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Al-Quds University

Assessing Quality of life of Cystic Fibrosis patients in West Bank and New Therapeutic Options

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Dedication

I dedicate this thesis to my family specially my mother, who gave me endless love, encouragement, and support every step of the way during my graduate education. To those children who are suffering from this dreadful disease and to their families who as well are suffering in silence but showing patience and understanding for their children. All the knowledge and experience I gained throughout this research project, I owe it them.

Declaration

I certify that this thesis submitted for the degree of master is the result of my own research, except where otherwise acknowledged and that this thesis has not been submitted for a higher degree to any other university or institution.

Signature: _____

Samya Izat Mohammed Salah

Date: 7/10/2017

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Abstract

Background

The number of cystic fibrosis patients is increasing around the world, Latest forecasts published in the European Respiratory Journal indicate an increase of approximately 50% by 2025 (20% in the child population; 75% in the adult population).
There is no accurate epidemiological data on CF disease in Palestine. The general impression has been that the disease is rare, but this is most likely the result of under-diagnosis or misdiagnosis due to limited awareness of the condition in the region.
This disease has high treatment burden and some of the novel technology used for drug delivery is highly beneficial because it may ease patient burden by decreasing administration time and offer more efficacy and safety. These options are not available for CF patients in Palestine, only basic traditional therapies are available and this is the fundamental problem.
Assessment of the patient's perspective of symptom improvement, satisfaction and their reported increase in health related quality of life (HRQoL) should be part of the treatment decision making. Most of the cystic fibrosis patients QoL studies have been conducted in developed countries and only a few in developing countries but no studies were done in Palestine.

Objective

The purpose of this project was to study the Palestinian health situation by using specific comparison tools including; Quality of life issues of Palestinian CF patients attending the Caritas baby hospital, their health status, their related cost effective treatment (Economical burden) and summarize the available evidence on the use of new options for the treatment by using a willingness to pay survey.

Method

A descriptive narrative study conducted for patients from West Bank suffering from cystic fibrosis disease. These patients used basic classic therapies and attending pediatric pulmonology clinic in Caritas Baby Hospital. Around 77 participants completed four quantitative assessment measures and provided demographic information. The status of CF patients were studied by using different aspect. Their quality of life score using CFQ-R questionnaire were measured. Their health status were screened by measuring different parameter; pulmonary function test, body mass index, their age at diagnosis and mortality rate related to CF disease. Their health related cost and the amount of money they are able to pay for improving their treatment options using a willingness to pay survey were calculated. Caritas Baby Hospital (CBH) Medical Research Committee/Ethical Review Board approved this study and a written informed consents form for the patients and their families were obtained. Results were analyzed using scoring software and SPSS software.

Results and conclusion

The overall score for CF patients QoL parameters is less than 60% (ranges from 14.5-55.6) which indicate poor quality of life relative to other countries worldwide. The lowest score is for body (14.5), treatment (17.5), and respiratory (27.5). The highest score appears to be for eat (55.6) and emotion (50). Illness severity as measured by FEV_1 percent predicted with mean value of 69.6%. BMI recorded with mean value 15.998 (Kg/m^2). With the overall mean age at diagnosis in our sample was 4.16 years of age. The study showed that 58.3% (7/12) of patients from Hebron district had high mortality rate related to CF disease.

The result revealed that quality of life for CF patients is influenced by age, gender, taking vacation without disease, work or school status, BMI measures, age at diagnosis for the patient's parameters. In addition, QoL as scored by their parents parameter which included: the age, educational level and work status of both parents and is also affected by total number of CF patients in each family.

QoL for CF patients is not influenced by marital status, geographic distribution, place of residency (city, village and camp), FEV_1 measures, willingness to pay answers, their parent's relationship (father or mother), monthly income, and the effect of taking influenza vaccine yearly.

For willingness to pay, results indicate that 93.5% said yes and 6.5% said no. 51.4% of patients are able to pay 100 NIS out of pocket to 2.7% able to pay 2000 NIS or more out of pocket to get new drugs. With economical evaluation for CF patient, the total costs for patient with the mean age of our sample 10.7 years of age were estimated to be around 35650.2 NIS per patient per year. Cost reduction were estimated after applying Dornase-alfa as a mucolytic drug and Tobramycin nebulizer solution. This added value can help in part of the cost for making these drugs available for CF patients in our region.

Overall, quality of life for patients with CF is poor relative to international standards, the medications used including Hypertonic saline and Gentamycin IV form used as nebulizer solution are not first line therapies around the world, patients and their families demand better treatment and are willing to pay to get better treatment. Now we have an objective proof to submit for the need of new therapies for CF patients in Palestine in order to improve their QoL, health status and longevity.

Table of contents

List of Tables

List of Appendices

List of Abbreviations

AZLI	Aztreonam for inhalation solution
BMI	Body mass index
CBH	Caritas Baby Hospital
CF	Cystic fibrosis
CFF	Cystic fibrosis foundation
CFQ-R	Cystic fibrosis questioner –revised
CFRD	Cystic fibrosis related diabetes
CFTR	Cystic fibrosis transmembrane conductance regulator
CHQ	Child health questionnaire
CRDQ	Chronic respiratory disease questionnaire
DISABKIDS	Disability kid screen project questionnaire
DNA	Deoxyribonucleic acid
FDA	Food and drug administration
FEV_1	Forced expiratory volume in 1 sec
FLZ-CF	Questions on life satisfaction – CF specific
GRQ	Global rate of change questionnaire
HRQoL	Health related quality of life
HS	Hypertonic saline
MIC	Minimum inhibitory concentration
MOH	Ministry of health
NHP	Nottingham health profile
NHS	National health service
PedsQL	Pediatric quality of life inventory
QALYs	Quality-adjusted life years
QoL	Quality of life
QWB	Quality of wellbeing scale
RhDNase	Recombinant human deoxyribonuclease
RSS	Respiratory symptom score
RTIs	Respiratory tract infections
SEIQOL	Schedule for the evaluation of individual quality of life
SF-36	Short-form 36
SGRQ	St George's respiratory questionnaire
SIP	Sickness impact profile
TIP	Tobramycin inhalation powder
TIS	Tobramycin inhalation solution
TSI	Tobramycin solution for inhalation
WTP	Willingness to pay

Chapter 1: Introduction

1.Background

1.1Cystic fibrosis disease

Cystic Fibrosis (CF), also called Mucoviscidosis, is a life threatening inherited disease defined by Flume et al., as "a recessive genetic disease characterized by dehydration of the airway surface liquid and impaired mucociliary clearance" [1]. The discovery of cystic fibrosis can be dated back to the Middle Ages, when people had the saying: "Woe to that child which when kissed on the forehead tastes salty. He is bewitched and soon must die." This is one of the earliest references to cystic fibrosis, recognizing the association between the salt loss in CF and illness, although the condition was unnamed at that time [2].

CF with a defective gene located on chromosome 7. A 3 base-pair deletion (~F508) causes about 70% of CF cases with the remainder arising from >600 different mutations of the gene [3]. The five classes of CF mutations affect cystic fibrosis transmembrane regulator (CFTR) protein through different molecular mechanisms – classes I and V affect CFTR production, and classes II, III, and IV affect CFTR processing, regulation and conduction, respectively [4].

It affects the functioning of several organ systems, which can result in significant discomfort and pain. Due to a defective gene, individuals with CF lack a protein (CFTR) needed to regulate the exchange of salt and water across the cell membrane. This leads to thick, sticky mucus secretions in the respiratory, digestive, pancreatic, and reproductive systems. Over time, thick mucus clogs the bronchi that carry air in and out of the lungs, causing persistent coughing, wheezing, mucus production, inflammation and recurrent infections. Additionally, mucus blocks tubes within the digestive track that carry enzymes from the pancreas to the small intestine. Thus, nutrients are not efficiently absorbed from food, resulting in poor weight gain and growth, abnormal bulky stools frequent greasy, constipation, and intestinal blockage. Females with CF may have difficulty getting pregnant due to thick vaginal secretions and 99% of males with CF are sterile due to blocking of the vas deferens in utero [5]. Also patients with CF diagnosed with electrolyte imbalance particularly in countries with warm weather [6].

There are three common tests used to diagnose cystic fibrosis: the newborn screening test, the sweat test, and the genetic test. The sweat test (high Cl level in sweat is a sign of the disease $\geq$ 60 mmol/L) is convenient and fast, with no needles involved. It can be done in less than an hour, and results can be obtained on the same day the test is performed. A genetic test could be further performed to confirm individuals with a positive sweat test result [7].

Due to advances in therapy in the world, the life expectancy of people with CF has increased. From 1992 to 2012, the predicted median survival increased from 29.4 to 41.1 years. During the same time period, the median age at diagnosis decreased from 6 months to 4 months, likely because of increased newborn screening. Earlier detection of CF prevents further functional deterioration that can occur without preventive care [8].

As per a Cystic Fibrosis Foundation annual report, more than 70,000 people across the world suffer from CF [6]. However, this estimate is based on the data available from the existing registries in developed countries (primarily the United States, Europe and Australia [6, 9]. And it shows that CF is most common in European and European-derived populations as the prevalence of CF is highest in Caucasians and Ashkenazi Jews; where one child in every 2,500 and 2,300 births is affected, respectively. Nevertheless, CF is present in other populations such as Native Americans (1 in 10,900), African Americans (1 in 15,000), and Asians (1 in 35,000). Although previously considered rare in those of non-Caucasian descent, CF has now been found in all ethnic groups, with an estimated prevalence of 1 in 10,000 births among Arabs and with affected individuals from India, Iran, South East Asia and Turkey. Determining the precise magnitude of prevalence of CF in South East Asian and Middle East countries remains elusive [6].

Although cystic fibrosis is not as common in Arab populations as it is in Europe and the United States, there are still very high rates of children born with CF in the Middle East. According to Middle East Cystic Fibrosis Association (MECFA) reports for every 100,000 live births, CF will affect approximately 7 babies in Oman and Qatar, 17 in Bahrain, 24 in Saudi Arabia, and 33-39 in Jordan. Cases of CF have also been reported in the UAE, Kuwait, Egypt, Lebanon, Palestine, Iraq, Iran, and Pakistan. Unfortunately, many of these babies are diagnosed after one year or more, and many die in childhood. A comprehensive neonatal screening program in Middle Eastern countries could identify babies born with CF in their first days of life and treat them sooner, thereby reducing morbidity and mortality of the disease in the region [6].

1.2Treatment

The management of CF pulmonary disease requires a multidisciplinary approach with numerous treatment options as daily medical treatment, including physiotherapy and oral and inhaled respiratory medication to minimize deterioration of lung function, and dietary supplementation with pancreatic enzymes and vitamin supplements to prevent mal-absorption [10]. Adoption of these techniques increased the median survival age of patients with CF by 10-fold, from 3 to at least 30 years [3]. The primary cause of morbidity and mortality among CF patients is pulmonary disease caused by the most common bacterial infection Pseudomonas aeruginosa; in 2010,

approximately 37.5 % of UK patients were reported to have chronic P. aeruginosa [11, 12].

All over the world, clinical management of cystic fibrosis (CF) has improved during the past years. Increased standardization of care and a focus on maintenance therapies, including nutrition, combined with the introduction of dornase-alfa a mucolytic agent in 1993, tobramycin inhalation solution (TIS) in 1998, and the widespread long-term use of azithromycin (a macrolide antibiotic) have been associated with an approximate 8-year increase in median predicted survival age (increase from 1990 to 2005 to 36.5 years of age) and a 10% increase in median FEV1 percent predicted (from 1990 to 2005) [13]. Unlike the treatment in Palestine which still depends on the traditional old basic treatment of hypertonic saline as mucolytic and gentamicin intravenous form used as nebulizer solution antibiotic.

