Research Article

# Outcomes of Sweat Conductivity Testing and Referral Patterns for Cystic Fibrosis: A 10-Year Retrospective Single-Center Study in Albania

Hamide Shllaku-Sefa[1*], Teuta Dedej-Kurti[2], Ndok Marku[1]

[1]*Laboratory Department, Catholic Hospital "Our Lady of Good Counsel", Tirana, Albania*
[2]*Laboratory Department, Faculty of Medicine, University of Medicine, Tirana, Albania*

**Article Info**

[*]***Corresponding Author:***
Hamide Shllaku-Sefa
Laboratory Department, Catholic Hospital "Our Lady of Good Counsel"
Street "Dritan Hoxha", Tirana, Albania
E-mail: sefadea@gmail.com
Phone.: 00355695305242

**Keywords**

Albania, Cystic Fibrosis, Immunoreactive Trypsinogen (IRT), Quantity Not Sufficient (QNS), Sweat Chloride Test

**Abstract**

**Introduction**: Cystic fibrosis (CF) is an autosomal recessive disorder. Sweat testing is a cornerstone of CF diagnosis and remains essential in settings where nationwide screening and registries are limited.

**Materials and Methods:** We performed a retrospective single-center analysis of all patients referred for sweat testing in our laboratory between May 2015 and May 2025 (n=567). Sweat induction and collection were performed using the Macroduct® system, and analysis was conducted via the Sweat-Chek™ Analyzer (Model 3120, ELITechGroup). Statistical analysis was performed using Jamovi software (version 2.3.28).

**Results**: The cohort included 302 males (53%) and 265 females (47%), with a mean age of 36.3 ±49.2 months (Median: 14; IQR: 4–48). The primary indications for referral were respiratory manifestations (57%), followed by gastrointestinal symptoms (14.1%), failure to thrive (6.2%), and others (4.2%). Asymptomatic individuals with no symptoms recorded at referral (18.2%). Diagnostic outcomes revealed that 83.4% of participants had normal results, 11.3% were positive, and 3% were borderline. A "quantity not sufficient" (QNS) rate of 2.3% was observed.

**Conclusions**: In this single-center referral cohort, most sweat test results were normal, with an overall positive rate of 11.3% and low QNS rates that are benchmark favorably against published quality targets. Clear referral pathways and strengthened early-life evaluation (including expansion of screening access) may support earlier diagnosis and reduce disease burden.

## Introduction

Cystic fibrosis (CF), an autosomal recessive disorder caused by biallelic pathogenic variants in the CFTR gene, disrupts epithelial ion transport, leading to viscous mucus accumulation, chronic multi-organ inflammation, and progressive respiratory failure [1]. The dysfunctional CFTR protein impairs chloride/bicarbonate secretion and sodium hyperabsorption, resulting in hallmark manifestations: recurrent pulmonary infections, pancreatic insufficiency, elevated sweat chloride concentrations, and male infertility due to obstructive azoospermia [2].

Globally, CF incidence varies significantly by population. While Ireland reports 1:1,353 live births [3], Finland observes 1:25,000 [4], with Western Europe averaging 1:4,500 [5] and Northern/Central Europe 1:6,000 [6]. In Albania, a Southeastern European nation with limited epidemiological data, CF prevalence was historically underreported due to fragmented registries. Before 2017, no national CF registry existed; however, the Department of Pediatrics at the University Hospital Center "Mother Teresa" (QSUNT) served as the sole national referral center, systematically documenting all pediatric CF cases since 1992. Retrospective analysis of QSUNT records (1992–2017) estimated an incidence of 1:4,041 live births [7], though this figure reflects hospital-based ascertainment rather than population-wide screening and requires validation through prospective studies. Importantly, the incidence figure is an estimate derived from QSUNT historical case counts and national birth rates, and it is not calculated from the referral cohort in the present study (which includes patients referred for evaluation rather than a population-based denominator).

