In 2023, the treatment regimen included hypertonic saline (86.9%, 60.8% of children), rhDNase (69.5%), inhaled antibiotics (56.5%), intravenous antibiotics (63%), macrolides (13%), pancreatic enzymes (93.4%), and oxygen therapy (6.5%).
Conclusion: The study highlights the diverse clinical presentations and challenges faced by CF patients in the Republic of Moldova. Improved access to neonatal screening, genetic testing, and modern therapies, along with enhanced awareness among healthcare providers, is essential for optimizing patient outcomes and addressing healthcare disparities.

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Incidence of cystic fibrosis in Brittany (western France): overview of 50 years of monitoring and 35 years of newborn screening

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Objectives: The incidence of cystic fibrosis (CF) appears to be declining in many countries, driven by factors such as demographic changes, the implementation of genetics-based health policies and evolving cultural attitudes towards testing. The expanding implementation of newborn screening (NBS) programmes for CF has allowed a better monitoring of the disease incidence and its evolution over time. The aim of this study was to examine long-term trends (50 years) in the incidence of CF in Brittany (France), a region where CF is common and where NBS has been in place for 35 years (since 1989).
Methods: The study focused on people with CF (pwCF) born in Brittany between 1970 and 2019 (n=634). Patients born after 1989 were easily identified from the NBS programme. Patients for born before 1989 were recorded by combining data sources and using capture-recapture studies. Temporal trends in incidence were analysed using Poisson regression and expressed as the average percentage change (APC) over time or between periods.
Results: Over 50 years, the incidence of CF dropped from 1/2303 (1970-79 period) to 1/3983 (2010-19 period), representing a 42.2% decrease ($p<0.001$). The average number of pwCF born annually in Brittany thus decreased from 17.4 to 8.6. The incidence declined significantly over the entire period (annual APC: -1.4%, $p<0.001$), but also since the introduction of NBS for CF (annual APC: -1.7%, $p=0.007$). A clear breakpoint in incidence was observed in the late 1980s, and a west-to-east gradient persists nowadays in Brittany (1/2783 in the western part *vs.* 1/6150 in the eastern part, which is similar to that observed in France).
Discussion: This study highlights the significant decline in the incidence of CF over the past 50 years in a region where the disease is common. It reports a clear decrease that coincides with the availability of prenatal diagnosis. Continued monitoring of the incidence of CF is essential to evaluate the impact of CFTR modulator therapies.

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Evaluation of rare cystic fibrosis transmembrane conductance regulator gene variants according to seven functional classes from Turkish National Cystic Fibrosis Patient Registry

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Objectives: Over 2,100 variants in the cystic fibrosis transmembrane conductance regulator(*CFTR)* gene have been documented.To address the need for effective therapies targeting *CFTR* defect in people with cystic fibrosis (pwCF) who are not eligible for existing treatments,*CFTR* mutations are categorized into seven functional groups according to Amaral et al.
Methods: In this study, based on the 2023 data from the Turkish National Cystic Fibrosis Patient Registry,*CFTR* variants were categorized into three groups Class I,Class VII,and Class II-VI according to literature.Variants identified in the population but with unknown effects were assessed using in silico tools,including MutationTaster,Sorting Intolerant from Tolerant,MutPred LOF,Functional Analysis Through Hidden Markov Models,Polymorphism Phenotyping v2,and GOR IV.The decision of eligibility for the CFTR modulators(CFTRm) was determined according to the'Vertex treatment-Finder'on the Vertex® website in January 2025.
Results: There were 2.258 registered patients from 34 centers,2.196 (97.2%) had genetic evaluation.Two alleles were identified in 1.916 (84.8%), which included 279 different *CFTR* alleles.Of these,61 pathogenic variants with a frequency higher than 0.2%(79.8% of all alleles)have been prioritized so far.In silico tools were applied to 23 variants with unknown effects,and at the end all variants were determined to be pathological. Among these variants,15(10.8% of all alleles)were classified as Class I and 6 (9.4%)as Class VII mutations.Remaining 40 variants(37.4%) were classified as Class II-VI.Between those Class II-VI,11 variants(10.3%)were found to be ineligible for CFTRm.

Conclusion: Patient-centered approach in cystic fibrosis care is crucial, particularly identifying the need for effective treatments in populations with a high prevalence of rare mutations. Functional studies have not yet been conducted in Türkiye but the results of this ongoing study will help address the unmet treatmetment needs.

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Clinical characteristics of cystic fibrosis children with intermediate sweat chloride test

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Objectives: Some CF patients can have intermediate sweat test values. In this study, our aim was to demonstrate the clinical and laboratotory findings of CF patients who had intermediate sweat chloride values and compare them to CF patients who had high values of sweat chloride.
Methods: We included CF patients who were followed up in our clinic in the last 1 year. CFTR-RD or CRMS patients were excluded.The patients were divided into two groups: those with a sweat chloride (Swcl) of 30-60 mmol/L(intermediate Swcl group) and Swcl of 60 mmol/L or more (high Swcl group). High Swcl group were determined in a 1:4 ratio and randomly selected from anonymised patient data in accordance with the age range of the study group.
Results: Among 80 included patients, 16 were in the intermediate Swcl group and 64 were in the high Swcl group. The clinical data of the intermediate Swcl group are shown in Table 1.
Mean age at diagnosis for the intermediate group was 1,7±3,2 years and 0,2±0,2 years for the high group(p<0,001).Median z-scores for height,mean faecal elastase and annual pulmonary exacerbation rates were statistically significantly higher in the intermediate group. Chronic colonisation status was in favour of MSSA, but MRSA and *Pseudomonas aeruginosa* colonisations were also present in the intermediate group. Although not statistically significant, nutritional status(BMI) and pulmonary functions(FEV1) were better in the group with intermediate Swcl group.
Conclusion: CF patients can have intermediate sweat chloride whose clinical and laboratory findings can be different. The reason for lower sweat chloride in these patients needs to be further evaluated.