1.2.1 Chronic Respiratory Complications

Active treatment against bacterial colonization and overgrowth is necessary to prevent and control CF-related respiratory exacerbations. The Cystic Fibrosis Foundation (CFF) guidelines on chronic CF respiratory care recommend inhaled tobramycin for patients aged ≥6 years that have persistent airway cultures growing Pseudomonas aeruginosa, including asymptomatic carriers, to reduce the incidence of exacerbations. Other inhaled antibiotics with activity against P aeruginosa, including colistin, gentamicin, and ceftazidime, have been found to have inconclusive evidence for routine chronic administration for prevention of exacerbations [1].

Mucolytic Therapies: Several none antibiotic agents may be utilized to control respiratory complications. Pulmozyme® (dornase alfa) is strongly recommended to improve lung function and prevent exacerbations by degrading free DNA within mucus secretions. This drug effect modifies the viscosity of the secretions and allows the patient to more easily clear the airway. Hypertonic saline should also be used chronically to prevent exacerbations by altering the viscosity of mucous secretions. Studies have used various concentrations, often 6% to 7% sodium chloride. Nebulized hypertonic saline may cause a reactive airway and may be used concomitantly with short-acting beta2-receptor agonists. For patients with airway cultures persistently positive for P aeruginosa, oral azithromycin is recommended and has been shown to be effective at preventing exacerbations of CF [14].

Bronchodilators have been evaluated in chronic CF respiratory care. Inhaled short-acting beta2-adrenergic receptor agonists should be used chronically; however, inhaled anticholinergic lack the data to recommend chronic administration. Chronic use of inhaled N-acetyl-cysteine lacks sufficient evidence of efficacy for exacerbation prophylaxis [1].

1.2.2 Chronic GI Complications

Due to the chloride channel mutation and thickened viscous secretions in CF, pancreatic and biliary ducts become obstructed, leading to hepatic and pancreatic fibrosis by retrogradation of digestive enzymes. The decreased clearance and fibrosis lead to respective enzyme deficiencies for various exocrine and endocrine functions. With the decreased amount of pancreatic enzymes secreted into the small intestine, nutritional absorption is further decreased, specifically of fat and protein along with fat-soluble vitamins. Pancreatic enzyme supplementation may help to decrease symptoms such as steatorrhea and abdominal pain. The addition of antacid therapy with a histamine H2 receptor blocker or a proton pump inhibitor may increase the amount of enzymes that are delivered to the small intestine for absorption by increasing the pH of the gastric acid [14].

A separate manifestation but also related to the pancreas, CF-related diabetes (CFRD) ultimately affects up to half of all adult patients with CF. Liver manifestations occur in up to 70% of patients, most commonly hepatic steatosis [15].

1.2.3 Fertility Issues

Nearly all males with CF are born without a vas deferens, resulting in infertility. Women with CF also can experience fertility issues due to mucus-related obstruction of the cervix. Advances in nutrition and lung function have also contributed to an increased number of healthy pregnancies in women with CF [14]. From 1997 to 2012, the number of women reported to be pregnant by the CFF Registry increased from 137 to 249 annually [16].

1.2.4 Pulmonary Exacerbations [14]

Respiratory administration of antibiotics has become a novel area for disease management. Potential systemic toxicities may be avoided by employing the local administration of nebulized medications.

Table (1): Specific approved nebulized antibiotics for CF exacerbations are listed

Drug	Route	Dosing	Indication	Comments
Cayston® (aztreonam for Inhalation solution)	Inhaled	75 mg nebulized tid for 28 days; administer in alternating 28-day periods	Management of pulmonary exacerbations in CF	For persons ≥7 y
TOBI® Podhaler (tobramycin Inhalation powder)	Inhaled	112 mg inhaled bid for 28 days; administer in alternating 28- day periods	Management of CF patients with pseudomonas aeruginosa	For persons ≥6 y
TOBI® (tobramycin Inhalation solution)	Inhaled	300 mg bid for 28 days; administer in alternating 28 day periods	Management of CF patients with P aeruginosa	For persons ≥6 y
Colistin Inhalation	Inhaled	Adults: 100-150 mg bid Children: 75 mg bid	Prevention or treatment of pneumonia in CF patients	Safety and efficacy not established in infants
Zithromax® (azithromycin)	Oral	250-500 mg 3 days weekly	Improving pulmonary function in CF patients colonized with P aeruginosa	For persons ≥6 y
Tobramycin Injection	IV	10 mg/kg q24h	Management of CF patients with pseudomonas aeruginosa	Doses up to 12-15 mg/kg/day have been investigated in children with CF
Colistin Injection	IV	2.5-5 mg/kg/day in 2-4 divided doses	Prevention or treatment of pneumonia in CF patients	May also be given via continuous IV infusion

Continuous infusion of beta-lactam antibiotics has become popular at some institutions for control of CF exacerbations; and consensus in the literature indicates 14 to 21 days based on the patient's response to therapy [17].

1.2.5 New or Emerging Therapies

CFTR (cystic fibrosis transmembrane conductance regulator) modulator therapies are designed to correct the function of the defective protein made by the CF gene. Because different mutations cause different defects in the protein, the medications that have been developed so far are effective only in people with specific mutations. There are currently two FDA-approved CFTR modulators: Ivacaftor (Kalydeco®) and lumacaftor/Ivacaftor (Orkambi®).

Ivacaftor (Kalydeco®) was FDA-approved in 2012 for treatment of CF in patients aged ≥6 years that have certain CFTR genetic mutations. Unfortunately, only 4.3% of patients with CF in 2012 had the necessary mutations to benefit from therapy. It is the first approved drug for CF that is disease-modifying rather than addressing only the consequences of the disease, thus giving hope for future pharmacologic targets [14]. According to FDA news release in May 2017, U.S. Food and Drug Administration expanded the approved use of Kalydeco (Ivacaftor) for treating cystic fibrosis. The approval triples the number of rare gene mutations that the drug can now treat, expanding the indication from the treatment of 10 mutations, to 33.

The lumacaftor/Ivacaftor combination therapy is prescribed for people ages 6 and older who have two copies of the F508del mutation, which is the most common CF mutation. Several problems are caused by the F508del mutation, which prevents

CFTR from achieving the correct shape and reaching the cell surface. The combination therapy works to correct this in two ways. Lumacaftor moves the defective CFTR protein to the correct place on the cell surface, and Ivacaftor increases the protein's activity once it is in place [18].

1.3Cystic fibrosis-related quality of life (CFQ)

Health-related quality of life (HRQoL) was established as a paradigm to include the patients' perspective in clinical practice and research. Typically, HRQoL is defined as a multidimensional construct comprising (at least) physical, psychological and social well-being and functioning as perceived by the individual. Asking the patient "how they are" or about the effectiveness of treatments is nothing new. HRQoL instruments, however, can provide a formal, standardized, valid and reliable way of gaining the patients' perspective as to the benefits and limitations of a specific intervention [19].

QoL questionnaires have been included as part of most clinical trials of CF new drugs, but in many cases the instrument used was not clearly identified. A commonly employed tool consisted of 5 questions on general well-being (feeling, energy, physical activity, appetite, sleep pattern) and 4 on CF-related symptoms (ease of sputum expectoration, cough frequency, cough severity, congestion). Responses were ranked on a Likert scale, where 1 is the worst and 5 is the best outcome. However, there appears to have been no assessment of the reliability, validity or responsiveness of this questionnaire [3].

Later on two types of measures can be used to assess quality of life: generic and disease- specific instrument. Different types of scales have previously been employed and include: global rating of change, ad hoc, generic (SIP, NHP, SF36; CHQ, PedsQL), utility (QWB, EuroQoL), non-standardized profiles (SEIQoL), respiratory (CRDQ, SGRQ) [19]. The SIP is reliable and valid, although lengthy and therefore unwieldy in practice. The SF-36 has the advantage of brevity and is a valid tool, but is generally only applicable to adults. The QWB Scale is designed for general populations and measures physical symptoms combined with functionality (mobility, physical activity and social activity). This scale has been positively correlated with pulmonary function and physical status in some studies of patients with CF but not others, and its usefulness in children and adolescents has been questioned [3].

The first evidence that the QWB scale may be useful in tracking general life quality over time in patients with CF from 1987-1989 was from Pittsburgh CF center, this scale (QWB) applied in 28 patients with CF before and after a two-week course of oral ciprofloxacin used to treat pulmonary exacerbations. There were significant correlations between changes in QWB and various pulmonary function test results; Most of the patients showed improved pulmonary function and improved QWB after two weeks of oral ciprofloxacin treatment of their pulmonary exacerbations [20].

Using the NHP, pulmonary function (FEV_1 values) has been identified by some investigators as the main determinant of quality of life in patients with CF. Aspects of

daily living, such as social life, sex life, holidays, hobbies, employment and looking after the home, have been rated as significantly better in patients with higher FEV_1 values (about >50% of predicted). In contrast, other researchers, using the SIP, have found that overall scores correlated strongly not with FEV_1 but with dyspnea scores. Dyspnea may therefore be an important surrogate measure of physical functioning [3]. CF specific scales (CFQ, CFQoL, FLZ-CF, DISABKIDS). Only the CFQ has scales for both children and adults. Apart from CF specific scales, the only scales that have CF psychometric evaluation data for investigators to consult are the SF36 and GRQ. Thus far, only the respiratory scale of the CFQ has been approved by the US Food and Drug Administration (FDA) for use as an endpoint in trials. It is noteworthy that it is the CFQ domain (adolescent and adult) with the most acceptable interclass correlation coefficient for test-retest reliability. The scale captures perceived respiratory function/symptoms which is only one aspect of the much broader construct of HRQoL [19].

The quality of life for CF patients in developed countries have improved dramatically the last decades, due to regular periodic evaluations, monitoring for complications of the disease, and new interventions by physicians and other healthcare workers specifically trained in management of CF. The Cystic Fibrosis Questionnaire-Revised (CFQ-R) has been validated as a subjective measure to assess multiple domains of patient quality of life and is approved by the FDA as a patient reported outcome measure to be used as disease specific questionnaire [21].

CFQ-R is currently the most widely used HRQoL instrument for CF and was rated "well-established" in the recent reviews. The CFQ-R has not only been translated into 34 languages, with validation studies in all countries, but has demonstrated responsively in several clinical trials of medications with different mechanisms of action (e.g., antibiotics, mucus hydrators, gene potentiators) [21].

1. Problem statement

According to Cystic fibrosis foundation, Respiratory Tract Infections (RTIs) are a major cause of hospitalization for CF patients. More than one-third of the CF patients are hospitalized each year, and 20% of the CF patients are hospitalized more than twice a year. Of all CF-related hospitalizations, more than 75% is for treatment of RTIs [22].

The treatment goals for patients with CF lung disease are to halt or slow disease progression by maintaining FEV1 and preventing pulmonary exacerbations, to provide symptom relief, and to improve quality of life. As discussed, despite the availability of proven therapies, significant variability exists in these outcomes and the use of medications. Many issues likely contribute to this variability, including genetic, medical, and environmental factors. Understanding how these factors affect outcomes and addressing the barriers to care is a critically important task. Some specific obstacles facing patients, clinicians, and researchers (Table 2) are considered. By targeting barriers in each group for intervention, we hope to advance the development and delivery of CF care [23].