The sweat chloride test (SCT) remains the diagnostic gold standard per Cystic Fibrosis Foundation guidelines [8], quantifying electrolyte concentrations following pilocarpine iontophoresis. Despite technical standardization, preanalytical errors, particularly insufficient sample volume (QNS), compromise reliability, with reported QNS rates ranging from 5–25% globally [9,10]. In resource-limited settings, suboptimal patient preparation (e.g., dehydration, skin barriers) and inconsistent collection protocols exacerbate these challenges. This study addresses a critical gap: no prior research has characterized SCT outcomes, referral patterns, or QNS determinants in Albania's high-prevalence cohort. Over a decade (2015–2025), we analyzed 567 SCTs performed at our laboratory to:

Quantify sweat chloride distributions across age groups and clinical indications,

Evaluate temporal trends in referral practices following updated international diagnostic criteria,

Identify modifiable preanalytical factors contributing to QNS events.

Our findings provide actionable insights to optimize diagnostic pathways, reduce diagnostic delays, and support evidence-based implementation of newborn screening in similar underserved regions.

## Materials and Methods

### *Study design and participants*

This was a retrospective single-center study including all consecutive patients referred for sweat testing in our laboratory between May 2015 and May 2025. Inclusion criteria were: (i) referral for sweat testing during the study period and (ii) availability of key variables (age, sex, referral indication, and sweat test outcome). Exclusion criteria were: (i) duplicate records/repeat tests for the same individual during the study period (only the last test was included in the analysis) and (ii) missing key variables required for analysis."

### *Definition of referral indication categories*

Referral indications were classified based on referral documentation and clinical notes. "Healthy individuals" refers to patients with no symptoms recorded at referral who were nevertheless referred for CF evaluation (e.g., screening or clinician concern without documented symptoms).

### *Definition of age categories*

Although the study included patients aged 1 month to 39 years, the vast majority were pediatric patients. Subgroup analysis was performed based on age categories (≤3 months and >3 months), but no formal comparison between pediatric and adult populations was conducted due to the very small number of adult subjects.

We used the SS-032 Macroduct Supply Kit (Pilogel Discs, Macroduct Collectors), Macroduct Sweat Collection System model 3700-SYS, and Sweat-Chek 3120 Sweat Conductivity Analyzer by Eli Tech Group Biomedical Systems. The test was conducted in the following phases [11]:

### *Phase one – stimulation of sweating*

The flexor surface of the child's forearm is cleaned with alcohol and deionized water and dried. Pilogel iontophoretic discs are applied to the skin with two stainless steel electrodes on the top, then fixed to the forearm. The electrodes are connected to a power supply, which automatically delivers pilocarpine equivalent to five minutes of iontophoresis at 1.5 mA, in accordance with international guidelines for sweat testing in both infants and adults [10].

### *Phase two – collection of sweat*

After sweat stimulation, the pilogel discs are removed by hand, and the skin is cleaned with water. Next, the disposable collector for sweat collection is fixed to the stimulated area, and sweat is collected for 30 minutes, during which the child can move, play, eat, and drink. When the sweat collection is over, the collector is removed from the child's forehand. The sweat specimen is handled with care before analysis to

avoid introducing air bubbles into the sweat column.

*Phase three – analytical phase*

The chloride concentration in the collected sweat is measured in the laboratory. The end of the specimen tube is connected to the inlet nipple of the conductivity cell in the left-hand nipple. The sweat specimen is transferred from the collector tube into the take-up tube via the conductivity cell. After the sweat specimen is transferred into the cell, its electrical conductivity is measured, the electrolyte concentration is calculated, and the result appears on the digital display.

**Statistics**

Categorical variables are presented as frequency and percentage. Continuous variables are summarized as median (range). Group comparisons for categorical variables were performed using Fisher's exact test when expected cell counts were <5; otherwise, chi-square tests were used. A p-value ≤0.05 was considered statistically significant. Analyses were performed using Jamovi Statistical Software version 2.3.28.

**Results**

A total of 567 patients were enrolled in our study. There was a slight predominance of males with 53%. The mean age of the participants was 36.3 ± 49.2 months. Given the non-normal distribution of the data (Shapiro-Wilk p<.001), the median age of 14 months (IQR: 4–48 months) provides a more accurate representation of the cohort's central tendency.

