EE182

Impact of CFTR Modulators on Real-World Healthcare Resource Utilisation in People With Cystic Fibrosis in Wales: A Retrospective, Observational Database Study Using Linked Data From the UK CF Registry and SAIL Databank

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BACKGROUND

- Cystic fibrosis (CF) is a rare, genetic, multi-organ, systemic disease that begins in utero. People with CF have a substantial disease burden and high levels of healthcare resource utilisation (HCRU) due to CF-specific symptoms and increased occurrence of comorbidities.[1,2]
- Cystic fibrosis transmembrane conductance regulator modulators (CFTRm) target the underlying cause of CF.[3] Ivacaftor (IVA) was the first CFTRm to become available and was followed by lumacaftor/ivacaftor, tezacaftor/ivacaftor, and elexacaftor/tezacaftor/ivacaftor (ELX/TEZ/IVA).
- The safety and efficacy of the CFTRm have been shown in clinical trials of people with CF.
- Real-world evidence (RWE) in people with CF treated with CFTRm has shown improvements in lung function[4–10], and reductions in pulmonary exacerbations[4–10], hospitalisations[4,6–11], mortality[12] and risk of lung transplant[4,6,12,13]. However, there is limited information on the real-world impact of CFTRm on HCRU in the UK.
- This study assessed the real-world HCRU of people with CF in Wales before and after CFTRm initiation, including all licensed CFTRm at the time of the study.

OBJECTIVE

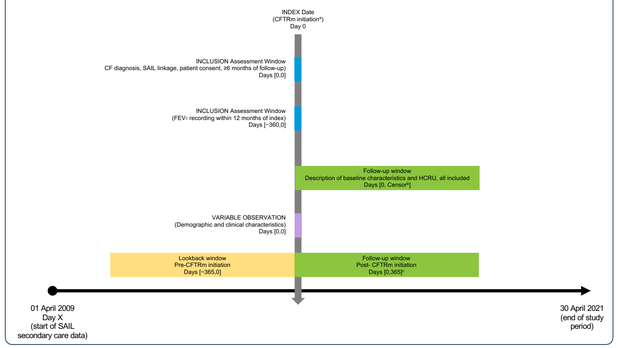
- To describe the impact of CFTRm on HCRU of people with CF in Wales before and after CFTRm treatment initiation.

METHODS

Study Design

- This was a non-interventional, observational, retrospective, cohort, linked-database study to assess the HCRU of people with CF in Wales.
- Data were extracted and linked from United Kingdom Cystic Fibrosis Registry (UKCFR) and electronic health records (EHRs) within the Secure Anonymised Information Linkage (SAIL) Databank.
  - The SAIL Databank provided information on HCRU.[14]
  - The UKCFR provided information on demographics, CFTRm treatment, and CF-specific health outcomes.[15]

Figure 1. Study Design



CF: cystic fibrosis; CFTRm: cystic fibrosis transmembrane conductance regulator modulator; ELX/TEZ/IVA: elexacaftor/tezacaftor/ivacaftor; HCRU: healthcare resource utilisation; IVA: ivacaftor; FEV$_1$: forced expiratory volume in 1 second; SAIL: Secure Anonymised Information Linkage.

[a] First initiation of IVA, lumacaftor/ivacaftor, tezacaftor/ivacaftor or ELX/TEZ/IVA. [b] End of study period, death, exit from SAIL database. [c] HCRU before and after CFTRm initiation.

Inclusion/Exclusion Criteria

- Inclusion criteria
  - Confirmed diagnosis of CF in the UKCFR
  - Record of any CFTRm use during the study period
  - ppFEV$_1$ recording within 12 months prior to or on index date
  - Linked data available across the UKCFR and SAIL Databank
  - ≥6 months of data available in the SAIL Databank from index date (post index)
- Exclusion criteria
  - Missing records of age, sex, or key linkage details
  - Withdrawn consent for data collection in the UKCFR

Study Design (cont)

- Description of baseline characteristics and HCRU included all people with CF who received any CFTRm and met all eligibility criteria.
- The analysis of HCRU before and after CFTRm treatment initiation included people who received any CFTRm and had ≥12 months of pre- and post-CFTRm initiation data.
- People were censored at CFTRm discontinuation. If people switched between CFTRm therapies, they continued to be followed until discontinuation.
- The group of people who received ELX/TEZ/IVA as their first and only CFTRm was analysed if they had ≥6 months of pre- and post-CFTRm initiation data.
  - The ELX/TEZ/IVA cohort allowed for <12 months of follow-up. The shorter follow-up time was necessary to ensure an analysis could be conducted. The maximum follow-up time possible within the study period was 8 months since full market authorisation was granted on 21 August 2020 in the UK.[14]