Table (2) Barriers to optimal therapy

Patient/family	Medical care providers	Researchers
- Adherence. - Treatment burden. - Mental health/depression. - Lack of insurance, underinsurance. - Lack of understanding (disease seriousness, treatment benefits, etc). - Heterogeneity of response (pharmacogenetics).	- Lack of resources/time. - Implementation of guidelines/evidence-based medicine. - Drug interactions. - Relaying hope vs. seriousness of disease. - Managing treatment failures, adverse events.	- Identifying appropriate outcome measures. - Need for large sample size. - Appropriate selection of controls. - Navigating regulatory guidelines. - Balancing need for new therapies with patient safety. - Lack of resources/time. - Competing clinical trials.

The status in Arab countries is more severe as the median survival for CF patients was estimated to be from 10 to 20 years of age, which reflects poor management strategy relative to other country for many reasons such as: delayed diagnosis due to decreased awareness of the variable presentation of the disease, lack of availability of diagnostic tool such as quantitative sweat chloride test and delayed institution of treatment due to delayed referral to a specialized CF center. Early pseudomonas colonization at 3 years compared to 7 years in the western countries. Poor compliance to treatment and chest physiotherapy, poor distribution of CF specialized centers, delayed nutritional rehabilitation [6], lack of more effective and potent medicines approved worldwide. In addition, poor adherence is a problem, especially during adolescence. The three most common barriers encountered were lack of time, forgetfulness, and unwillingness to take medication in public [10].

Also the major problem of CF in our countries is that CF is costly disease; patients with Cystic Fibrosis have thick, tenacious sputum. They are chronically colonized with bacteria. This leads to frequent exacerbations and is a burden for these patients. Of the patients in UK which are hospitalized each year (around 33%), 75% is treated for pulmonary infections [22].

Costs of patients with chronic P. aeruginosa infection were more than three times higher than of uninfected patients [24]. Therefore, medical professionals worldwide have limited treatment options that have shown to be both safe and effective in P. aeruginosa treatment. With continued research and patient compliance, CF patients will have improved quality of life and clinical outcomes [12]. Unfortunately, this medical progress isn't applicable in Palestine since old traditional treatment is available, this contributes to accelerated progressive obstructive disease which leads to major morbidity, reduced quality of life and, ultimately, high mortality rate. Wherefore the automatic therapeutic substitution is one method utilized to reduce healthcare costs while sustaining patient quality of care. The characteristics of these new medications are described below:

Table (3): Hypertonic saline compared to Dornase alfa (rhDNase) solution

	New: Pulmozyme® (Dornase alfa sol. rhDNase)	**Available:** Hypertonic saline
Packaging and mechanism of delivery	Inhalation solution in single-use ampules (2.5mg/2.5ml) delivered by nebulizer. It is new world wide available medication.	3%, 7% inhalation solution vial made to order by hospital pharmacy sterile products personnel in accordance with standards issued by pharmacopeia. Delivered by nebulizer.
Compliance and Adherence	_ less potential problems with drug stability. _ High dose uniformity as it given by nebulization and performance doesn't depend on patient's inspiratory flow profile.	_ potential problems with drug stability as it prepared locally in hospital. _ High dose uniformity as it given by nebulization and performance doesn't depend on patient's inspiratory flow profile.
Efficacy	_ According to the studies it's the most efficient mucolytic agent used for CF patients. _ It offers a therapeutic opportunity to reduce RTI-related health care use. _ Reduce number of hospitalization and the need to parenteral antibiotic and other antibiotics. _ Reduce the side effect of hypersensitivity and bronchospasm caused by HTS. (no need for bronchodilator). _ Improve general health perceptions and so the ability to function during the daily life (QOL).	_ It is approved to use in CF patients but not the first choice. _ may cause bronchospasm which necessitates the need to use bronchodilator as pre-medication.
Cost	Expensive	Less expensive

Table (4): Gentamycin compared to Tobramycin and Azetreonam lysine

	New: TOBI®(tobramycin)	**Available:** Zetamycin® (gentamycin)	**New:** Cayston® (azetreonam lysine)
Packaging and mechanism of delivery	- TOBI Podhaler (TIP) consists of a dry powder formulation filled into clear, colorless hypromellose capsules (28mg) for oral inhalation only with the podhalar device twice daily on cycle of 28-day. - TOBI 300 mg (TIS) single-use ampule, administered by inhalation, using a hand-held PARI LC PLUS Reusable Nebulizer with a DeVilbissPulmo-Aide compressor.	Intravenous gentamycin ampule (20, 40, 80mg) given as inhalation solution by nebulizer.	Single-use vial (75 mg of aztreonam) reconstituted with 1 mL of sterile diluent (0.17% sodium chloride) administered 3 times a day for a 28-day course by inhalation using an Altera® Nebulizer System.
Compliance and Adherence	- Propellant and preservative free if used TIP which reduce hypersensitivity RXN probability. - They have high deposition efficiency. - Short administration time (mobility). - Less potential problems with drug stability. - No need for power supply or pressurized air (immobility) with TIP use. - Performance depends on the patient's inspiratory flow profile in case of TIP and so there is a potential difficulties to obtain dose uniformity but it is opposite for TIS.	- There is a Preservative to be used for IV injection which may cause hyper sensitivity RXN such as bronchospasm. - It is delivered by simple type of nebulizer or by IV injection route so it need an medical intervention or hospital admission to give. - Low deposition efficiency. - Long administration time. - Need for power supply or pressurized air (immobility). - They have potential problems with drug stability. - High dose uniformity as it given by nebulization and performance doesn't depend on patient's inspiratory flow profile.	- Patients should use a bronchodilator before administration. - It is delivered by specific nebulizer. - High deposition efficiency. - Short administration time (mobility). - No potential problems with drug stability as it delivered by specific nebulization technique. - High dose uniformity and performance doesn't depend on patient's inspiratory flow profile.
Efficacy study	- Studies show that it is more effective against pseudomonas aeruginosa infection in CF patient than aminoglycoside drugs in reducing; - Total Hospital resource use and cost; By improve pulmonary function test FEV_1, FVC and ability to function during the daily life (QOL). _ Community service use and cost.	Less efficient than tobramycin and used as added on therapy for CF patients in the world.	It is the most effective antibiotic drug used for CF patients with pseudomonas aeruginosa infection as it Reduce total Hospital resource use and community service use and cost more efficiently.
Cost	Expensive	Less expensive than TOBI	Very expensive

The cost of administering aerosolized tobramycin three times a day is one-half the daily cost of administering two intravenous antibiotics at home and one-fifth the daily cost of administering two intravenous antibiotics in hospitals [25].

3. Aim of Current Study

To obtain a comprehensive understanding of CF patient's health status, one must monitor variables, such as disease severity related to health status, treatment adherence relative to health related cost, social support, and HRQoL. Health related Quality of life (HRQoL) issues are important when one considers that CF is a disease with high morbidity (mostly related to pulmonary involvement) and early mortality. With the various treatment options for CF pulmonary disease, the question to optimize medical treatment is a crucial issue in CF care and, basically, the approach of a survey on evidence based therapy in CF can give some answers to this basic question.

The overall objective of this study was to evaluate the Palestinian CF Patients health situation by studying quality of life issues, health status and economic burden. In addition, the study summarizes the available evidence on the use of new treatment options and examines its application in Palestine by using a willingness to pay survey. To date, few studies were done on CF disease in Palestine and the studies done only determined the CF mutation spectrum in our patient population [26, 27], but no study have discussed QoL of cystic fibrosis patients and factors that affect it.

The following objectives and hypotheses were evaluated.

Study aims and hypotheses:

1. The first aim was to measure quality of life (QoL) scores for children, teens, and adults with CF and parent caregivers to provide data about their status.

    a. Hypothesis 1: Low quality of life scores for adult group than children group with the treatment domain as the most one.
    b. Hypothesis 2: A good agreement between the mean scores on the CFQ Parents 6-13 and the information obtained by means of the questionnaires applied to their patients. Differences are expected especially regarding physical, weight and emotional aspects.

2. The second aim was to compare QoL score for our patients (using basic therapies) to patients in developed countries (using advanced therapies).

    a. Hypothesis 3: Low quality of life (QoL) domain scores for CF- patients in Palestine compared with other population worldwide.

3. The third aim was to correlate the relationship between HRQoL and clinical (lung functional test, BMI and diagnostic age) and with demographic factors of patients using basic therapies.

    a. Hypothesis 4: There is a correlation between CFQ-R scores and gender, Females may be expected to have lower QoL score on specific domains of functioning than male.
    b. Hypothesis 5: In general, as both education and income levels increase, the QoL parameter would be enhanced.
    c. Hypothesis 6: Most of patients suffering from CF disease was from southern region countries with more than one CF patient in each family.
    d. Hypothesis 7: There is a high percentage of families we interviewed have a child died from CF disease.
    e. Hypothesis 8: Most of patients diagnosed later on not at the first year of their life. And so for the patients diagnosed earlier in their life, CFQ-R scores are higher than patients diagnosed later on their life.

4. The fourth aim was to examine the total healthcare resources use and cost of our patients then looked up literature to see the percentage of reduction in the cost after using such new medication and using this percentage to apply to our cost.

    a. Hypothesis 9: healthcare resources costs of our patients are very high and expensive and will be decreased as the new advanced therapeutic options supplied to our patients.

5. The fifth aim was to assess the willingness of CF patients/families to contribute to the cost of new therapies and to examine the association between the QoL and willingness to pay survey.

    a. Hypothesis 10: Patients willing to pay the highest amount in order to reduce symptoms of CF disease.

Chapter 2: Literature review

Issues:

• What evidence is available for the efficacy and safety of inhaled tobramycin, aztreonam, and dornase alfa for cystic fibrosis (CF)?

• Is there comparative evidence that either inhaled tobramycin or aztreonam is superior in efficacy or safety?

• Are there specific subpopulations or clinical situations in which one inhaled antibiotic provides clear benefit over another?

Systematic search of all the published literature that has considered the evidence for antimicrobial therapies in CF with key findings were as follows: inhaled antipseudomonal antibiotic improves lung function, and probably the safest/most effective therapy; anti staphylococcal antibiotic prophylaxis increases the risk of acquiring P. aeruginosa; azithromycin significantly improves respiratory function after 6 months of treatment; a 28-day treatment with aztreonam or tobramycin significantly improves respiratory symptoms and pulmonary function; aztreonam lysine might be superior to tobramycin inhaled solution in chronic P. aeruginosa infection; oral ciprofloxacin does not produce additional benefit in those with chronic persistent pseudomonas infection but may have a role in early or first infection [28].

And also published clinical data show that inhaled tobramycin reduces the bacterial load, improves lung function and reduces the number of hospital admissions. Inhaled tobramycin has been used successfully to eradicate P. aeruginosa in patients with early infection. Maintaining clinical benefits requires chronic tobramycin treatment, and the concept of chronic intermittent inhaled treatment (typically, alternating drug and drug-free periods of 28 days) was introduced to minimize the emergence of aminoglycoside resistant P. aeruginosa strains. Other therapeutic advances include the development of different tobramycin formulations and nebulizers that reduce delivery time without compromising efficacy [9].

RhDNase offers a therapeutic opportunity to reduce RTI-related health care use in CF patients. The objective behind therapy with rhDNase is improving health related quality of life and additionally lowering the costs of CF including several cost components hospitalization, exacerbations, symptoms, therapy, RTI related, antibiotics, etc. [22].