The study analyzed a cohort primarily composed of patients older than 3 months (80%) and outpatients (69%). Clinical referrals were driven primarily by the Department of Pediatric Pulmonology (57%), with respiratory tract manifestations as the most common clinical sign for testing (57.3%). Detailed demographic and referral distributions are provided in Table 1.

**Table 1:** Descriptive statistics of the participants.

| | N | % |
|---|---|---|
| **Gender** | | |
| Males | 302 | 53 |
| Females | 265 | 47 |
| **Age** | | |
| ≤ 3 months | 116 | 20 |
| > 3 months | 451 | 80 |
| **QNS** | | |
| No | 554 | 97.7 |
| Yes | 13 | 2.3 |
| **Result** | | |
| Normal | 473 | 83.4 |
| Positive | 64 | 11.3 |
| Borderline | 17 | 3 |
| No results | 13 | 2.3 |
| **Department** | | |
| Pediatric Pulmonology | 321 | 57 |
| General Pediatric Policlinic | 90 | 16 |
| Pediatric Gastroenterology | 66 | 12 |
| Pediatric Immunology-Allergy | 42 | 7 |
| Pediatric Intensive Care | 22 | 4 |
| Neonatal Department | 7 | 1 |
| Others | 19 | 3 |
| **Signs and Symptoms** | | |
| Respiratory tract manifestations | 325 | 57.3 |
| Gastrointestinal tract manifestations | 80 | 14.1 |

| | N | % |
|---|---|---|
| Healthy individuals | 70 | 12.3 |
| Failure to thrive | 35 | 6.2 |
| Family history | 13 | 2.3 |
| IRT + | 11 | 2 |
| Confirmed mutations in the CFTR gene | 9 | 1.6 |
| Other manifestations | 24 | 4.2 |
| **Hospitalization** | | |
| Inpatients | 177 | 31 |
| Outpatients | 390 | 69 |

While the majority of tests yielded normal results (83.4%), a definitive positive diagnosis was reached in 11.3% of the cases. Statistical analysis revealed that a positive cystic fibrosis diagnosis was significantly associated with age, clinical symptoms, and hospitalization status ($p < .001$), whereas gender is not a relevant factor ($p = 0.346$). Table 2 provides the full breakdown of these diagnostic correlations.

**Table 2:** Demographic and clinical characteristics of participants by diagnostic result.

| | Result | | | | | | | | p |
|---|---|---|---|---|---|---|---|---|---|
| | Overall | | Positive | | Normal | | Borderline | | |
| | N | % | N | % | N | % | N | % | |
| **Age** | | | | | | | | | |
| ≤ 3 months | 112 | 20 | 26 | 23.2 | 85 | 75.9 | 1 | 0.9 | <.001 |
| > 3 months | 442 | 80 | 38 | 8.6 | 388 | 87.8 | 16 | 3.6 | |
| **Gender** | | | | | | | | | |
| M | 294 | 53 | 39 | 13.3 | 245 | 83.3 | 10 | 3.4 | 0.377 |
| F | 260 | 47 | 25 | 9.6 | 228 | 87.7 | 7 | 2.7 | |
| **Signs and Symptoms** | | | | | | | | | |
| Respiratory tract manifestations | 318 | 57.4 | 25 | 7.9 | 283 | 89 | 10 | 3.1 | <.001 |
| Gastrointestinal tract manifestations | 78 | 14.1 | 10 | 12.8 | 65 | 83.3 | 3 | 3.9 | |
| Healthy individuals | 70 | 12.6 | 2 | 2.9 | 67 | 95.7 | 1 | 1.4 | |
| Failure to thrive | 33 | 6 | 3 | 9.1 | 30 | 90.9 | 0 | 0 | |
| Family history | 13 | 2.3 | 3 | 23.1 | 10 | 76.9 | 0 | 0 | |
| IRT + | 11 | 2 | 4 | 36.4 | 6 | 54.5 | 1 | 9.1 | |
| Confirmed mutations in the CFTR gene | 9 | 1.6 | 8 | 88.9 | 0 | 0 | 1 | 11.1 | |
| Other manifestations | 22 | 4 | 9 | 41 | 12 | 54.5 | 1 | 4.5 | |
| **Hospitalization** | | | | | | | | | |
| Inpatients | 169 | 30 | 32 | 19 | 130 | 77 | 7 | 4 | <.001 |
| Outpatients | 385 | 70 | 32 | 8.3 | 343 | 89.1 | 10 | 2.6 | |

Notably, in the subgroup of patients with confirmed CFTR mutations, 88.9% returned positive sweat tests, with the remaining 11.1% showing borderline results due to active modulator therapy (Table 2).

