7
Unit cost per EmERGE pharmacy patient excluding ARV costs	70.4
Annual cost of ARVs for EmERGE patients	11,585.8
Unit cost per EmERGE biochemistry laboratory test	1.1
Unit cost per EmERGE haematology laboratory test	3.2
Unit cost per EmERGE microbiology laboratory test	20.5
Unit cost per EmERGE immunology laboratory test	31.5
Unit cost per EmERGE patient radiology investigation	62.0
Hospital Capuchos, Centro Hospitalar De Lisboa Central, Lisbon	**Cost/unit cost**
Unit cost per EmERGE HIV outpatient visit	165.8
Annual cost per pharmacy service for EmERGE patient excluding ARVs	1728.8
Annual unit cost of ARVs per EmERGE patient	17,229.7
Unit cost per EmERGE combined laboratory test	5.2
Unit cost per EmERGE radiological investigation	62.2
Brighton and Sussex University Hospitals NHS Trust, Brighton[a]	**Cost/unit cost**
Unit cost per EmERGE outpatient clinic visit	195
Annual unit cost of ARVs per EmERGE patient	9595.3

ARV anti-retroviral drugs, *BSUH* Brighton and Sussex University Hospitals NHS Trust, *DEXA* dual-energy X-ray absorptiometry, *PPP* purchasing power parities

[a]A top-down overall unit cost per outpatient visit, incorporating SCOPE expenditures, was agreed with the Head of Income and Costing at the BSUH based on HIV outpatient expenditure provided by the BSUH to the UK Department of Health in 2019[11]

2.7 Primary and Secondary Outcome Measures

The primary outcome measures were changes in CD4 counts and viral load measurements, 12 months before and after the implementation of EmERGE. Secondary outcomes measures included patient activation as reflected by the PAM13 [36] and for quality-of-life measures the PROQOL-HIV was used [37]; changes in PAM13 and PROQOL-HIV were monitored during the 12 months post-implementation of EmERGE.

2.8 Out-of-Pocket Expenditure for EmERGE Participants

The clinic analyses provide information on the direct costs of the implementation of EmERGE. Data were also collected on some of the indirect costs, including time off work for clinic appointments, return travelling time and costs for clinic appointments, and the socio-economic status of the participants [38]. Where appropriate, these were analysed in terms of their medium values and interquartile ranges (IQRs).

3 Results

There were 2251 participants recruited across five sites, with a range from 244 to 586 per site (Table 4); 87–93% were male and the mean age at recruitment ranged from 41.0 years (95% confidence interval 39.9–41.9) to 47.0 years (95% confidence interval 46.2–47.8). Participants in full-time employment ranged from 70% to 84%, working a median 37.5 or more hours per week, with the lowest median monthly income of $1580. Monthly income was higher for Barcelona participants compared with those from Lisbon and Zagreb; 12% of Antwerp and 25% of Brighton participants had incomes less than $1948 and $2183 per month respectively. Of all participants, 5–16% received additional social services support; median monthly support ranged from $318 in Zagreb to $1558 in Antwerp (Table 4).

Sick days 3 months before enrolment was a median 0 days (IQR 0–1); 50–82% of participants did not take a day off work to visit the clinic. Median time for a return trip to their clinic ranged from 1.5 hours (IQR 1–2 hours) in Brighton to 2.0 hours (IQR 1–3) in Lisbon; median costs for a return trip ranged from $5 (IQR $0–13) to $41 (IQR $6–90).

3.1 Primary and Secondary Outcome Measures

None of the participants had substantial changes in their primary outcome measures, with CD4 counts either remaining the same or increased; viral load for all participants was and remained undetectable during the study (Fig. 2). For patient activation and quality-of-life measures, based on PAM13 and PROQOL-HIV respectively, no substantive changes were observed during the 12 months post-implementation [39]. Given the lack of substantial changes in primary and secondary outcomes, a cost-minimisation analysis was conducted in each of the sites.

3.2 Unit Costs

The cost per outpatient visit ranged from $166 in Zagreb to $210 in Antwerp. The average unit costs for outpatient visits across the three Barcelona HIV outpatient clinics was $180 (Table 3); unit costs ranged from $80 for the virtual clinic to $186 and $272, respectively, for the two F2F clinics [25, 29].