1. Efficacy studies

A J MARTIN, Birmingham Children's Hospital study results show that P. aeruginosa can successfully be eliminated or suppressed with high-dose aminoglycoside plus carbenicillin, but such elimination is usually short lived**.** In vitro studies showed gentamicin to be 2- to 4-fold less active against isolates of mucoid P. aeruginosa than tobramycin. The MIC to tobramycin ranged from 0.5 to 1 mg/l and from 0.5 to 2 mg/l for gentamicin [29].

Some studies suggest that tobramycin may be less nephrotoxic than gentamicin. Acute renal failure has been very rarely reported in patients with CF. Smyth et al. recently published a case-control study of 24 patients with CF from 20 UK centers. They found that use of intravenous aminoglycoside is a risk factor for renal impairment, with gentamicin being more nephrotoxic than tobramycin [9].

TIP via the Podhaler has been shown to be safe, similarly effective to Tobramycin inhalation solution (TIS) and faster to deliver if compared to TIS delivered through the PARI LC PLUS jet nebulizer (mean time for delivery 5.7 versus 19.7 minutes respectively) though delivery would have been faster through other commonly used vibrating mesh nebulizers such as the e-Flow. Patient-rated satisfaction scores favor TIP over TIS, though there was a higher rate of cough, dysphonia and taste disturbance and of discontinuation of TIP [30].

The EAGER trial enrolled 553 CF patients comparing TIP to TIS over 3 cycles of treatment. The EVOLVE trial, including 102 CF patients, was placebo-controlled for 1 cycle followed by open label treatment with the TOBI Podhaler for 2 additional cycles of treatment. The Podhaler formulation displayed similar tolerability and efficacy to TIS and significantly improved FEV1 compared with placebo. Cough was the most frequently reported adverse reaction related to the dry powder in both clinical studies. The recommended dose is 112 mg (four 28 mg capsules) inhaled twice daily in alternating cycles of 28 days on treatment followed by 28 days off treatment. TIP is currently available in some European countries, South America, and Canada [31].

In several clinical studies Cayston® (aztreonam) has been shown to be safe and efficacious in suppressing chronic P. aeruginosa lung infection in CF patients. In a randomized, placebo-controlled study of 164 CF patients, Cayston® significantly improved CFQ-R Respiratory Symptoms Score (RSS) and FEV_1 after one cycle of use at 28 days, with a treatment difference compared to placebo of 9.7 points and 10.3%, respectively. In a second pivotal trial of 211 patients with CF, Cayston® increased the median time to need for additional anti-pseudomonas antibiotics for symptoms of pulmonary exacerbation by 21 days, versus placebo. In the open-label follow-on study of these two trials, Cayston® safety and efficacy was examined in 274 patients over 18. FEV1 values, CFQ-R RSS, and body weight increased with each 28 day course of Cayston®, and this effect was maintained over 18 months. No significant safety concerns were observed in studies over 12 months and 18 months; including no evidence of development of antibiotic resistance [31].

In a 6 month active comparator trial of 273 CF patients receiving either Cayston® (aztreonam) or TIS, Cayston® was superior to TIS with regard to lung function improvements, with a treatment difference of 7.8% at 28 days and 2.7% at 24 weeks. Significant reductions in pulmonary exacerbations and mean change in CFQ-R RSS after 28 days of Cayston® treatment were also seen, compared to TIS. In the follow-on 6 month open-label extension of this active comparator trial, the FEV_1 response of previous TIS subjects who were switched to Cayston® improved and was sustained over time. Patients receiving Cayston® also gained weight throughout the 12 month trial, compared to those who received TIS who initially lost weight and then improved

upon switch to Cayston®. Cayston® is available in the EU, Switzerland, USA and Canada. Cayston® is licensed for use in patients 6 years and older [31].

The Pulmozyme (rhDNase) Early Intervention Trial (PEIT) of Robinson et al, showed reduction in the risk of pulmonary exacerbations and thereby a reduction of 34% in parenteral antibiotic therapy. This study also showed an improved forced expiratory flow at 25 to 75% of FVC and improvement in FEV_1 over a 2 year period in CF patients with almost normal lung function. The results of this study, conducted at 49 sites in 12 countries in a randomized trial (placebo-controlled) design, showed benefits from rhDNase in CF patients from early intervention in the course of their lung disease. In another, this time short term, study of rhDNase of Robinson et al, an increase of 7.5% in FEV_1 and 5.4% in FVC from baseline was seen in patients who received rhDNase compared with placebo [22].

Fuchs et al. found a reduction in exacerbations of respiratory symptoms and a slight improvement in pulmonary function after 2.5mg rhDNase therapy in a randomized, double-blind, placebo-controlled study in which 968 patients participated. One or more exacerbations occurred in 27% of the patients who received a placebo, 22% in patients who received once daily rhDNase and 19% in patients who received twice daily rhDNase (2 x 2.5 mg). The FEV_1 improved with about 6% in patients who received rhDNase [22].

Hypertonic saline and recombinant human DNase: a randomized crossover pilot study in patients with cystic fibrosis demonstrated the first evidence that the effects of HS and rhDNase on FEV_1 (% predicted) were comparable in a group of mild to moderately severe ill children with CF. Approximately 30% of patients showed a clinically relevant increase of FEV_1 (>10%) with rhDNase and the same was observed for HS. The substantial variations in the same individual in the response to HS or rhDNase might reflect the diverse influences of HS (viscoelasticity) and rhDNase (spinnability) on sputum which might have different relevance in the individual patient. Thus, a patient not respond to HS might be successfully treated with rhDNase and vice versa [32].

Suri et al. compared the consequences of three therapies in children: 1) daily rhDNase (2.5 mg), 2) alternate day rhDNase (2.5 mg) and 3) hypertonic saline (two times per day) during 12 weeks. The study was an open randomized cross-over trial, in which 48 children with CF were allocated. This resulted in a significant greater increase in mean FEV1 (2-14%) with daily rhDNase compared with hypertonic saline, while daily and alternate daily rhDNase did not differ significantly [33].

In another clinical trial, Grieve et al. investigated the effect of 12 weeks treatment with daily rhDNase, alternate day rhDNase or hypertonic saline (HS) in a randomized, crossover study, in which 40 children with CF were allocated. They found a 14% (5-23%) improvement in FEV1 for daily rhDNase compared with HS, while alternate day rhDNase compared to HS resulted in a 12% (2-22%) improvement in FEV1. There was, as also described by Suri et al, little difference between FEV1 of daily and alternate day rhDNase [22].

Ballmann and colleagues did a pilot cross-over trial comparing 3 weeks of daily rhDNase with 5.85% hypertonic saline in 14 patients. Both drugs were administered

by jet nebulizer. Increases in mean FEV_1 were 8% and 9% for hypertonic saline and rhDNase, respectively. Statistical testing was not done owing to small numbers [33].

2. Studies of Quality of Life considerations

The respiratory symptoms of CF can adversely affect daily activities of the patient with CF, because of the unpredictability of these symptoms and serious consequences of exacerbations. It is difficult to predict the degree to which the quality of life of an individual can be affected by CF. Some studies mention that the great majority of CF patients live well in adulthood with an acceptable quality of life, due to basic therapies. New therapies can help to improve the quality of life. However, all patients suffer from deterioration in their disease, which leads to limitations and thus ultimately reduces quality of life significant. The majority of morbidity and mortality in CF results from inflammation and infection of the airway lumen, which leads to a certain degree of disability in patients with CF. In one study, the impact of pulmonary exacerbations on quality of life in CF patients was studied. The objective was to compare health-related quality of life (HRQoL) of CF patients to general population and to determine the relationship between HRQoL and clinical and demographic factors [22].

HRQoL measures the individual ability to function in different area and the individual's evaluation of their functioning. The study of Britt et al. showed that exacerbations do not have a profound negative impact on HRQoL that is not explained by differences in function of lungs, nutrition status or demographic factors. In spite of this, lung function, nutrition, 6-min walk, age, gender, and insurance status were not significantly associated with HRQoL in this study population [34].

On short term, well-being and quality of life of CF patients is improved by rhDNase, through improvement in lung function and a reduction of RTI incidence. In the study of Oster et al, questionnaires were developed to evaluate well-being (feeling, energy, activity, sleep, appetite) and physical symptoms (sputum production, frequency and severity of cough, chest congestion). The results mentioned that compared to the placebo group, there was significantly less dyspnea, significantly improved wellbeing and there were significantly fewer CF related symptoms in the rhDNase-group. This implies that when CF patients are treated with rhDNase they have a better quality of life compared to patients who are not treated with rhDNase [35].

Another study noted that baseline HRQoL assessments show that adults with CF, reported decrements in health status and functioning. In this study, a significant association was found between the rhDNase therapy and one-year change in HRQoL. One of their suggestions was that a further evaluation of the relation between hospital admission and changes in HRQoL is required [36].

As opposed to life expectancy, morbidity and mortality, quality of life is mainly not affected by the CF disease as such (e.g. dietary requirements), but much more by the symptoms and respiratory tract inflammations and infections. Hospitalization affects quality of life also in a negative sense. RhDNase has a positive short-term effect on the quality of life as mentioned above [22].

Three-month data from the 24-week Australian rhDNase Phase IIIb Study in 69 patients demonstrated significant improvements from baseline ($p < 0.05$) in total CF-specific score (3%) and SF- 36 total score (7.5%) with dornase alfa 2.5mg once daily. Significant improvements also occurred in the domains of emotional functioning, energy levels, coughing, sputum production, congestion, chest pain and sleep patterns [3].

Alexandra L. Quittner study examined the effects of TSI on global ratings of health-related quality of life (HRQoL) by patients (or their parents) in 520 patients with CF and chronic pseudomonas aeruginosa infections were analyzed retrospectively. They receive 24 weeks of placebo or treatment with TSI 300 mg bid both in 3 cycles of 28 days followed by 28mg days off, there was strong agreement between the paired patient/parent and physician global HRQoL rating across the three cycles. And they more likely report improvements in HRQoL than were patients in placebo group. And change in FEV1% predicted values was rated significant improvement only at the end of the cycle 1. The result of this provide consistent evidence that TSI was associated with improved global ratings of HRQoL completed by both patients or parents and physicians [37].

3. Economic evaluation studies

There have been relatively few economic evaluations of antibiotic treatments in CF, with three different areas of interest: (a) the economic value of home- versus hospital-based intravenous therapy, (b) assessment of cost-effectiveness of inhaled antibiotics, specifically TIS and AZLI and (c) the relationship between costs, including patient co-payments and out of pocket expenses, and adherence and (d) the economic value of antibiotic eradication therapy [31].

The main economic findings were that (i) the annual costs of care for CF vary greatly with disease severity; (ii) hospitalizations account for the greatest portion of costs for CF patients; and (iii) the costs of expensive therapies may be partly offset by savings in other resources [38]**.**

One of the economic evaluations of TIS have been conducted in the UK from the perspective of the National Health Service (NHS) and in Canada from the perspective of the Canadian Health Service in Ontario and Quebec. In Canada, the acquisition cost of TIS was estimated to be CA$8602 over a 24-week period. Mean offsets in direct medical costs for all patients treated with TIS versus placebo were CA$4916 in Quebec and CA$4055 in Ontario. In the UK, in all patients the cost of TIS was partially offset by savings of £3719 per year compared with placebo in 2001. This was primarily because of a reduction in the mean number of days spent in the hospital (7.8 days), resulting in savings of £2345 and a reduction in the mean number of days treatment with intravenous antibiotics (6.4 days), resulting in savings of £1344. The net direct cost was £6292 per year, based on a TIS acquisition cost to the NHS of £10,010 in 2001. Inpatients aged ≤18 years, the direct cost offset was £6180, resulting in a net cost versus placebo of £3830 [39].