Among infants referred following a positive IRT screening, only 36.4% were confirmed positive by sweat testing, while over 54% returned normal results (Table 2). This highlights the critical role of SCT in resolving false positives from newborn screening.

Table 3 compares clinical characteristics by hospitalization status for patients with positive sweat test results. Analysis shows that signs and symptoms (p=0.005) represent the only variable with a statistically significant difference between inpatients and outpatients.

**Table 3:** Comparison of age, gender, and symptoms between inpatients and outpatients with positive sweat tests.

| | Hospitalization | | | | | | p |
|---|---|---|---|---|---|---|---|
| | Overall | | Inpatients | | Outpatients | | |
| | N | % | N | % | N | % | |
| **Age** | | | | | | | |
| ≤ 3 months | 26 | 41 | 13 | 50 | 13 | 50 | 1.000 |
| > 3 months | 38 | 59 | 19 | 50 | 19 | 50 | |
| **Gender** | | | | | | | |
| M | 39 | 61 | 17 | 44 | 22 | 56 | 0.305 |
| F | 25 | 39 | 15 | 60 | 10 | 40 | |
| **Signs and Symptoms** | | | | | | | |
| Respiratory tract manifestations | 25 | 39 | 12 | 48 | 13 | 52 | 0.005 |
| Gastrointestinal tract manifestations | 10 | 16 | 9 | 90 | 1 | 10 | |
| Healthy individuals | 2 | 3 | 0 | 0 | 2 | 100 | |
| Failure to thrive | 3 | 5 | 2 | 67 | 1 | 33 | |
| Family history | 3 | 5 | 0 | 0 | 3 | 100 | |
| IRT + | 4 | 6 | 1 | 25 | 3 | 75 | |
| Confirmed mutations in the CFTR gene | 8 | 12 | 1 | 12.5 | 7 | 87.5 | |
| Other manifestations | 9 | 14 | 7 | 78 | 2 | 22 | |

The overall rate of insufficient sweat volume was low at 2.3% (n=13). Analysis of sample failure showed:

Non-significant factors: Age (p=0.351), gender (p=0.545), and specific clinical symptoms (p=0.315) did not significantly affect the ability to collect sufficient sweat.

Significant factors: A statistically significant difference was seen based on patient location (p=0.016), with inpatients exhibiting a higher QNS rate (4.5%) compared to outpatients (1.3%).

Detailed QNS distributions across all variables are summarized in Table 4.

**Table 4:** The distribution of the patients according to sweat volume, age, gender, symptoms and hospitalization.

| | Sweat volume | | | | | | p |
|---|---|---|---|---|---|---|---|
| | Overall | | QNS | | Sufficient | | |
| | N | % | N | % | N | % | |
| **Age** | | | | | | | |
| ≤ 3 months | 116 | 20 | 4 | 3.4 | 112 | 96.6 | 0.315 |
| > 3 months | 451 | 80 | 9 | 2 | 442 | 98 | |
| **Gender** | | | | | | | |
| M | 302 | 53 | 8 | 2.6 | 294 | 97.4 | 0.587 |
| F | 265 | 47 | 5 | 2 | 260 | 98 | |