Statistical Analysis

- For continuous variables, descriptive summary statistics (eg, mean, standard deviations, and n) are reported at baseline (defined as the closest record prior to CFTRm initiation), and post-baseline period.
- The mean difference and 95% CI were calculated for the continuous HCRU measures (eg, event rates and event duration) after CFTRm initiation relative to the "pre-CFTRm initiation" period.
  - The rate difference ($Y_{diff} = Y_{after} - Y_{before}$) was calculated for each outcome measure for each person separately and then averaged for the total population.
  - Assuming the rate difference (Y_{diff}) was normally distributed, the 95% CI was calculated as rate difference ± (1.96 × SE [rate difference]) with SE being the standard error of the rate difference.
- Seasonality was adjusted for in the analysis of the ELX/TEZ/IVA cohort because <1 full year of data was available.
- Categorical variables for counts and percentages are reported. No tests of significance were performed.
- People were categorised by deprivation score, a measure of, but not limited to socioeconomic factors.
- General practitioner (GP) events comprehensively included any patient interactions with primary care health services, which may not be directly comparable with specific data collected in other healthcare settings, such as clinical trials.

RESULTS

Demographics, Clinical Characteristics, and HCRU of People Who Initiated a CFTRm

- 240 people met all study eligibility criteria and were included in the CFTRm cohort. Demographics, clinical characteristics, and HCRU for this cohort are listed in **Tables 1**, **2**, and **3**, respectively.
- On average, people in this cohort had contact with their GP approximately 31 times annually and received approximately 82 prescriptions annually; they were hospitalised approximately once per year (**Table 3**).

Table 1. Demographic Characteristics of People Receiving a CFTRm

Demographic Characteristics	N = 240
Age at index, mean (SD), years	22.7 (13.9)
Categorical age at index, n (%), years	
0–1	0
2–5	23 (9.58)
6–11	36 (15.00)
12–17	40 (16.67)
>18	141 (58.75)
Female, n (%)	106 (44.17)
Height at index, mean (SD), cm[a]	169 (8.4); n = 138
Weight at index, mean (SD), kg[a]	65.3 (13.9); n = 138
BMI at index, mean (SD)[a]	22.8 (4.1); n = 138
BMI categorical at index, n (%)	
Underweight [<18.5]	16 (11.59); n = 138
Healthy [18.5–24.9]	88 (63.77); n = 138
Overweight [25–29.9]	27 (19.57); n = 138
Obese [≥30]	7 (5.07); n = 138
Deprivation score, mean (SD)[b]	3.1 (1.4)
Deprivation score, categorical, n (%)	
1	44 (18.33)
2	46 (19.17)
3	50 (20.83)
4	46 (19.17)
5	54 (22.50)

BMI: body mass index; CFTRm: cystic fibrosis transmembrane conductance regulator modulator.

[a] Adults. [b] Score ranged from 1 to 5 with a score of 1 defined as most deprived and 5 defined as least deprived.

Table 2. Clinical Characteristics of People Receiving a CFTRm

Clinical Characteristics	N = 240
Age at diagnosis, mean (SD), years	2.5 (7.8)
Age group at diagnosis, n (%), years	
0–1	188 (78.33)
2–5	29 (12.08)
6–11	8 (3.33)
12–17	5 (2.08)
≥18	10 (4.17)
Mode of CF presentation, n (%)	
Family history	34 (14.17)
Newborn screening	85 (35.42)
Genotype	12 (5.00)
Prenatal/antenatal	5 (2.08)
CFTR genotype, n (%)	
F/F	167 (69.58)
*F/*MF	19 (7.92)
*F/*RF	10 (4.17)
*F/*gating or R117H	22 (9.17)
Gating or R117H/other or missing	5 (2.08)
F/(other or missing) or other/other	17 (7.08)
ppFEV$_1$ at index, mean (SD)	67.1 (24.3); n = 185
ppFEV$_1$ group at index, n (%)	
<40%	35 (18.92); n = 185
40%–70%	54 (29.19); n = 185
70%–90%	57 (30.81); n = 185
>90%	39 (21.08); n = 185
First CFTRm initiated, n (%)	
IVA	29 (12.08)
Lumacaftor/ivacaftor	76 (31.67)
Tezacaftor/ivacaftor	99 (41.25)
ELX/TEZ/IVA	36 (15.00)
Ever received specific CFTRm, n (%)	
IVA	30 (12.50)
Lumacaftor/ivacaftor	76 (31.67)
Tezacaftor/ivacaftor	104 (43.33)
ELX/TEZ/IVA	72 (30.00)

CF: cystic fibrosis; CFTRm: cystic fibrosis transmembrane conductance regulator modulator; ELX/TEZ/IVA: elexacaftor/tezacaftor/ivacaftor; *F/F*: homozygous for *F508del*-CFTR; *F/*gating: heterozygous for *F508del*-CFTR and a CFTR gating mutation; *F/*MF: heterozygous for *F508del*-CFTR and a minimal function mutation; *F/*other: heterozygous for *F508del*-CFTR and another mutation that is not MF, RF, or gating; *F/*RF: heterozygous for *F508del*-CFTR and a CFTR residual function mutation; IVA: ivacaftor; other/other: any genotype without an *F508del*-CFTR mutation; ppFEV$_1$: percent predicted forced expiratory volume in 1 second; SAIL: Secure Anonymised Information Linkage.

