**Supplementary appendices**

**1. Derivation of health state costs**

The table below provides further detail of the unit costs and assumptions used to estimate health state costs in the economic model.

**Table S1: Summary of unit costs and assumptions used to estimate health state costs in the economic model**

| **Resource type** | **Resource component** | **Unit cost (GBP)** | **Assumptions**  | **Source**  |
| --- | --- | --- | --- | --- |
| IV drugs - hospital\* | Ceftazidime 3g (per dose) | 3.38 | 42 doses in 14 days | Personal communication (ClinicalPharmacist)a |
| Tobramycin 481-560mg (per dose) | 16.25 | 14 doses in 14 days |
| Sodium chloride 0.9% (per dose) | 0.06  | 28 doses in 14 days |
| Heparin 50units in 5ml (per dose) | 0.44 | 42 doses in 14 days |
| **Total (per IV day)** | **27.82** |  |
| IV drugs - homecare\* | Ceftazidime 3g (per dose) | 32.88 | 42 doses in 14 days | Personal communication (ClinicalPharmacist)a |
| Tobramycin 481-560mg (per dose) | 48.04 | 14 doses in 14 days |
| Sodium Chloride 0.9% (per dose) | 0.64  | 28 doses in 14 days |
| Heparin 50units in 5ml (per dose) | 3.22  | 42 doses in 14 days |
| 30L WIVA waste bin (per 14-day course) | 5.99  | 1 unit |
| 1x100 Sani-cloth wipes (per 14-day course) | 24.85  | 1 unit |
| Delivery (per 14-day course) | 77.64 | 1 unit |
| **Total (per IV day)** | **165.36** |  |
| Nebulised drugs‡ | Tobramycin solution (per year) | 1,739.56 | Tobramycin 300mg/5ml; daily dose: 600mg | BNF (1), CF Registry Report 2018 (2), personal communication (ClinicalPharmacist,a Consultant in Respiratory Medicine and Adult Cystic Fibrosisb)  |
| Other aminoglycoside | 5.89 | Gentamicin 80ml/2ml; daily dose: 160mg |
| Colistin | 442.19 | Colomycin 2 million unit powder; daily dose: 2 million units |
| Promixin | 1,158.39 | Promixin 1million unit powder; daily dose: 4 million units |
| Aztreonam | 1,506.06 | Cayston 75mg powder; daily dose: 225mg |
| Colistimethate dry powder | 923.62 | Colobreathe 1.6 million units powder capsules; Daily dose: 3.32 million units |
| Tobramycin dry powder | 1,212.22 | Tobramycin 28mg powder capsules; daily dose: 224mg |
| Azithromycin | 47.51 | Azithromycin 250mg tablets; daily dose: 250mg |
| Prophylactic flucloxacillin | 4.00 | Flucloxacillin 250mg or 500mg capsules; daily dose:1g |
| Mannitol | 341.04 | Bronchitol 40mg inhalation powder capsules; daily dose: 800mg |
| DNase | 4,160.35 | Pulmozyme 2.5mg; daily dose: 2.5mg |
| Hypertonic saline | 91.33 | 6% or 7% inhalation solution; daily dose: 8ml |
| **Total** | **11,632.15** | **-** |
| Adherence intervention | Data transfer | **N/A (CD)** | Commercial value | PARI GmbH |
| Monitoring | **N/A (CD)** | Same costs as in the trial, conversion rate €1= £0.88756 (01/10/2019) | PARI GmbH |
| Data platform (management, maintenance, costumer support, hosting & penetration testing) | 20.60 | Costs of running the CFHealthHub plataform for 12 months divided by 5,900 patients eligible for the intervention | Farr Institute |
| Interventionists training | 21.37 | Three trainers (2 × 180.5 hours and 61 hours for developing training, delivering face-to-face and competency assessment), 30 interventionists (grade 7 physiotherapists); includes overheads for academic staff; divided by 5,900 patients eligible for the intervention; applicable only for the first year of the model | University of Sheffield (wages); PSSRU report 2021 (3) personal communication (hours and personnel involved)c |
| Ongoing fidelity support | 3.62 | Includes the costs of 15 interventionists, one programme manager, one data specialist, two research assistants, one trainer and overheads for academic staff; divided by 5,900 patients eligible for the intervention |
| Initial data set-up visit | 195.00 | Includes the costs of grade 7 physiotherapists and total of 3 hours of visits per patient; applicable only for the first year of the model | PSSRU report 2021 (3); personal communication c  |
| Delivery of intervention | 315.19 | Data from the intervention log from the trial, assumed the same average cost per patient for the 305 trial patients in the intervention arm  | PSSRU Report 2021 (3); ACtiF trial |
| **Total 1st year (annual costs)** | 777.18 |  |  |
|  | **Total subsequent years (annual costs)** | 560.81 |  |  |
| Nebuliser – intervention | eTrack | **N/A (CD)** | Annuitised cost per patient; equipment lifetime of 5 years and discount rate of 3.5% | PARI GmbH |
| Nebuliser – intervention | eflow | **N/A (CD)** |
| Resource use | IV in hospital (days) | 410.75 | Assumed to reflect cost of bronchiectasis, cost per non-elective bed-day (codes DZ12C to DZ12F), weighted by FCEs and average length of stay  | NHS Reference Costs 2020/2021 [(4) |
| Other hospitalisation IVs (total days) | 349.25 | Cost per non-elective excess bed-day weighted by FCEs; weighted average across all interventions |
| GP (mins) - surgery and at home | 4.23 | GP appointments of 9.22 minutes were assumed; unit cost includes direct care staff and qualification costs, and carbon emissions | PSSRU report 2021 (3) |
| Consultant hospital visits (no.) | 219.17 | Consultant-led services for respiratory medicine (service code 340) | NHS Reference Costs 2020/2021(4) (total outpatient attendances data) |
| Non-consultant hospital visits (no.) | 165.83 | Non-consultant led services for respiratory medicine (service code 340)  |
| Physiotherapist (no.) | 118.88 | Total services for physiotherapy (consultant and non-consultant led, service code 650) |
| Dietician (no.) | 107.30 | Total services for dietetics (consultant andnon-consultant led, service code 654) |
| Nurse (mins) | 0.85 | Cost per working hour for band 6 community or hospital-based nurses (nurse specialist/team leader) | PSSRU Report 2021 (3) |
| Social worker (min) | 0.87 | Costs for per working hour for social worker (adult services), unit cost includes qualifications |
| Phone contact (call) | 11.47 | Based on average unit costs between GP-led and nurse-led services for telephone triage |
| Psychologist visits (no.) | 221.52 | Total services for clinical psychology (consultant and nonconsultant led, service code 656) | NHS Reference Costs 2020/2021(4) (total outpatient attendances data) |
| Occupational therapist visits (no.) | 117.66 | Total services for occupational therapy (consultant and non-consultant led, service code 651) |
| Radiographer visits (no.) | 50.20 | Total services for diagnostic imaging (consultant and non-consultant led, service code 812) |
| A&E (no.) | 170.46 | Total services for A&E (consultant and non-consultant led, service code 180) |
| Other visits (no.) | 177.09 | Assumed all interventions for total outpatient attendances, excluding paediatric (and related) items; weighted by FCEs |
| Transplant | 88,823.49 | Assumed the costs of total services for lung and heart and lung transplants (elective inpatient, elective inpatient excess bed-days and non-elective long stay, codes DZ01Z and ED01Z); weighted by FCEs | NHS Reference Costs 2020/2021 (4) |