| | Sweat volume | | | | | | p |
|---|---|---|---|---|---|---|---|
| | Overall | | QNS | | Sufficient | | |
| | N | % | N | % | N | % | |
| **Signs and Symptoms** | | | | | | | |
| Respiratory tract manifestations | 325 | 57.3 | 7 | 2.2 | 318 | 97.8 | 0.315 |
| Gastrointestinal tract manifestations | 80 | 14.1 | 2 | 2.5 | 78 | 97.5 | |
| Healthy individuals | 70 | 12.3 | 0 | 0 | 70 | 100 | |
| Failure to thrive | 35 | 6.2 | 2 | 5.7 | 33 | 94.3 | |
| Family history | 13 | 2.3 | 0 | 0 | 13 | 100 | |
| IRT + | 11 | 2 | 0 | 0 | 11 | 100 | |
| Confirmed mutations in the CFTR gene | 9 | 1.6 | 0 | 0 | 9 | 100 | |
| Other manifestations | 24 | 4.2 | 2 | 8.3 | 22 | 91.7 | |
| **Hospitalization** | | | | | | | |
| Inpatients | 177 | 31 | 8 | 4.5 | 169 | 95.5 | 0.029 |
| Outpatients | 390 | 69 | 5 | 1.3 | 385 | 98.7 | |

## Discussion

Cystic fibrosis is an autosomal recessive disease, common in Europe, including the Albanian population, but a national cystic fibrosis registry was not established in Albania until 2017 [7].

Sweat testing services have been provided since 2015, with an annual average of 57 tests. To ensure competency and quality, all tests are performed by a single laboratory professional. This volume exceeds the minimum requirements set by the Cystic Fibrosis Foundation and other professional bodies, which recommend at least 50 tests per laboratory and 10 per technician annually. [12].

While global literature often indicates a more severe disease trajectory in females, often attributed to the onset of estrogen-related complications post-puberty [13], our data did not reflect significant gender-based disparities in clinical presentation. We saw a slight male predominance (53%) and a higher positivity rate in males (13.3%) compared to females (9.6%), yet no significant differences were found in symptoms ($p=0.879$) or hospitalization rates ($p=0.204$). This lack of divergence is consistent with a prepubescent cohort, where the hormonal drivers typically associated with gender-specific CF morbidity have not yet manifested. Furthermore, since our study used cross-sectional data at the point of diagnosis without longitudinal follow-up, these findings represent the initial clinical state rather than long-term disease progression. Consequently, our results suggest that in the early pediatric stages of CF in Albania, gender does not appear to be a primary determinant of acute clinical severity.

The diagnoses of CF can be made at various ages, but with newborn screening, it's often diagnosed within the first month of life, before symptoms appear [14]. Most children are diagnosed by age 2, either through newborn screening or when symptoms become clear [15]. However, some individuals, particularly those with milder or atypical forms of the disease, may not be diagnosed until adolescence or adulthood [16]. Although we do not have a national program for newborn screening (NBS), since this is only offered in private hospitals in Albania, we have found a significant difference between the diagnosis of cystic fibrosis and age ($p<.001$) where it resulted that 23.2% of patients with a positive diagnosis were ≤3 months and only 8.6% were >3 months. The data prove that diagnosis typically occurs within the first three months of life, despite the lack of a universal screening program. This early detection points to effective diagnostic pathways and strong awareness among both caregivers and medical professionals. Most referrals originated from the Pediatric Pulmonology Department (57%), followed by General Pediatrics (16%), Gastroenterology (12%), and Immunology-Allergy (7%), with the remainder from Intensive Care (4%) and Neonatology (1%). These patterns diverge from international guidelines, such as those of the Croatian Society of Medical Biochemistry and Laboratory Medicine and University Hospital Centre Zagreb, which advocate for primary care physicians to initiate referrals to CF specialists [17]. Furthermore, our findings contrast with data from Turkey, where general pediatric clinics serve as the primary source of referrals [18]. We suggest these discrepancies reflect distinct national variations in diagnostic and management strategies for cystic fibrosis.

Since 1992, patients with CF in Albania have been managed and followed at the Department of Pediatrics within the University Hospital Center "Mother Teresa". The CF diagnosis

is based predominantly on clinical criteria and two positive sweat test results for patients suspected of the disease. The diagnosis is confirmed by the identification of two CF-causing mutations. Genetic assessment has been in practice since 2004, when the search for genetic mutations in patients with cystic fibrosis began to be recorded. Unfortunately, there was no national registry for cystic fibrosis in Albania until 2017. However, every pediatric patient diagnosed in the Department of Pediatrics at QSUNT has been documented throughout the course of the disease. Practically, this is the only center that diagnoses and follows cystic fibrosis patients in our country. Since 2017, Albania has been part of the European Cystic Fibrosis Society Patient Registry (ECFSPR), which collects anonymized demographic and clinical data from consenting people in Europe with CF [7].