A study was designed to investigate in a British population the impact of TNS on usage of costly health care resources that have a high consumption in CF. The study set out to compare utilization of specified healthcare resources over two 1 year periods before and during treatment with TNS in patients with CF. Use of inhaled TNS for 12 months in the study population of moderately severely affected CF patients gave rise to important clinical and social benefits such as reduction of hospitalization and the use of intravenous antibiotics, which would be expected to improve patients' quality of life as well as to reduce interference with work and schooling. Its acquisition cost was partially offset by the savings that occurred in these expensive components of patient care [38].

Recently, a cost-effectiveness analysis of the AZLI–TIS active comparator study was performed using a Markov model with health states defined principally by FEV1 % predicted levels. Over 3 years, AZLI use was associated with increased life-years, reduced number of hospitalizations, increased QALYs, and a subsequent cost savings of over $6000 over TIS [31].

Oster et al. used data from a U.S. clinical trial that compared the effectiveness of rhDNase with placebo in adults with CF. However, this study excluded the cost of rhDNase and only assessed respiratory tract infection–related health costs. The study suggested that rhDNase (administered once or twice daily) improved patients' lung function and reduced hospitalizations, which could potentially offset around 25% of the drug's cost. Menzin et al. used data from the same U.S. trial to compare the costs of rhDNase with placebo in four different European countries. The analysis used expert opinion to adapt the resource use observed in the trial to a European context, and concluded that rhDNase could reduce health service costs by between US $700 and $1,000 over 6 months. The validity of the latter study was limited by the extent to which data could be transferred between the United States and Europe [40].

The cost effectiveness of dornase alfa was evaluated in the North-West region of England (cost per in-hospital day avoided, £2857) was found to be considerably less than for clozapine in schizophrenia but much better than for interferon in multiple sclerosis. A caveat to such comparisons is that costs and drug use are influenced by differences in approaches to treatment for the various diseases and among different countries [3].

Suri et al. compared mean incremental costs of daily and alternate day rhDNase with hypertonic saline (HS) over a 12 week period as investigated in a clinical trial, in which they labeled themselves a cost-consequence analysis. The mean incremental costs of daily rhDNase compared with HS were €1409 and the incremental cost of using daily over alternate day rhDNase was €513. A formal cost-effectiveness analysis to analyse whether the increased effectiveness of daily rhDNase compared to HS twice daily delivered by nebulizer was not done. It was merely concluded that daily rhDNase was more expensive and significantly increases health care costs. Administering rhDNase on an alternate day rather than on daily basis may be as effective, with a potential cost saving [33].

A U.K. study has recently compared the effectiveness and costs of treating children with CF with daily rhDNase (2.5 mg), alternate day rhDNase (2.5 mg) and HS. The

study was based on a randomized controlled trial with a crossover design, with 40 patients receiving each treatment for 12 weeks, with a 2-week washout period between treatments. The primary outcome measure was the patients' lung function measured by forced expiratory volume in 1 second (FEV1). Comparing mean FEV1 between the treatments, the trial reported an 8% (95% CI, 2% to 14%, $p = .01$) advantage for daily rhDNase over HS, but none for daily compared with alternate day rhDNase (2%, 95% CI, −4% to 9%, $p = .55$) [40].

Grieve et al. study show compared the relative cost-effectiveness of daily recombinant human deoxyribonuclease (rhDNase), with alternate day rhDNase and hypertonic saline (HS) for treating children with cystic fibrosis (CF). A randomized controlled trial with a crossover design allocated 40 CF children consecutively to 12 weeks of daily rhDNase, alternate day rhDNase, or HS. The primary outcome measure was forced expiratory volume in 1 second (FEV_1), a measure of lung function. All health resource use was prospectively documented for each patient and multiplied by unit costs to give a total health service cost for each 12-week treatment period. The non-parametric bootstrap method was used to present cost effectiveness acceptability curves and net benefit statistics for each treatment comparison, for various hypothetical levels of the decision maker's ceiling ratio. Compared with HS, there was a 14% improvement in FEV1 for daily rhDNase (95% CI, 5% to 23%), and a 12% improvement (95% CI, 2% to 22%) for alternate day rhDNase. For a ceiling ratio of £200 per 1% gain in FEV1, the mean net benefits of daily and alternate day rhDNase compared with HS were £1,158 (95% CI, −£621 to 2,842) and £1,188 (95% CI, −847 to 3,343), respectively; the mean net benefit of daily compared with alternate day rhDNase was −£30 (95% CI, −£2,091 to 1,576). If decision makers are prepared to pay £200 for a 1% gain in FEV1 over a 12-week period, then on average either rhDNase strategy is cost-effective [40].

4. CF in Palestine

The rate of consanguineous marriages in Palestine, was found to be 45% in 2004 [41], indicating that Palestine has a very high risk of congenital disorders including CF, but there are no accurate epidemiological data on CF. The general impression has been that the disease is rare, but this is most likely the result of under-diagnosis or misdiagnosis due to limited awareness of the condition in the region.

In Palestine, the only studies published discussed the disease and the mutation causing it. As the mutation of the disease in the Cystic Fibrosis Transmembrane Conductance Regulator gene (CFTR) that contributes to the clinical presentation of CF are ill defined. Two studies have been done to determine these mutation one of them was from September 2011 until November 2012, Caritas Baby Hospital (CBH) personnel conducted it to determine the CFTR mutations in a Palestinian cohort affected with CF. A total of thirty three patients from twenty one different families residing in the central and southern part of Palestine with the exception to Gaza district were incorporated in this study. Nine different CFTR mutations were identified, c.1393-1G>A, appeared to be the most common (28.6%), followed by F508del (19%) and W1282 (14.3%) in the cohort of Palestinian families evaluated in West Bank only

[26]. Unlike other countries where F508del is the most common mutation, c.1393-1G>A is the most occurring CFTR mutation among a cohort of Palestinians affected by CF despite the fact that this mutation is infrequent in the neighboring countries, and considered rare worldwide [26].

Another broader study was in Clinical Laboratory Science, Birzeit University published on December 2014 [27]. Samples from 60 unrelated CF patients residing in the West Bank and Gaza were collected and their respective CF mutations were determined. Eighteen different CF-causing mutations were identified. Although most mutations are rare, the three-base-pair deletion p.(Phe508del) is most common (35% of the positive cases). mutations c.1393-1G>A, p.(Gly85Glu), p.(Trp1282X), and p.(Asn1303Lys) were only present among Palestinians in the West Bank, while mutations p.(Lys684Serfs∗38) and c.1585-1G>A were only present among Palestinians residing in Gaza. Interestingly, the p.(Phe508del) mutation was primarily prevalent among patients living in Gaza (68%) as compared to patients in the West Bank (32%) [27].

Unfortunately, all of the mutations observed and studied in our CF patients are not mentioned in approved mutations for CFTR genetic treatment options as Ivacaftor (Kalydeco®) drug until now.

Status in Gaza

A project was established by Dr. Mahmoud Shamaly to manage CF resources poor settings in Gaza resulted on the following data [42]:

"After yearlong training period, a CF center was opened in Gaza. A database was established to register all known CF patients. They are currently aware of 80 patients with CF in the Gaza strip. Based on population projections, it is estimated that there are between 140-321 patients with CF in Gaza, a large number of which have not been diagnosed and others whom have died of CF complications without an established diagnosis. Limited resources under the current government continue to be problematic. Medications are still in short supply and are available mainly by private donations. Prior to the arrival of the trained CF team, the medical staff frequently dosed those medications that were available such as pancreatic enzymes incorrectly. Trained personnel are still unable to provide physiotherapy to many patients. Appropriate and effective inhalation machines are not available and have been replaced by cheaper, less efficient units. Hypertonic Saline is the standard mucolytic/secretion clearance treatment. Families commonly prepare this at home by mixing 15% Hypertonic Saline with 0.9% Normal Saline. Inhaled antibiotics such as TOBI are not available and are replaced by inhalation of intravenous solutions such as Gentamicin. Nutritional supplements are rarely available and again, only by private donation. Food enrichment is done by families by mixing cereal with oil. Appropriate next steps in the evolution of the CF program in Gaza are to work with health authorities to understand the importance of providing basic therapies to patients".

5. Role of pharmacist in CF disease

Pharmacotherapy has long been the cornerstone of effective treatment for cystic fibrosis. To a growing extent, pharmacists become involved in developing formularies for CF care and in supporting disease management pathways for CF. Pharmacists play a unique role in managing complex pharmacotherapy regimens around unique pharmacokinetic profiles. Novel formulations of medications and unusual sites of administration make a pharmacist a central provider of proper CF care. The document specifically cites that a dedicated CF clinical pharmacist reduces medication errors and increases availability of medications [14].

The European Cystic Fibrosis Society (ECFS) Cystic Fibrosis Centre, describes the CF Clinical Pharmacist as pivotal to the medicines management program to support the optimization of medicines for patients, and describes the role of the CF clinical pharmacist [43].

Common roles and responsibilities of the pharmacist:

- Managing formularies, clinical guidelines and treatment protocols.
- Medication reconciliation/history taking.
- Prescription monitoring and medication review service.
- Identifying patient and medication risk factors.
- Preventing, detecting and reporting adverse drug reactions.
- Individualizing drug and dosage requirements.
- Educating and counseling patients and cares.
- Evaluating medicine use and assess patient compliance.
- Order and evaluate appropriate laboratory tests.
- Pharmacists today intend to collaborate with doctors to develop treatment algorithms and evidence based guidelines for drug classes and disease states as well as to write monographs describing the use of specific agents.

The benefits of a dedicated CF pharmacist have been described, including benefits in terms of financial savings, improvements in patient care, adherence and efficient use of resources as they may use prescription records in order to provide information for improving quality of treatment and to ameliorate patient satisfaction [44].

Off-label use of medicines

During the clinical care of people with CF, there is often a need to use medicines outside of their product license. A new medicine, for example, may not have been subject to the rigorous trials necessary to gain a pediatric product license; or it may be necessary to manipulate a formulation so that it can be administered via an unlicensed route, such as nebulization of an intravenous drug formulation. Although off-label use of medicines is not routinely recommended, it is often necessary in the CF population due to the complexities of the disease, and heterogeneity of the complications encountered. The CF pharmacist will be involved in ensuring these medicines are used in the most safe and effective way and can apply pharmacokinetic and pharmacodynamics principles to determine appropriate dosing [43].

Chapter 3: Method

Design

This was a descriptive narrative study for patients with cystic fibrosis who visited the pediatric pulmonologist clinic of Caritas Baby Hospital from January 2017 until May 2017. Participants completed four quantitative assessment measures and provided demographic information. The patients' routine medication was not altered during the study. According to Caritas Baby Hospital records and files there is around 86 patients from West Bank suffered from cystic fibrosis disease.