Unit costs for tests and procedures differed between clinics, depending on the number and type performed within each outpatient service [25]. The annual costs for antiretroviral drugs (ARVs) ranged from $9593 in Brighton to $11,586 in Barcelona with Zagreb and Antwerp prices falling within this range: the annual ARV cost in Lisbon was the highest at $17,230.

3.3 Annual Use and Cost of Services Pre- and Post-EmERGE

The MPPY outpatient visits decreased by 9% to 35% in four clinics except for the Barcelona site where MPPY of outpatient visits increased by 8% between periods (Table 5). A 5–33% reduction was observed in average annual cost for providing outpatient services in the four clinics (Table 5), while the cost for the Barcelona site increased by 8%. In this patient group, the main annual cost driver were ARVs, which comprised between 83% and 91% of the annual cost. The total annual cost of services did not decrease substantially because of the high ARV costs. Based on gross domestic product (PPP), in 2017, the UK was the 'wealthiest' of the five countries, followed by Spain and Belgium, while Portugal and Croatia were the least wealthy (Table 5).

4 Discussion

The introduction of the EmERGE platform reduced average costs between 5% and 33% and the number of outpatient visits between 9% and 31% in four clinics. The 8% increase in outpatient visits in the Barcelona site was due to the closure of the virtual HIV outpatient clinic and the transfer of participants back to the more expensive F2F clinics. Barcelona participants who only used F2F clinics, recorded a 5% reduction in the use and cost of services, while EmERGE participants transferred from V-visits to the F2F clinics increased their annual costs [8]. A switch from F2F to V-visits was also observed in Brighton [11] and associated with a reduction in outpatient services and their costs [12].

The cost of outpatient services is governed by many factors apart from the number and nature of outpatient visits. For instance, the reduction in outpatient costs at the Zagreb clinic was related to a reduction in outpatient visits and fewer CD4 tests being performed: the latter owing to a breakdown of the flow cytometer. Furthermore, in the UK National Health Service, F2F and V-visits are currently reimbursed at similar rates, without having established their actual costs; in Spain, the V-visits had lower unit costs compared with the F2F visits [8].

Table 4 Number of EmERGE study participants, mean age at study entry, socio-economic, out-of-pocket expenditure (2018 US$ PPP) and sick days (previous 3 months) for EmERGE participants

	Institute of Tropical Medicine, Antwerp	University Hospital for Infectious Diseases, Zagreb	Infectious Diseases Department, Hospital Clínic, IDIBAPS, Barcelona	Hospital Capuchos, Centro Hospitalar De Lisboa Central, Lisbon	Brighton and Sussex University Hospitals NHS Trust, Brighton
Number of participants	*N* = 244; 90% men	*n* = 293; 90% men	*N* = 546; 92% men	*n* = 586; 87% men	*N* = 565; 93% men
Mean age at study entry, years (95 CI)	44.9 (95% CI 43.6–46.2)	41.0 (95% CI 39.9–41.9)	43.3 (95% CI 42.0-44–6)	42.0 (95% CI 39.2–44.8)	47.0 (95% CI 46.2–47.8)
In full-time employment	81%	75%	84%	78%	70%
Median (IQR) number of hours worked	40 (IQR 40-45)	40 (IQR 40-45)	40 (IQR 34-40)	40 (IQR 36-44)	37.5 (IQR 35–40)
Median (IQR) monthly income	12% participants had monthly income less than $1948	$1801 (IQR $1351–$2402)	$2284 (IQR $1654–$3228)	$1580 (IQR $1097–2504)	25% participants had monthly income less than $2183
Percentage participants receiving social services or additional benefits	13%	16%	5%	14%	14%
Additional median monthly income (IQR)	$1558 (IQR $1164–$1818)	$318 (IQR $150–$468)	$732 (IQR $630–$1162)	$383 (IQR $307–$1149)	$761 (IQR $393–$1237)
Median (IQR) number of days off sick last 3 months	0 days (IQR 0–1)	0 days (IQR 0–0)	0 (IQR 0–0)	0 (IQR 0–0)	0 days (IQR 0–1)
Percentage that did not take day off to visit clinic	59%	59%	50%	67%	82%
Median time of return visit, hours (IQR)	1.8 (IQR 1–2.5)	1.5 (IQR 0.5–2.5)	1.5 (IQR 0.5–2.5)	2.0 (IQR 1–3)	1.5 (IQR 1–2)
Median (IQR) cost of return visit	$5 (IQR $0–$13)	$41 (IQR $6–$90)	$5 (IQR $0–$13)	$9 (IQR $5–$17)	$7 (IQR $0–$9)