Our study confirms that respiratory and gastrointestinal manifestations are still the primary drivers for sweat test referrals, accounting for 57.4% and 14.1% of our cohort, respectively. The strong correlation between age, symptoms, and test results ($p<.001$) aligns with established literature [2] about the early clinical presentation of cystic fibrosis.

Beyond clinical symptoms, other primary indications for sweat test referral by pediatricians include family history, positive IRT results on newborn screening, and confirmed CFTR mutations via molecular analysis.

In our cohort, only 23.1% of patients with a family history of CF yielded positive sweat test results. While family history indicates an increased carrier probability, and thus a higher risk of having an affected child, the actual clinical risk depends on the specific CFTR mutations present in the family. Consequently, genetic counseling and molecular testing are essential to determine the precise reproductive risk for individuals and their offspring [19].

Approximately 97% of infants with a single CFTR mutation identified through newborn screening for immunoreactive trypsinogen are false positives [20]. Consequently, CF has become a primary model in the United States for integrating DNA analysis into NBS programs [21]. While genetic-based NBS can find presymptomatic infants, it also finds asymptomatic heterozygote carriers and infants without disease-causing mutations. In such cases, at least one parent is typically a carrier, placing the couple at risk for future affected pregnancies [22]. While false-positive rates vary by screening methodology and ethnic background [23], our data revealed a false-positive IRT rate of 54.5%. It is critical to clarify that these referrals do not stem from a centralized national screening program, as a universal NBS for cystic fibrosis is not yet implemented in the Albanian public health sector. Instead, these cases represent a specific population of infants born in private maternity hospitals where elective screening is available. This distinction is vital for interpreting our data, as it reflects a self-selected or higher-socioeconomic demographic rather than a cross-section of the general population. Our findings underscore that even in these private settings, the SCT remains the indispensable "gold standard" in resolving the diagnostic uncertainty created by initial IRT elevations.

While it may initially appear that identifying CFTR mutations is sufficient for diagnosis, the sweat chloride test remains the gold standard for confirming a clinical diagnosis by verifying the functional defect of the CFTR protein [24,25]. This is particularly critical in cases involving a single identified mutation or indeterminate results [26]. In our study, nine patients presented with confirmed F508del mutations; eight yielded positive sweat test results, while one returned a borderline result. The latter case involved a patient previously diagnosed with CF who had been receiving CFTR modulator therapy in the United Kingdom for nearly a year. This case underscores an evolving role for the SCT, moving beyond initial diagnosis to become a key metric for assessing the effectiveness of CFTR modulators, which work by enhancing salt and water transport across cell membranes [27].

Children with cystic fibrosis experience significantly higher rates of hospitalization and outpatient visits compared to children without CF, with inpatient hospitalization rates often exceeding 30 times those of their peers [28]. In our cohort, patients with a positive SCT had a hospitalization rate of 19%, which was more than double the outpatient management rate of 8.3%. Additionally, we found a statistically significant association between positive SCT results and hospitalization ($p < 0.001$). These findings call for more research on diagnosis, care, and treatment to improve patient outcomes, prevent complications, and reduce hospitalizations.

The determination of QNS rates serves as a primary metric for assessing the quality of pre-analytical sweat collection. The QNS rates observed in our laboratory were well below the thresholds recommended by the Cystic Fibrosis Foundation (<10% for infants ≤3 months and <5% for older children) [10], reflecting strong adherence to preanalytical quality standards. These results provide strong evidence of the high technical proficiency of our laboratory staff. Furthermore, while literature suggests that physiological variables like body weight or skin condition can influence volume [2, 18, 29], our statistical analysis demonstrated that age ($p=0.315$), gender ($p=0.587$), and clinical symptoms ($p=0.315$) did not compromise sample adequacy. This stability across diverse pediatric subgroups underscores the robustness of our standardized collection protocols.