Participants

Participants were recruited through their normal routine visit to the clinic or by contact with them to come to the clinic. A total of seventy seven eligible participants from fifty eight different families residing in the northern, central and southern part of Palestine with the exception to Gaza district consented to take part in the study. Questionnaires were fully completed by all participants and calculations were carried out to establish the size of correlation which could be confidently detected for a sample size of 77. The majority of the families 38 (65.52%) came from Hebron district, followed by 5 (8.62%) from Jenin district, 4 (6.89%) from Nablus, 4 (6.89%) from Bethlehem district, 4 (6.89%) from Ramallah district, 1 (1.73%) from Jerusalem district, 1 (1.73%) from Tulkarem district and 1 (1.73%) from Qalqilia district. Potential participants and their parents were approached during routine clinic visits while waiting for their appointments.

Inclusion and exclusion criteria:

Patients were included in the study if they met the following criteria: a proven clinical diagnosis of CF as evidenced by a positive sweat test or the presence of two known CF mutations; which confirmed by a pediatric pulmonologist doctor based on their clinical manifestations. The principal inclusion criteria were:

1. The caregiver must have a child diagnosed with CF.
2. The diagnosis of CF must have been made by specialist doctor.
3. The caregiver must have a reasonable understanding of the study, understand what is involved of them and be competent enough to refuse participation.

Participants were excluded from the study if their Caregivers or children have physical or mental disabilities which prohibit them from participating in the study successfully. But in our study we don't exclude any family member diagnosed with

CF disease. There were other CF patients that Caritas was aware of, but three of them refused to participate as they do not acknowledge the existence of the disease and three others cannot be reached because they traveled to other countries for treatment.

Procedure

After recruiting and screening participants and standardized the study protocol, we interviewed family that came to the clinic, administered consent forms, and instructed to administer questionnaires to both children and their parents. The protocol and consent forms were approved by the ethical review board at the hospital.
The CFQ-R versions were administered to all patients. Parents of participants were asked to complete a demographics, health status, socioeconomic burden, willing to pay questionnaire and the CFQ-Parent version, a proxy measure of HRQoL for children with CF. After completion the versions of the CFQ and all questionnaires, pulmonary functioning tests, BMI (weight/length percentile) and physical exams were conducted to assess health status. We confirmed the data by reviewing the medical charts and files for each patient.
We contacted Dr. Alexandra L. Quittner professor and director in Department of Pediatrics and Otolaryngology, Head & Neck Surgery, University of Miami/School of Medicine, Miami, Florida to get the international data for QoL to compare it with our result and to demonstrate the status of our CF patients.

Measures

1. Cystic Fibrosis Questionnaire – Revised (CFQ-R)

In this study Cystic Fibrosis Questionnaire-Revised a Health Survey was used to find the QoL of CF patients. CFQ-R is a disease-specific health-related qualify of life (HRQoL) measure for children, adolescents and adults with cystic fibrosis (CF). It is a profile measure of HRQoL with several different domains. It was initially developed through focus groups and interviews with CF patients and health care professionals and has undergone extensive reliability and validity testing [45]. It is one of the most widely used HRQoL measures for CF and was judged as "well-established" in a review of evidence-based measures. It is being used in the United States and internationally in a number of clinical trials. It is also used clinically during routine CF care.
The CFQ-R has been translated into several languages including Arabic-Israel is the one we used in this study without any modification. Linguistic validation has been conducted with input from Dr. Alexandra Quittner [45].

There are 4 versions of the CFQ-R currently available we used in this study:

- Teen/Adult version (≥14 years).
- Child version with two formats
  - Interviewer-administered format for 6-11 years
  - Self-report format for 12-13 years
- Parent version for children 6-13 years.
- Preschool version for ages less than 6 years [46, 47].

Cystic Fibrosis Questionnaire–adult Version

CFQ-Teen/Adult for ages ≥ 14 years (self-report) contains 50-items within twelve domains [48]. Which include Physical functioning; this part contains questions such as climbing stairs, kneeling and walking, Role limitations; limitations because of physical functioning, Vitality, Emotional functioning, Social functioning; this part contains questions about the effect of physical and emotional health on social life, Body image, Eating disturbances, Treatment burden, Health perceptions, Weight problems, Respiratory symptoms, Digestive symptoms.

CFQ-R subscales items of physical functioning (eight items), emotional functioning (five items), role functioning (four items), social functioning (six items), vitality functioning (four items), body (three items), eat (three items), treat (three items), health (three items), weight (one item), respiratory (seven items) and digest (three items) were rated on a four-point Likert scale. A standardized score ranging between 0 – 100 is obtained for each subscale, with higher scores indicating better functioning.

Cystic Fibrosis Questionnaire–Child Version. The CFQ-Child is a disease-specific HRQoL measure for children with CF between the ages of 6 and 13 [49]. Two format of the CFQ-Child were established: an interviewer-administered format for children 6 –11 years of age and a self-report format for 12 –13 year olds. The CFQ-Child is a 35-items instrument that assesses multiple domains of HRQoL. This questionnaire includes three broad domains of HRQoL, including Physical Symptoms (6 items), Emotional Functioning (8 items), and Social Functioning (7 items). The CFQ-Child also assesses five domains specific to CF, which include Body Image (3 items), Eating Disturbances (3 items), Treatment Burden (3 items), Respiratory Symptoms (4 items), and Digestive Symptoms (1 item). Nineteen items required a true or false rating on a 4-point scale ranging from not at all true to very true. Sixteen items required a frequency response ranging from always to never on a 4-point scale. The CFQ-Child took approximately 15 minutes to complete. Raw scores for each of the eight scales were converted into standardized scores (0-100), with higher scores representing better HRQoL.

Cystic Fibrosis Questionnaire–Parent Version. The CFQ-Parent is a measure of the parent's report of their child's HRQoL for children aged 6 to 13 [48, 49]. It is a 44-item self-report measure that assesses four broad domains: Physical Symptoms (8 items), Emotional Functioning (5 items), Vitality (5 items), and School Functioning (4 items); and seven CF specific domains: Eating Disturbances (2 items), Body Image (3 items), Treatment Burden (3 items), Respiratory Symptoms (7 items), Digestive

Symptoms (3 items), and Weight (1 item), along with an overall Health Perception scale (3 items). The CFQ-Parent took approximately 15 – 20 minutes to complete. Raw scores were converted into standardized scores (0 –100) for each of the 11 scales, with higher scores indicating better HRQoL.

2. Health status and Socio-economic sheet

The health profile and Socio-economic information sheet covered the following areas of interest:

a. Current used medication and influenza vaccine.
b. Forced expiratory volume in one second as a percent of predicted (FEV_1%).

Health Status/Spirometry. Pulmonary function tests are the gold standard for measuring respiratory functioning and lung damage for individuals with CF. Illness severity ratings are based on established cutoffs for mild (≥ 70%), moderate (40–69%), and severe (≤ 39%) disease [50].

c. Body mass index (weight/length percentile for ages less than 2 years). This measure used as a reflection of growth.

   These values (FEV_1% and BMI) were both included as measures of health status and were taken from the last clinical visit.

d. Patient's knowledge about his disease.
e. Age at CF diagnosis.
f. Number of deaths per family we interviewed.
g. Income status.
h. Address and any external help.
i. Health related economical end point:
   Total health care resources use and cost.

j. The third part contained themes asked about financial situation, support, patients believes about management strategies and mechanism of treatment, and asked about the effect of disease burden on social life. They were graded on a scale of 1-4 (1= never, 2= sometimes, 3= often, 4= always).

3. Willingness to Pay (WTP) section

Willingness to pay (WTP) survey was used in this study to examine the patient's preference for the new treatment options and their willingness to pay for them.

WTP is the maximum amount of money that the individual would pay to get the benefits of a service or intervention. WTP will be different between patients depending on the preferences and income. In order for healthcare decision makers to determine to reimburse a certain intervention or treatment the incremental benefits are

found, the incremental benefits are the sum that each patient is willing to pay; if the incremental benefits are higher than the incremental costs then the treatment is preferred [51].

WTP questions are either closed-ended question, in which the patients are asked if they would pay a specific amount of money for the health service, the answer will be yes or no, or open ended question, in which the patients can be asked what is the maximum amount they are willing to pay or a payment scale can be used, in which the patients are presented with a scale of possible WTP values [52].

In this study, we asked about their willingness to pay for new therapies with yes or no answer and a payment scale was used in order to ask about the amount of money they are willing to pay for the new medication if they answered yes to first question. Then we asked about the most important factors they want to achieve through their contribution to payment.

The health status, Socio-economic and willingness to pay parts of the questionnaire translated into Arabic and validated by two experts in clinical research.

Data analysis

The Statistical Package for the Social Sciences, version 22.0 (SPSS) was used for data processing. The scores are expressed as means and standard deviations. The Mann-Whitney test was used for comparing two groups, whereas the Kruskal-Wallis test was used for comparing more than two groups. Pearson correlation coefficients (r) were calculated between CFQ-R scores and clinical outcomes such as BMI, The level of significance was set at $p<0.05$. The data from health status, socioeconomic and WTP questionnaires were analyzed using SPSS program. Descriptive statistics (means and standard deviations) were used to characterize the demographic variables.

Patient oriented outcomes measured included change in different area specificity respiratory symptoms measured by the Cystic Fibrosis Questionnaire-Revised where points ranged from 0-100 and increasing scores indicated improvement of symptoms.

CFQ-Child data for ages 6–11 and 12–13 years were combined because they contain the same questions. We assessed parent-child reporting concordance by including indicators for parent versus child report, CFQ-Child versus CFQ-Teen/Adult version, and their interaction in the model. We calculated to determine the relationship between health status (FEV1 % predicted and BMI) and CFQ-R scaled scores (predictive validity). Next, correlations were conducted to examine demographic data differences in the HRQoL score. And a comparison between the QoL international data and our QoL score was done.

Ethical consideration

This study was approved by Caritas Baby Hospital (CBH) Medical Research Committee/Ethical Review Board (approval number: MRC-21). Written informed consents were obtained from the patients and parents (father or mother) of the children involved in this study. All signed informed consent forms were deposited in the patient's hospital medical chart.

Chapter 4: Results

Part one

Descriptive statistics

1.1Demographic characteristics

A total of 77 cystic fibrosis patients (58 families) have participated in this study. There were 46.75 % (36/77) male patients and 53.25 % (41/77) females. The patients were divided into groups by age: those < 6 years of age ($CFQ_{<6}$), ≥ 6 and < 12 years of age ($CFQ_{6\text{-}11}$ group); those ≥ 12 and < 14 years of age ($CFQ_{12\text{-}13}$ group); and those ≥ 14 years of age (CFQ_{14+} group). Table (5) shows the distribution of the data for cystic fibrosis patients and table (6) for their parents. The mean age of the patients was 10.7 years (range: 0.5-36 years). Most of the patients were children (6-13 years old) as shown. The patients were distributed throughout the different regions of the West Bank, as shown in Table (7).