Table 3. HCRU of People Receiving a CFTRm

HCRU Characteristics	N = 240
Total follow-up time, mean (SD), days	603 (569)
Hospitalisations: rate per year	
People with ≥1 event, n (%)	96 (40.00)
Total number of events, n	410
Event rate (95% CI)	1.03 (0.79, 1.34)
GP events: rate per year	
People with ≥1 event, n (%)	198 (82.50)
Total number of events, n	12,305
Event rate (95% CI)	31.01 (28.2, 34.1)
Emergency department visits: rate per year	
People with ≥1 event, n (%)	13 (5.42)
Total number of events, n	20
Event rate (95% CI)	0.05 (0.03, 0.10)
Prescriptions: rate per year	
People with ≥1 event, n (%)	197 (82.08)
Total number of events, n	32,517
Event rate (95% CI)	81.95 (72.23, 92.99)

CFTRm: cystic fibrosis transmembrane conductance regulator modulator; CI: confidence interval; GP: general practitioner; HCRU: healthcare resource utilisation.

Comparison of HCRU 12 Months Before and After Initiation of a CFTRm

- Out of the 240 people who initiated a CFTRm during the study period, 166 had ≥12 months of follow up available.
- **Table 4** shows the difference in HCRU 12 months before and after initiation of any CFTRm for this cohort.
- After CFTRm initiation, people had a lower mean annual hospitalisation rate (0.89 vs 1.78) and reductions in mean hospital length of stay (7.4 vs 15.2 days) compared with before CFTRm initiation, respectively.

Table 4. Comparison of HCRU 12 Months Before and After Initiation of a CFTRm

HCRU Characteristics	Before Initiating Any CFTRm n = 166	After Initiating Any CFTRm n = 166	Difference (95% CI)[a]
Total follow-up time, days, n (%)	365 (0)	365 (0)	
Hospitalisations: rate per year			
People with ≥1 event, n (%)	98 (59.04)	61 (36.75)	
Total number of events, n	296	149	
Event rate (95% CI)	1.78 (1.40, 2.27)	0.89 (0.66, 1.21)	−0.89 (−1.13, −0.64)
Length of stay in hospital, mean (SD), days[b]	15.2 (27.5)	7.4 (21.4)	−7.89 (−11.54, −4.23)
GP events: rate per year			
People with ≥1 event, n (%)	143 (86.14)	143 (86.14)	
Total number of events, n	5186	5431	
Event rate (95% CI)	31.24 (28.38, 34.40)	32.7 (29.68, 36.06)	1.48 (0.26, 2.69)
Prescriptions: rate per year			
People with ≥1 event, n (%)	143 (86.14)	143 (86.14)	
Total number of events, n	13,901	14,658	
Event rate (95% CI)	83.74 (73.45, 95.48)	88.3 (76.91, 101.37)	
IV antibiotics in hospital: rate per year			
People with ≥1 event, n (%)	60 (36.14)	62 (37.35)	
Total number of events, n	129	129	
Event rate (95% CI)	0.8 (0.58, 1.03)	0.8 (0.58, 1.03)	0.00 (−0.19, 0.19)
IV antibiotics at home: rate per year			
People with ≥1 event, n (%)	32 (19.28)	35 (21.08)	
Total number of events, n	82	72	
Event rate (95% CI)	0.5 (0.33, 0.74)	0.43 (0.30, 0.64)	−0.06 (−0.21, 0.09)
Time on IV antibiotics in hospital, mean (SD), days	9.5 (19.9)	9.4 (18.2)	−0.13 (−2.71, 2.44)
Time on IV antibiotics at home, mean (SD), days	5.7 (18.4)	5.0 (16.2)	−0.67 (−2.56, 1.21)

CFTRm: cystic fibrosis transmembrane conductance regulator modulator; CI: confidence interval; GP: general practitioner; HCRU: healthcare resource utilisation; IV: Intravenous.

[a] A negative sign (−) indicates a decline or reduction in HCRU after CFTRm initiation. [b] Among those with no hospital stay have 0 days.