## Conclusions

In this single-center referral cohort, sweat testing yielded normal results, with an overall positive rate of 11.3% and low QNS rates that benchmark favorably against published targets. Expanding access to early-life evaluation (including broader screening availability), strengthening referral pathways, and

maintaining high-quality sweat testing procedures may support earlier CF diagnosis and improved outcomes.

**Disclosure**

The authors have nothing to declare.

**Ethical Approval**

Our study involved human subjects and followed the ethical principles for medical research involving human subjects, in accordance with the Declaration of Helsinki.

**Authors contributions**

Hamide Shllaku-Sefa contributed to conceptualization, data curation, formal analysis, investigation, validation, methodology, visualization, and writing – original draft. Ndok Marku, role in conceptualization, data curation, supervision, and project administration. Teuta Dedej-Kurti contributed to writing - review & editing.

**Funding sources**

None.

**Data Availability Statement**

Data will be provided on request.

**References**

1. Davis PB. Cystic fibrosis since 1938. Am J Respir Crit Care Med. 2006;173(5):475-482.
2. Farrell PM, Rosenstein BJ, White TB, Accurso FJ, Castellani C, Cutting GR, et al. Guidelines for diagnosis of cystic fibrosis in newborns through older adults: cystic Fibrosis Foundation consensus report. J Pediatr 2008;153: S4–S14.
3. Farrell PM, Joffe S, Foley L, Canny GJ, Mayne P, Rosenberg M. Diagnosis of cystic fibrosis in the Republic of Ireland: Epidemiology and costs. Ir. Med. J. 2007; 100:557–560.
4. Kere J, Estivill X, Chillon M, Morral N, Nunes V, Norio R, et al. Cystic fibrosis in a low-incidence population: Two major mutations in Finland. Hum. Genet. 1994; 93:162–166.
5. Dankert-Roelse JE, Bouva MJ, Jakobs BS, Janssens HM, de Winter-de Groot KM, Schonbeck Y, et al. Newborn blood spot screening for cystic fibrosis with a four-step screening strategy in the Netherlands. J. Cyst. Fibros. 2019; 18:54–63.
6. Skov M, Baekvad-Hansen M, Hougaard DM, Skogstrand K, Lund AM, Pressler T, et al. Cystic fibrosis newborn screening in Denmark: Experience from the first 2 years. Pediatr. Pulmonol. 2020; 55:549–555.
7. Kasmi I, Kasmi G, Basholli B, Sefa HS, Vevecka E. The Spectrum and Frequency of Cystic Fibrosis Mutations in Albanian Patients. Balkan J Med Genet. 2024;27(1):31-36.
8. Castellani C, Southern KW, Brownlee K, Dankert Roelse J, Duff A, Farrell M, et al. European best practice guidelines for cystic fibrosis neonatal screening. J Cyst Fibros 2009;8(3):153–173.
9. Coakley J, Scott S, Doery J, Greaves R, Talsma P, Whitham E, et al. Australian guidelines for the performance of the sweat test for the diagnosis of cystic fibrosis: report from the AACB Sweat Testing Working Party. Clin Biochem Rev 2006;27(2): S1–7.
10. LeGrys VA, Yankaskas JR, Quittell LM, Marshall BC, Mogayzel PJ Jr. Cystic Fibrosis Foundation. Diagnostic sweat testing: the Cystic Fibrosis Foundation guidelines. J Pediatr 2007;151(1):85–89.
11. ELITechGroup. 3120 SWEAT CHEK™ Sweat Conductivity Analyzer Instruction Manual. Logan, UT: Wescor, Inc.; 2005.
12. Massie J, Greaves R, Metz M, Wiley V, Graham P, Shepherd S, et al. Australasian Guideline (2nd Edition): an Annex to the CLSI and UK Guidelines for the Performance of the Sweat Test for the Diagnosis of Cystic Fibrosis. Clin Biochem Rev. 2017;38(3):115-130.
13. McNally E, Casey M. Sex disparities in cystic fibrosis in the era of highly effective modulator treatment. BMC Pulm Med. 2025;25(1):212.
14. Borowitz D, Robinson KA, Rosenfeld M, Davis SD, Sabadosa KA, Spear SL, et al. Cystic Fibrosis Foundation evidence-based guidelines for management of infants with cystic fibrosis. J Pediatr. 2009;155(6 Suppl): S73-93.
15. A.D.A.M. Medical Encyclopedia [Internet]. Cystic Fibrosis; [reviewed 2024 Feb 17; cited 2025 Sep 03]; [about 5 p.]. Available from: https://medlineplus.gov/ency/article/000107.htm#:~:text=Many%20people%20carry%20a%20CF,Symptoms%20in%20newborns%20may%20include: (accessed:30/10/2025)
16. Padoan R, Quattrucci S, Amato A, Carnovale V, Salvatore D, Salvatore M et al. The Diagnosis of Cystic Fibrosis in Adult Age. Data from the Italian Registry. Diagnostics (Basel). 2021;11(2):321.
17. Leničeк Krleža J, Aralica M, Tješić-Drinković D, Crneković K, Culej J, Fressl Juroš G, et al. National Guidelines for the Performance of the Sweat Test in Diagnosis of Cystic Fibrosis on behalf of the Croatian Society of Medical Biochemistry and Laboratory Medicine and the Cystic Fibrosis Centre - Paediatrics and adults, University Hospital Centre Zagreb. Biochem Med. 2022;32(1):010501.
18. Ozgenc A, Yasar NE, Kucur M, Bolayirli I M, Konukoglu D. The most common preanalytic problem of sweat testing: Insufficient sweat volume. Int J Med Biochem. 2020; 3(2), 62-66.
19. Mishra A, Greaves R, Massie J. The Relevance of Sweat testing for the Diagnosis of Cystic Fibrosis in the Genomic Era. Clin. Biochem. Rev. 2005; 26, 135–153.
20. Rock MJ, Hoffman G, Laessig RH, Kopish GJ, Litsheim TJ, Farrell PM. Newborn screening for cystic fibrosis in