Table 1: Clinical data of intermediate Swcl group

patient no	Age at diagnosis (years)	mutation 1	mutation 2	sweat chloride-1	Sweat chloride -2	Newborn screening (NBS)#
1	0,6	E831X*	E831X*	38	33	negative
2	1	R347P*	711+3A>G**	54	33	positive
3	0,08	R347H**	deltaF508*	45	38	positive
4	1	1677delTA*	E831X*	54	47	positive
5	0,42	R117C**	R334W*	55	53	negative
6	0,17	S945L**	S1196X*	51	48	not done
7	0,42	1677delTA*	R117C**	59	50	positive
8	0,5	deltaF508*	deltaF508*	57	47	not done
9	0,58	deltaF508*	R117C**	50	46	not done
10	10	deltaF508*	3849+ 10kbC>T**	51	22	not done
11	0,42	CFTRdele2*	D110H**	59	44	not done
12	0,83	G126D*	1802delC*	57	53	negative
13	2	R117C**	R117C**	45		not done
14	10	3849+ 10kbC>T**	3849+ 10kbC>T**	46	35	not done
15	0,25	H1054D*	1525-1G>A*	59	39	positive
16	0,33	G194V**	deltaF508*	57	52	not done

• #:NBS: 2 IRT values,*:CF causing, **:VCC

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Health outcomes for PwCF switching from a CFTR modulator therapy (CFTRm) to elexaftor/tezacaftor/ivacaftor (ETI) compared with those starting on ETI naively. A study using Irish registry data

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Objective: This study compares long-term clinical outcomes of people with cystic fibrosis (PwCF) who were CFTRm naïve at initiation of ETI versus those who switched from another CFTRm.
Methods: This preliminary analysis included 908 PwCF across three cohorts: C1 (naïve to CFTRm before ETI initiation, N=228), C2 (switched from Ivacaftor, N=116), and C3 (switched from another CFTRm, N=564). Baseline was defined as ETI initiation, with follow-up between 6 and 58 months (through end of 2023). Linear regression was used to analyse baseline and annualised change in BMI and $ppFEV_1$, adjusting for cohort and age at ETI initiation. A Chi-square test compared the incidence of *Pseudomonas aeruginosa* (Pa) before and after ETI initiation across cohorts.
Results: C2 had significantly higher baseline BMI (mean=22.2 kg/m^2) compared to C1 (mean=20.0 kg/m^2, p<0.001) and C3 (mean=20.6 kg/m^2, p<0.001), with no significant difference between C1 and C3 (p=0.113). Baseline ppFEV1 was highest in C2 (mean=75.3%), but the difference with C1 (mean=74.4%, p=0.777) and C3 (mean=70.3%, p=0.064) was not significant. Post-ETI, there was a significant increase in BMI in all cohorts: C1 (Δ=0.74, 95% CI=0.58-0.91), C2 (Δ=0.84, 95% CI=0.64-1.07), C3 (Δ=0.81, 95% CI=0.72-0.90), with no significant cohort differences. Similarly, $ppFEV_1$ increased significantly in all cohorts: C1 (Δ=5.2, 95% CI=4.2-6.4), C2 (Δ=4.2, 95% CI=3.1-5.3), C3 (Δ=4.0, 95% CI=3.6-4.6), with no significant differences between cohorts. The incidence of Pa was similar across cohorts both before and after ETI initiation (C1=40%, C2=36%, C3=41% (p=0.66) and C1=27%, C2=27%, C3=0.25% (p= 0.88), respectively).
Conclusion: This preliminary analysis suggests that despite C2's higher baseline BMI, PwCF who switched from Ivacaftor displayed similar patterns to modulator-naïve patients and those who switched from a less effective CFTRm. Further analysis will include 2024 data, and stratification by genotype and disease severity.

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Ensuring Excellence: The Data Quality Programme of the cystic fibrosis Registry of Ireland

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Objectives: The Cystic Fibrosis Registry of Ireland (CFRI) plays a key role in managing health data for individuals with cystic fibrosis (CF) in Ireland. Our data quality programme ensures the data is accurate, complete and reliable, supporting clinical decision-making, research, and policy development in CF care.
Methods: The CFRI data quality programme uses a multi-faceted approach, including data validation, monitoring, and continuous improvement. Key components include:

- Standardised protocols for consistency and completeness.
- Training for research associates who enter data.
- Automated checks to identify and correct common data entry errors.
- Manual review to address more complex discrepancies.

In 2022, an ECFS patient registry (ECFSPR) team conducted onsite data validation visits at two Irish CF centres. This process proved invaluable, and CFRI have continued these visits in 2023 and 2024, following ECFSPR procedures. Here, we present findings from three years of this programme.