CI confidence interval, *IQR* interquartile range, *PPP* purchasing power parity

We did not perform sensitivity analyses nor external data comparisons, which limits our findings; however, the before-and-after study provided a robust method for this health-technology assessment [22]. The reduction in outpatient services was associated with a stable or increasing CD4 count and viral loads remained undetectable during the study period among all participants. Patient activation measure PAM13 [36] and quality-of-life measure PROQOL-HIV [37] did not display substantial changes during the 12 months follow-up post-implementation [39]. However, these conclusions are limited as these secondary outcome measures were not compared with a control group.

Some privacy concerns existed especially among black and migrant women. Some of these individuals were anxious about using the App, as they were afraid that the App could be seen on the phone by friends or family members, some of whom might ask questions. These issues were discussed with relevant caregivers or community members at the time and in some cases resulted in these participants being able to discuss and disclose their sero-status with relevant friends or family members. For others, where this was not possible, they were able to use the App in what for them was a 'safe place'. The majority of participants, however, expressed trust in the privacy and security of the EmERGE platform, a trust that grew over time [40].

The EmERGE Pathway also changed the way staff interacted with participants, which may have added to the reduction in costs; however, these changes were not quantified. Protecting the confidentiality and security of information is of paramount importance to mHealth [41]. Readers are referred to other publications for a thorough discussion of these issues [18, 42].

The cost savings will have increased the fiscal space of each of the clinics, potentially enabling resources to be freed and channelled towards other needs. Savings so far were relatively small, owing to the dominant price of ARVs in managing MS-PLHIV; these comprised 83%–91% of annual outpatient costs. However, the relative cost of ARVs was