Wisconsin: Nine-year experience with routine trypsinogen/DNA testing. Journal of Pediatrics. 2005;147(Suppl. 3): S73–S77.
21. Sharp JK, Rock MJ. Newborn screening for cystic fibrosis. Clinical Reviews in Allergy and Immunology. 2008; 35:107–115.
22. Tluczek A, Orland KM, Cavanagh L. Psychosocial consequences of false-positive newborn screens for cystic fibrosis. Qual Health Res. 2011;21(2):174-186.
23. Giusti R. Elevated IRT levels in African American infants: Implications for newborn screening in an ethnically diverse population. Pediatric Pulmonology. 2008; 43:638–641.
24. Farrell PM, White TB, Ren CL, Hempstead SE, Accurso F, Derichs N, et al. Diagnosis of Cystic Fibrosis: Consensus Guidelines from the Cystic Fibrosis Foundation. J Pediatr. 2017;181 S: S4-S15: e1.
25. Massie J, Greaves R, Metz M, Wiley V, Graham P, Shepherd S, et al. Australasian Guideline (2nd Edition): an Annex to the CLSI and UK Guidelines for the Performance of the Sweat Test for the Diagnosis of Cystic Fibrosis. Clin Biochem Rev. 2017;38(3):115-130.
26. Mishra A, Greaves R, Massie J. The relevance of sweat testing for the diagnosis of cystic fibrosis in the genomic era. Clin Biochem Rev. 2005;26(4):135-153.
27. Zemanick ET, Ramsey B, Sands D, McKone EF, Fajac I, Taylor-Cousar JL, et al. Sweat chloride reflects CFTR function and correlates with clinical outcomes following CFTR modulator treatment. J Cyst Fibros. 2025;24(2):246-254.
28. Malmivaara K, Pölkki M, Prami T, Raittinen P, Heikkilä E, Aalto A, et al. Cystic fibrosis patient characteristics and healthcare resource utilization in Finland using linked registries. Heliyon. 2024. 22;10(13): e33439.
29. Camargos P, Bedran RM, Alvim CG, Sader OG. Rate and predictors of insufficient sweat volume in very young infants after pilocarpine gel iontophoresis: prospective, population-based study. Arch Dis Child. 2024;109(4):304-307.