Table (5): Demographic data distribution for Cystic fibrosis

Characteristic	**Group**		
	$CFQ_{<6}$	**$CFQ_{6\text{-}11}$**	**$CFQ_{12\text{-}13}$** **CFQ_{14+}**
	n (22)	**n (24)** **n (9)** **n (33)**	**n (22)**
Age (mean/SD)	3.159 (1.475)	9.21 (2.118)	19.36 (5.77)
Gender Male/Female, n/n %	11/11 (50% / 50%)	12/21 (36.4% / 63.6%)	13/9 (59.1%/40.9%)
Vacation not related to disease			
Yes		8 (24.2%)	9 (40.9%)
No	22 (100%)	25 (75.8%)	13 (59.1%)
Marital status			
Single	22 (100%)	33 (100%)	20 (90.9%)
Married			2 (9.1%)

Education			
- Some high school or less	9 (40.9%)	33 (100%)	15 (68.2%)
- High school diploma/GED			2 (9.1%)
- College degree			4 (18.2%)
- Professional or graduate degree			1 (4.5%)
Current work or school status			
- Attending school outside the home	9 (40.9%)	33 (100%)	12 (54.5%)
- Taking educational courses at home			1 (4.5%)
- Seeking work			1 (4.5%)
- Working full or part time (either outside the home or at a home-based business)			5 (22.7%)
- Not attending school or working due to my health.			3 (13.6%)
Monthly income (NIS)			
o < 1500	6 (27.3%)	11 (33.3%)	3 (13.6%)
o 1500-3000	15 (68.2%)	19 (57.6%)	17 (77.3%)
o 3001-5000	1 (4.5%)	3 (9.1%)	2 (9.1%)
o > 5000			

CFQ: Cystic Fibrosis Questionnaire; CFQ_{6-11}: patients ≥ 6 and < 12 years of age; CFQ_{12-13}: patients ≥ 12 and < 14 years of age; and CFQ_{14+}: patients ≥ 14 years of age and n: number of patients. SD: standard deviation. Values expressed as frequency and percent.

- Parent's demographic data:

Demographic data for parents of CF child 6-13 years of age and children less than 6 years of age were determined as following.

Table (6): Demographic data distribution for parents

Characteristic	Parent's group	
	CFQ $_{<6}$ **n(22)**	**CFQ $_{6-13}$** **n(33)**
Age (mean/SD)	29.27 (6.356)	34.67 (7.326)
	Parents of CFQ $_{<6}$	**Parents of CFQ $_{6-13}$**
Family relationship with patients		
Mother	22 (100%)	28 (84.8%)
Father		3 (9.1%)
Grandfather		1 (3%)
Other		1 (3%)
Vacation not related to disease		
Yes		11 (33.3%)
No	22 (100%)	22 (66.7%)
Marital status		
Married	22 (100%)	31 (93.9%)
Divorced		2 (6.1%)
Education		
- Some high school or less	9 (40.9%)	17 (51.5%)
- High school diploma/GED	8 (36.4%)	9 (27.3%)
- Some college	4 (18.2%)	3 (9.1%)
- College degree	1 (4.5%)	4 (12.1%)
Work status		
- Seeking Work	1 (4.5%)	1 (3%)
- Working full or part time (either outside the home or at a home-based business)		9 (27.3%)
- Full time homemaker	20 (90.9%)	22 (66.7%)
- Not working due to my health		1 (3%)
- Not working for other reasons	1 (4.5%)	

SD: standard deviation; CFQ: Cystic Fibrosis Questionnaire; CFQ_{6-11}: patients ≥ 6 and < 12 years of age; $CFQ_{<6}$: patients < 6 years of age and n: number of patients. Values expressed as frequency and percent.

Table (7): Geographical Distribution of the participants

City	Number of patients	Number of families
Jerusalem	1 (1.3%)	1
Bethlehem	6 (7.8%)	4
Hebron	50 (64.9%)	38
Ramallah	5 (6.5%)	4
Nablus	7 (9.1%)	4
Jenin	6 (7.8%)	5
Qalqilia	1 (1.3%)	1
Tulkarem	1 (1.3%)	1
Total	**77 (100%)**	**58**

Cystic Fibrosis Questionnaire-Revised

Quality of life dimensions were assessed using Likert scales and scores were standardized from 0 to 100, with higher scores indicating better HRQoL. Scores above 50 are considered to reflect good QoL.

All participants completed the questionnaires without any problems. And the result was determined in Table (8). In the CFQ_{14+} group, the mean scores ranged from 20.2 for the treatment domain to 55.6 for eat domain. The lowest mean score was for question 10 'You felt energetic?' with a value of 13.6 for vitality domain. And the highest score was for question 25 'I think I look different from others my age?' with a value of 83.3 for body domain.

Table (8): Descriptive Statistics of the score for CFQ_{14+} group

	N	Minimum	Maximum	Mean	Std. Deviation
Physical	22	.00	91.67	31.0614	24.42242
Vitality	22	.00	91.67	28.4095	22.95386
Emotion	22	6.67	100.00	47.2727	24.85114
Eat	22	11.11	100.00	55.5568	22.48673
Treatment	22	.00	66.67	20.2005	17.69651
Health	22	.00	100.00	26.7664	23.67253
Social	22	11.11	66.67	44.9486	12.70508
Body	22	.00	88.89	22.7268	27.32017
Role	22	.00	91.67	40.1527	21.76737
Weight	22	.00	100.00	22.7264	27.95759
Respiratory	22	.00	77.78	28.2832	22.73846
Digest	22	.00	100.00	39.8986	28.20616
Valid N (list wise)	22				

In the CFQ_{6-13} group Table (9), the mean scores ranged from 14.48 for the body domain to 48.23 for the emotion domain. The lowest mean score was for question 30 'Doing your treatments bothered you?' with a value of 9.09 for treatment domain and the highest score was for question 23 'You felt left out?' with a value of 91.92 for social domain.

Table (9): Descriptive statistics of the score for CFQ_{6-13} group

	N	Minimum	Maximum	Mean	Std. Deviation
Physical	33	.00	72.22	26.4310	19.59418
Emotion	33	12.50	87.50	48.2323	15.13217
Social	33	28.57	61.90	45.4545	9.22837
Eat	33	.00	100.00	46.1279	26.94891
Treatment	33	.00	55.56	17.5084	13.61686
Body	33	.00	55.56	14.4781	17.67436
Respiratory	33	.00	66.67	27.5253	19.92661
Digest	33	.00	66.67	23.2323	26.98360
Valid N (list wise)	33				

In the $CFQ_{<6}$ parent version Table (10), the mean scores ranged from 25.76 for the weight domain to 59.26 for the school domain. The lowest mean score was for question 30 'My child spends a lot of time on his/her treatments every day?' with a value of 15.15 for treatment domain and the highest score for question 14 'The extent to which your child participated in sports and other physical activities, such as gym class?' with a value of 90.91 for physical domain.

Table (10): Descriptive statistics of the score for $CFQ_{<6}$ group

	N	Minimum	Maximum	Mean	Std. Deviation
Physical	21	16.67	83.33	49.7222	18.22569
Emotion	22	13.33	73.33	50.0000	14.94257
Vitality	22	13.33	60.00	36.9697	16.55228
School	9	41.67	83.33	59.2593	15.27778
Eat	22	.00	100.00	43.1818	28.94032
Body	22	.00	100.00	32.8283	30.76093
Treatment	22	11.11	66.67	38.3838	14.83885
Health	22	22.22	66.67	41.4141	13.79356
Respiratory	22	19.05	85.71	42.2078	14.49547
Digest	22	.00	100.00	39.3939	30.61726
Weight	22	.00	66.67	25.7576	28.97147
Valid N (list wise)	9				

Table (11) shows the data regarding the questionnaire completed by the parents for children 6-13 years of age. In the $CFQ_{\text{Parents 6-13}}$ the mean scores ranged from 14.8 for the body domain to 51.1 in eat domain. The lowest was mean score for question 21 'My child thinks that he/she is too thin?' is 11.1for body domain and the highest score was for question 31 'How difficult is it for your child to do his/her treatments each day?' with a value of 73.7374 for treatment domain.

Table (11): Descriptive statistics of the score for CFQ $_{Parents\ 6\text{-}13}$ group

	N	Minimum	Maximum	Mean	Std. Deviation
Physical	33	12.50	83.33	37.6263	14.30102
Emotion	33	6.67	93.33	45.8586	22.09560
Vitality	33	.00	73.33	33.9394	21.94460
School	33	.00	91.67	45.9596	22.44991
Eat	33	.00	100.00	51.0101	28.54680
Body	33	.00	44.44	14.8148	16.35511
Treatment	33	22.22	55.56	41.4141	8.45865
Health	33	22.22	77.78	46.1279	15.24522
Respiratory	33	9.52	61.90	31.7460	14.41738
Digest	33	.00	77.78	30.6397	22.05323
Weight	33	.00	100.00	15.1515	23.70377
Valid N (list wise)	33				

Health profile section

After screening the outpatient medication all patients took Vitamin A&D (Adol®) drops, Tocopherol (Evitol®) tablet, Vitamin K 2mg ampoule, Hypertonic saline (3%, 7%) solution, Creon 10000 IU tablet, Salbutamol 5mg/ml (Ventolin®) nebulized solution, Gentamycin 80 mg ampoule (every other month) and other oral antibiotic.

Pulmonary function test (FEV_1)

Illness severity as measured by FEV1 for only 26 patients, ranged from 33 to 111 percent predicted with mean value of 69.6, the majority of patients (53.8% from the available data) fell into the moderate category ($40\leq FEV_1<70\%$ predicted). Of the 26 patients evaluated, 2 patients had an $FEV_1 < 40\%$ of predicted (mean = 36), 14 patients had $40\leq FEV_1<70\%$ (mean = 61.3), 10 patients had $FEV1_1\geq 70$ (mean = 88). Table 12 shows the spirometry data results by group.

Table (12): Distribution of the spirometry values in cystic fibrosis patients, by group

Parameter	**Group**			
	CFQ_{14+}	**$CFQ_{6\text{-}13}$**	**Total sample [a]**	**Mean**
FEV_1	**n (=22)**	**n (=33)**	**n (=77)**	**of FEV_1**
$FEV_1 \geq 70$	2 (9.1%)	8 (24.2%)	10 (13%)	88
$70 > FEV_1 \geq 40$	9 (40.9%)	5 (15.2%)	14 (18.2%)	61.3
$FEV_1 < 40$	2 (9.1%)		2 (2.6%)	36
NA	9 (40.9%)	20 (60.6%)	51 (66.2%)[a]	

Values expressed as frequency and percent. CFQ: Cystic Fibrosis Questionnaire; CFQ6-13: patients ≥ 6 and < 14 years of age; and CFQ14+: patients ≥ 14 years of age. n: number of patients and NA: not available. a: 22 patients in the $CFQ_{<6}$ group did not undergo spirometry test.

Body mass index (Kg/m^2) and Weight/Length percentile.

BMI recorded for 72 patients sample with mean value 15.998 ranged from 9.60-23.12.

Table (13): BMI results

Group	N	Minimum	Maximum	Mean	Std. Deviation
CFQ_{14+}	22	14.00	23.12	18.3118	2.48902
CFQ_{6-13}	33	9.60	16.70	14.4185	1.40554
$CFQ_{<6}$	17	13.29	20.9	16.0688	1.79721
Total sample [a] (N = 77)	72	9.60	23.12	15.9978	2.50407

CFQ: Cystic Fibrosis Questionnaire; CFQ6-13: patients ≥ 6 and < 14 years of age; and CFQ14+: patients ≥ 14 years of age and $CFQ_{<6}$ patients < 6 years of age. N: number of patients; a: five patients less than 2 years cannot measured BMI and have weight/length percentile.

There were five patients that were less than 2 years of age, we used weight per length percentile to measure their health status. Their percentile's result were less than 5th % so they in sever status (2.9kg/51cm, 9.7kg/79cm, 9kg/75cm, 11kg/88cm, 2.65kg/49cm).

Patients' knowledge and consultation about CF disease was screened with result in table below: 92.2% of patients have knowledge about the disease from Caritas Baby Hospital lectures (Table 14).