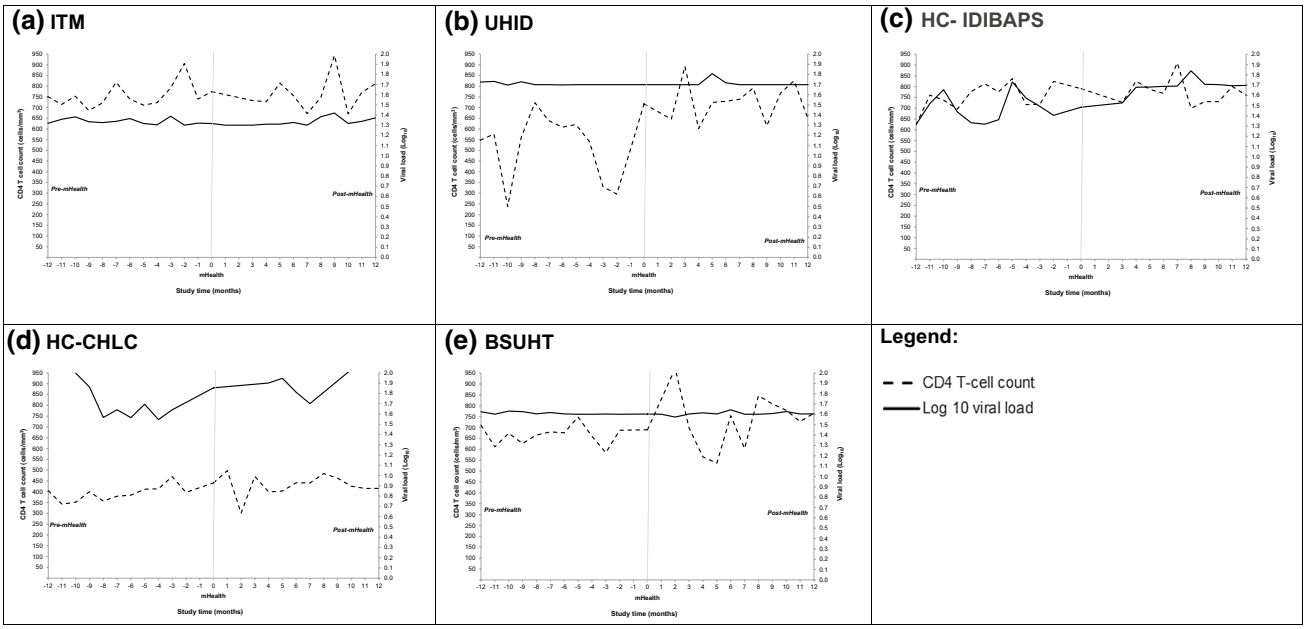

Fig. 2 Mean CD4 cell count and HIV viral load at implementation of the EmERGE Pathway (month 0) and 12 months before and after the start of the follow-up in each of the five participating centres. *BSUHT* Brighton and Sussex University Hospitals NHS Trust, Brighton, *HC-CHLC* Hospital Capuchos, Centro Hospitalar De Lisboa Central, Lisbon, *HC-IDIBAPS* Infectious Diseases Department, Hospital Clinic-IDIBAPS, Barcelona, *ITM* Institute of Tropical Medicine, Antwerp, *UHID* University Hospital for Infectious Diseases, Zagreb

higher in Portugal compared with the other countries, which becomes more apparent in terms of US$PPP: ARV prices in Portugal were the highest among all sites. Conversely, Croatia, the least wealthy of the five economies, pays similar ARV prices as England, Belgium and Spain. Measures to reduce ARV costs include switching to quality-assured and affordable generic forms of the ARVs, although the use of generic drugs is not without its issues. While most generic drugs are cheaper than branded drugs, this may not be the case in situations when there is lack of market competition, as has been seen with triple-line antiretroviral therapy [43]. Furthermore, off-patent drugs may be converted into 'specialty drugs' for which some producers may demand high prices [43]. Healthcare costs can be further reduced when using single daily pill regimes [44, 45].

Accounting practices in each of the hospital, which were not well developed within departments and at some central administrative levels, and these were major rate-limiting steps to obtain data for this study. All sites had a pre-costing visit to discuss the study with local stakeholders, followed by one of the investigators (PY) performing the on-site micro-costing study. When required, data collection was completed after the actual site visits. Data on departmental workload and SCOPE were the most difficult to obtain. It was possible to use the bottom-up method, *mutatis mutandis*, for four clinics but for Brighton the top-down method had to be used, resulting in less granularity of the Brighton analyses compared with the other sites. Collection of individual-level data that were stored electronically was the easiest to obtain [25]. Internal organisational changes also hampered the retrieval of information and this especially affected the Barcelona and Brighton sites.

Some of the staff, external to the HIV clinics, refused to participate as it "unnecessarily increased their workload" while others indicated that they did not "want the study to produce results that differed from those estimated by their staff". None of the hospitals in the study had integrated health information systems that linked individual and departmental process data to the use of services, their costs and outcomes.

5 Conclusions

The development and implementation of the *EmERGE Pathway* for MS-PLHIV have been demonstrated to work successfully in the five countries where the study was performed, despite their differences in socio-economic and cultural conditions. The EmERGE Pathway was found to be useful and acceptable to users and providers of services and provided cost savings in the clinics. Pilot sites are investing in the ongoing development and implementation of the EmERGE Pathway in their HIV clinic.

While most users and providers of HIV services liked the EmERGE Pathway, security and confidentiality issues with software-based interventions remain an issue at the

Table 5 Annual mean outpatient visits and average annual service costs in 2018 US$ PPP for each clinic and GDP: PPP (2017 OECD estimates)