*Abbreviations: A&E, accident and emergency; FCE, finished consultant episode; GP, general practitioner; N/A (CD) – data not available for being confidential commercial data; ScHARR, School of Health and Related Research.*

*\* Unit costs presented by dose.*

*‡ the costs for each nebulised drug was calculated by weighting the estimated annual cost by the proportion of patients in CF registry; the lowest pack price between the NHS indicative and drug tariff prices from BNF for the correspondent dosage was used.*

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**2. Model validation**

## (a) Multistate model prevalence plots, observed versus expected, by age-category

Figures S1 to S5 show comparisons of the msm predictions against the observed data from the CF Registry (5).

**Figure S1: *msm* prevalence plots age 30-34 years**



**Figure S2: *msm* prevalence plots age 35-39 years**

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**Figure S3: *msm* prevalence plots age 40-44 years**

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**Figure S4: *msm* prevalence plots age 45-49 years**

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**Figure S5: *msm* prevalence plots age 50+ years**

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**(b) Comparison of model-predicted overall survival versus spline model reported by Keogh *et al***

Figure S6 presents a comparison of overall survival (OS) predicted by the CFHH model versus OS predictions obtained from Keogh *et al* (6).

**Figure S6: Modelled overall survival versus Keogh *et al* spline model (weighted by prevalence of covariate groupings)**



## FEV1% pred. stratum by age

Figure S7 presents a comparison of the probability of being in each of the three FEV1% pred. groups predicted by the model compared against estimates from the CF Registry dataset.

**Figure S7: FEV1% pred. by age category, model-predicted versus CF Registry estimates**



**3. Cost-effectiveness acceptability curves**

**Figure S8: Cost-effectiveness acceptability curves – CFHH adherence intervention versus usual care**



**References**

1. Joint Formulary Committee. British National Formulary (online). London, 2022.

2. Cystic Fibrosis Trust. UK Cystic Fibrosis Registry Annual Data Report 2018. BMJ Group and Pharmaceutical Press: London, UK, 2019.

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5. Cystic Fibrosis Trust. CF Registry bespoke dataset (years 2006-2015; data held on file). CF Trust: London, UK; 2019.

6. Keogh RH, Szczesniak R, Taylor-Robinson D, et al. Up-to-date and projected estimates of survival for people with cystic fibrosis using baseline characteristics: A longitudinal study using UK patient registry data. Journal of Cystic Fibrosis 2018;17(2):218-27.