Comparison of HCRU 12 Months Before and After Initiation of ELX/TEZ/IVA

- Out of the 240 people who initiated any CFTRm during the study period, 36 were included in the ELX/TEZ/IVA cohort.
- Demographics and clinical characteristics for this cohort are reported in **Table 5,** and the HCRU difference is reported in **Table 6**.
- There was a lower mean hospital event rate (0.60 vs 1.99) after ELX/TEZ/IVA initiation compared with before its initiation (adjusted for seasonality).
- When the differences between the 2 cohorts were compared, a greater decrease in hospitalisation rate was seen in the ELX/TEZ/IVA cohort vs the CFTRm-12mo cohort (**Figure 2**).

Table 5. Demographic and Clinical Characteristics of People Receiving ELX/TEZ/IVA

Demographic Characteristics	n = 36
Age at diagnosis, mean (SD), years	4.1 (11.3)
Age at index, mean (SD), years	31.3 (14.6)
Categorical age at index, n (%), years	
0–1	0
2–5	0
6–11	0
12–17	8 (22.22)
≥18	28 (77.78)
Female, n (%)	15 (41.67)
Height at index, mean (SD), cm[a]	169.3 (9.3); n = 25
Weight at index, mean (SD), kg[a]	67.7 (16.6); n = 25
BMI at index, mean (SD)[a]	23.5 (4.9); n = 25
Deprivation score, mean (SD)[b]	3.1 (1.1); n = 36
ppFEV$_1$ at index, mean (SD)	64.8 (20.6); n = 26
CFTR genotype, n (%)	
F/F	9 (25.00)
*F/*MF	17 (47.22)
F/(other or missing) or other/other	10 (27.78)

BMI: body mass index; CFTRm: cystic fibrosis transmembrane conductance regulator modulator; *F/F*: homozygous for *F508del-CFTR*; *F/*MF: heterozygous for *F508del-CFTR* and a minimal function mutation; *F/*other: heterozygous for *F508del-CFTR* and another mutation that is not MF, RF, or gating; other/other: any genotype without an *F508del-CFTR* mutation; ppFEV$_1$: percent predicted forced expiratory volume in 1 second.

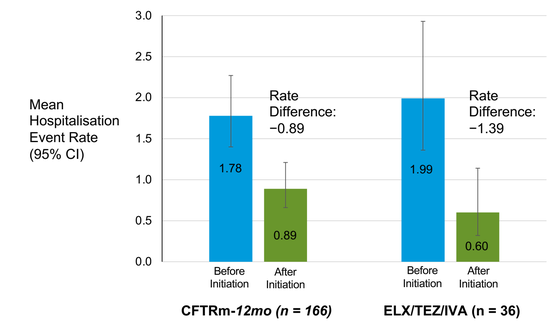
[a] Adults. [b] Score ranged from 1 to 5, with a score of 1 defined as most deprived and 5 defined as least deprived.

Table 6. Comparison of HCRU Before and After ELX/TEZ/IVA Initiation

Characteristics	Before ELX/TEZ/IVA Initiation n = 36	After ELX/TEZ/IVA Initiation n = 36
Total follow-up time, mean (SD), days	230 (104)	218 (79)
Hospitalisations: rate per year		
People with ≥1 event, n (%)	17 (47.22)	8 (22.22)
Total number of events, n	43	13
Event rate (95% CI)	2.00 (1.36, 2.93)	0.60 (0.32, 1.14)
GP events: rate per year		
People with ≥1 event, n (%)	26 (72.22)	25 (69.44)
Total number of events, n	714	684
Event rate (95% CI)	33.16 (26.35, 41.72)	31.76 (24.24, 41.61)

CI: confidence interval; ELX/TEZ/IVA: elexacaftor/tezacaftor/ivacaftor; GP: general practitioner; HCRU: healthcare resource utilisation.

Figure 2. Mean Hospitalisation Rate Before and After Initiation of a CFTRm or ELX/TEZ/IVA[a]



CFTRm: cystic fibrosis transmembrane conductance regulator modulator; CI: confidence interval; ELX/TEZ/IVA: elexacaftor/tezacaftor/ivacaftor.

[a] Analysis before and after initiation of any CFTRm was in the cohort of people who initiated any CFTRm and had ≥12 months of follow up. Analysis before and after ELX/TEZ/IVA initiation was in the cohort of people who initiated ELX/TEZ/IVA as their first CFTRm, even if they had <12 months of follow up.

CONCLUSIONS

- People with CF in Wales who initiated a CFTRm used fewer healthcare resources, as assessed by hospitalisation, admission rates, and length of stay in the 12 months after initiation of a CFTRm treatment.
- People who initiated ELX/TEZ/IVA as their first CFTRm experienced a more pronounced decline in hospitalisation rates compared with those who initially started any other CFTRm.
- To the best of our knowledge, this is the first study using data linkage to evaluate the impact of CFTRm use on HCRU in people with CF in the UK.

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AUTHOR DISCLOSURES

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