	pre-EmERGE	post- EmERGE	Percentage change
Institute of Tropical Medicine, Antwerp			
Annual outpatient visits	2.6 (95% CI 2.4–2.8)	1.8 (95 CI 1.6–2.0)	31% decrease
Annual service costs	$1804 (95% CI $1730–$1882)	$1558 (95% CI $1505–$1622)	14% decrease
Annual ARV costs	$11,477		
Annual service costs and ARVs (%)	$13,281 (86%) (95% CI 13,207–13,359)	$13,035 (88%) (95% CI $12,982–$13,099)	2% decrease
Belgium GDP PPP	$529,200,000,000		
University Hospital for Infectious Diseases, Zagreb			
Annual outpatient visits	4.0 (95% CI 3.8–4.3)	3.3 (95% CI 3.1–3.5)	17% decrease
Annual service costs	$2143 (95% CI $2031–$2260)	$1435 (95% CI $1352–$1523)	33% decrease
ARV costs	$10,671		
Annual service costs and ARVs (%)	$12,814 (83%) (95% CI $12,702–$12,931)	$12,106 (87%) (95% CI $12,023–$12,194)	6% decrease
Croatia GDP PPP	$102,100,000,000		
Infectious Diseases Department, Hospital Clinic -IDIBAPS, Barcelona			
Annual outpatient visits	5.2 (95% CI 5.0–5.4)	5.6 (95% CI 5.4–5.8)	8% increase
Annual service costs	$1690 (95% CI $1573–$1822)	$1824 (95% CI $1707–$1950)	8% increase
ARV costs	$11,586		
Annual service costs and ARVs (%)	$13,276 (87%) (95% CI $13,159–$13,408)	$13,410 (86%) (95% CI $13,293–$13,535)	1% increase
Spain GDP PPP	$1,778,000,000,000		
Hospital Capuchos, Centro Hospitalar De Lisboa Central, Lisbon			
Annual outpatient visits	3.1 (95% CI 3.0–3.3)	2.0 (95% CI 1.9–2.1)	35% decrease
Annual service costs	$3615 (95% CI $3577–3648)	$3427 (95% CI $3400–$3456)	5% decrease
ARV costs	$17,230		
Annual service costs and ARVs (%)	$20,845 (83%) (95% CI $20,807–$20,878)	$20,657 (83%) (95% CI $20,630–$20,686)	1% decrease
Portugal GDP PPP	$314,100,000,000		
Brighton and Sussex University Hospitals NHS Trust, Brighton			
Annual outpatient visits	5.6 (95% CI 5.4–5.8)	5.1 (95% CI 4.9–5.3)	9% decrease
Annual service costs	$1093 (95% CI $1051–$1135)	$987 (95% CI $951–$1026)	9% decrease
ARV costs	$9595		
Annual service costs and ARVs (%)	$10,689 (90%) (95% CI $10,646–$10,730)	$10,582 (91%) (95% CI $10,546–$10,622)	1% decrease
UK GDP PPP	$2,925,000,000,000		

ARV antiretroviral drugs, *CI* confidence interval, *GDP* gross domestic product, *PPP* purchasing power parity

development and implementation stages. The implementation of complex systems in different countries may result in the loss of sites because of local conditions, which can range from the changes to or closures of services or sites, to the impact of local political inference.

Costing exercises may be hampered by a lack of local data, data that are difficult to access or political considerations when local financial staff are concerned that the findings generated by the costing exercise may differ from those that were generated by local financial staff, and which had been used to generate national information.

For MS-PLHIV, the EmERGE Pathway may not result in substantial cost savings especially in countries where ARVs are priced very high compared with the country's purchasing power parity index. In those countries, ARV prices should be set within the context of such PPP indices and where this has not yet been done, ARV prices could be re-negotiated.

Broader implementation of the use of the EmERGE Pathway to all PLHIV and other diseases will likely increase its efficiency. However, this should be systematically monitored, and funding should be made available by relevant agencies for such assessment over time. The use of mHealth has become an important method for "ensuring that all people can access the health services they need—without facing financial hardship—… key to improving the well-being of a country's population". [46].

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Declarations

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Consent for publication and Availability of data and materials Consent was obtained from participants to participate in the Study, and their consent for the publication andavailability of data and materials

Authors' contributions EJB, SM and PY developed the health economic aspects of the EMERGE Project in collaboration with AL, FG, LA, JB, MdFB and JW; PY, EJB, SM, AL, MJM, FG, MW, AL, IB, SZ, JB, ASC, ET, GR, MdFB, DF, JV and JW were responsible for the data collection; EJB, SM and PY were responsible for the analyses; EJB and SM were the lead authors in collaboration with PY, AL, MJM, FG, MW, LA, IB, SZ, JB, ASC, ET, GR, MdFB, DF, JV and JW, who all reviewed and commented on drafts of the paper.

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