Table 14: Patients' knowledge and consultation about CF disease

Knowledge		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	No	6	7.8	7.8	7.8
	Yes	71	92.2	92.2	100.0
	Total	77	100.0	100.0	

Age at CF diagnosis is determined in Table 15 with the overall mean age of diagnosis for CF patients in our sample is **4.16** years of age.

Table 15: Age at time of diagnosis (years)

Group	N	Minimum	Maximum	Mean	Std. Deviation
CFQ_{14+}	22	1	30	9.68	9.068
CFQ_{6-13}	33	1	11	2.48	2.874
$CFQ_{<6}$	22	<1	2	1.14	0.3513
Total sample (N = 77)	77	<1	30	4.16	6.239

Socio-economic status section;

Table (16): Different parameter for CF patients

Parameter	N	Minimum	Maximum	Mean	Std. Deviation
Number of Family member	77	2	18	6.18	2.018
Total number of people live in the same place	77	2	18	6.21	2.325
CF patients in each family	77	1	4	1.6	0.845
Number of death related to CF disease	77	0	4	0.364	0.742

- 74.1% of families have one patient suffer from CF disease, 20.7% having two patients, 3.5% having three patients and 1.7% have four patients as determined below

(Table 17): Number of CF patients in each family

Number of CF patients in each family		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	1	43	74.1	74.1	74.1
	2	12	20.7	20.7	94.8
	3	2	3.5	3.5	98.3
	4	1	1.7	1.7	100.0
	Total	58	100.0	100.0	

- 19.5% of patients have one case of death due to CF disease, 3.9% having two case of death, 1.3% having three case of death and 1.3 have four cases as described below

(Table 18): Death cases due to CF disease

CF Death cases		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	0	57	74.0	74.0	74.0
	1	15	19.5	19.5	93.5
	2	3	3.9	3.9	97.4
	3	1	1.3	1.3	98.7
	4	1	1.3	1.3	100.0
	Total	77	100.0	100.0	

- 29.9% of patients live in cities, 61% live in villages and 9.1% live in camps as described below.

(Table 19): Place of living

Place of living		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	City	23	29.9	29.9	29.9
	Village	47	61.0	61.0	90.9
	Camp	7	9.1	9.1	100.0
	Total	77	100.0	100.0	

- 89.6% of patients have property house and 10.4 have a rented house as described below.

(Table 20): Type of housing

Type of housing		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	Property	69	89.6	89.6	89.6
	Rent	8	10.4	10.4	100.0
	Total	77	100.0	100.0	

(Table 21): Transportation cost (NIS)

Mean average traveler cost to receive care is 81.033 NIS

	N	Minimum	Maximum	Mean	Standard Deviation
Transportation cost (NIS)	77	6.00	500.00	81.033	108.36137
Valid N (list wise)	77				

- Average monthly income of the families (66.2%) between 1500-3000 NIS, 26% less than 1500 NIS and 7.8% between 3001-5000 NIS

(Table 22): Monthly income

Monthly income		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	1500>	20	26.0	26.0	26.0
	1500-3000	51	66.2	66.2	92.2
	3001-5000	6	7.8	7.8	100.0
	Total	77	100.0	100.0	

NIS; new Israel shekel

- Only 3.9% of CF patients have an external support from social affairs and children's village SOS (save our souls or selves) organization as described below.

Table 23: External support for CF cases

External support		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	No	74	96.1	96.1	96.1
	Yes	3	3.9	3.9	100.0
	Total	77	100.0	100.0	

1.3 Health related economic endpoint section

Table (24): Economic endpoint

Health care resources	N	Minimum	Maximum	Mean	Std. Deviation
1. Monthly use of nebulized antibiotics per year.	77	0	12	5.58	3.833
2. Hospital admission per year.	77	0	15	2.99	2.458
3. Total inpatient days receiving parenteral antibiotic in hospital.	77	0	21	7.51	6.752
4. Out patients visits (no. of clinic visits per year).	77	1	12	3.52	3.633
5. Number of times doing sputum culture test yearly.	77	4	6	4.39	2.537
6. Number of times doing blood tests yearly.	77	1	2	1.16	.365
7. Number of times doing radiology exams yearly.	77	1	2	1.04	.195
8. Monthly productivity loss (No. of days at home due to CF illness per month [a]).	64	1	30	4.88	6.909
Valid N (list wise)[a]	64				

***a**: thirteen patient under 6 years of age who don't enter school or kindergarten,* ***N**: number of patients.*

- 53.2% of CF patients take influenza vaccine yearly as described below.

(Table 25): Influenza vaccine

Influenza vaccine		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	Yes	41	53.2	53.2	53.2
	No	36	46.8	46.8	100.0
	Total	77	100.0	100.0	

- 7.8% of CF patients take drugs for treatment of other diseases. Such as Thyroxine (Eltroxin®) tablets, Ursolit® tablets (Ursodeoxycholic acid), Omega-3, Diabetic insulin pens, Growth hormone, Triple therapy for peptic ulcer disease and Normalax® Polyethylene glycol 3350 powder for oral solution for treatment of constipation.

Table (26): Drugs used by CF patients for other diseases

Other drugs		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	No	71	92.2	92.2	92.2
	Yes	6	7.8	7.8	100.0
	Total	77	100.0	100.0	

- The themes asked about financial situation, support, patients believes about management strategies and mechanism of treatment, and asked about the effect of disease burden on social life, results are demonstrated as following [a].

(Table 27): Themes

Items [a]	Themes	Always	Often	Sometimes	Never
Are you thinking about your financial situation?	Financial situation	88.3%	9.1%	2.6%	0%
Do you have confidence that your treatment will be available at all times?	Support and occupation	0%	13%	20.8%	66.2%
Are you satisfied with your access to health services?	Mechanism of treatment	5.2%	9.1%	19.5%	66.2%
Does the treatment currently used affect your social life?	Mechanism of treatment	51.9%	22.1%	23.4%	2.6%
Do you have sufficient financial resources for treatment?	Financial situation	0%	2.6%	28.6%	68.8%
Do you think your current treatment needs to be changed?	Mechanism of treatment	79.2%	15.6%	3.9%	1.3%

***a**: The data determined by percent of total number of patients 77.*

Willingness to pay (WTP) section

When we told CF families to assume that inhaled TOBI® or CASTON® and Pulmozyme® are a new medications that are available for reducing disease symptom and improving general health in different ways. Keeping in mind their income and household budget, would they have a willingness to pay out of pocket each month to get these new drugs?, 93.5% said yes and 6.5% said no. (the five families said no one of them from adult (14+) group; two from 6-13 group and two from group less than 6 years of age).

Table (28): Willingness to pay answers.

WTP		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	Yes	72	93.5	93.5	93.5
	No	5	6.5	6.5	100.0
	Total	77	100.0	100.0	

- 51.4% of patients are willing to pay 100 NIS out of pocket each month to get these new drugs, 37.5% are able to pay 50 NIS, 8.3% able to pay 500 NIS and 2.7% able to pay 2000 NIS or more to get these new drugs.

(Table 29): Money to pay each month (NIS)

Money to pay each month (NIS)		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	50	27	35.1	37.5	37.5
	100	37	48.1	51.4	88.9
	500	6	7.8	8.3	97.2
	2000 or more	2	2.6	2.8	100.0
	Total	72	93.5	100.0	
Missing	System	5	6.5		
Total		77	100.0		

NIS: new Israel shekel.

- When we asked about the important things they are willing to pay for, the results as following:

(Table 30):The important things they are willing to pay for

	Characteristic	Items	Yes	No	N[a]
1	Providing new medicines reduce disease symptom and improve general health in different ways.	General health status	98.6% (71)	1.4% (1)	72
2	Facilitate the mechanism of treatment by providing modern equipment for treatment.	Mechanism of treatment and time	100% (72)		72
3	Minimize the time it takes to receive the treatment by nebulizer.		100% (72)		72
4	Reduce monthly health related costs by reducing the number of visits and admission to the hospital.	Health related costs/visits	98.6% (71)	1.4% (1)	72
5	Improve the ability to live daily life normally.	Performance	100% (72)		72

***N**: the number of patients answered the questions. **a**: five of patient answered NO to pay so subtract from the total sample 77. Data demonstrated by percent and frequency.*

- Some patients preferred to add comments about things they are concerned about and requested to achieve them:

    1. The need of medical centers that care for CF patients, help in their treatment and follow up on their status.
    2. The need of community awareness and education about CF disease.
    3. Inpatient cases' ages in Caritas baby hospital should be less than 15 years as instructed, which cause a big problem for CF patients older than 15 years and need for hospital admission.
    4. They request for complete recovery from the disease by a drug that treats the genetic cause of CF disease completely and cure them.
    5. Change the dosage form of Creon® (pancrelipase, pancreatic enzyme replacement therapy) tablet into drops form for children.
    6. The need of one dosage form of A, D, E, and K vitamins.

- Table 31 shows rank order of the items by order of importance for the patient:
  40.3% of patients chose the most important thing they needed is characteristic number 2: Facilitate the mechanism of treatment by providing modern equipment

for treatment and 33.3% of patients chose characteristic number 1: Providing new medicines reduce disease symptom and improve general health in different ways, these results described below

(Table 31): Rank order of the items by order of importance for the patient

Number of characteristic		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	1	24	31.2	33.3	33.3
	2	29	37.7	40.3	73.6
	4	4	5.2	5.6	79.2
	5	6	7.8	8.3	87.5
	1 + 2	2	2.6	2.8	90.3
	1 + 4	4	5.2	5.6	95.8
	1 + 5	2	2.6	2.8	98.6
	4 + 5	1	1.3	1.4	100.0
	Total	72	93.5	100.0	
Missing	System	5	6.5		
Total		77	100.0		

- The main reason for patients who do not want to pay (answer No), is poor financial situation and poverty. As described below

(Table 32): Poverty cause

Poverty cause		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	Yes	5	6.5	100.0	100.0
Missing	System	72	93.5		
Total		77	100.0		

(Table 33): The items used for patient saying No for willingness to pay

	Items	Yes	No	N[a]
1	Poor financial situation and poverty	100% (5)		5
2	Lack of desire for change		100% (5)	5
3	I see the situation as appropriate		100% (5)	5
4	Get used to the available medications		100% (5)	5
5	Not want to treat at all		100% (5)	5

N*: the number of patients answered the questions.* ***a****: 72 of patient answered YES to pay so subtract from the total sample 77. Data demonstrated by percent and frequency.*

PART 2

Correlation and comparisons statistics

Cystic Fibrosis Questionnaire-Revised scores related comparison

The overall scoring for CF patients in this study is less than 50% which indicate poor quality of life (Table 34). The data appears to show the lowest score is for treatment, body and respiratory. The highest score appears to be for eat and emotion.

When we compare the mean scores of the CFQ_{14+} group with CFQ_{6-13}, we observed no statistically significant difference between them (Table 35) only in eat domain. As determined the scores for adult (14+) are slightly higher than child (6-13) scores except for emotion and social domain. But the score for patients less than 6 years of age is much higher than both.

Table (36) below compare the data collected from questionnaires completed by the parents relative to patients. We observed good agreement between the mean scores on the CFQ Parents 6-13 and the information obtained by means of the questionnaires applied to the patients. But we found a statistically significant difference only in the physical domain (p = 0.010) and treatment domain (p = 0.000) as determined in table (37).

Table (34): Quality of life scores from the questionnaires related to cystic fibrosis patients, by group [a].

Domain	Groups			
	CFQ_{14+} n (22)	**CFQ_{6-13}** n (33)	**$CFQ_{parent\ 6-13}$** n (33)	**$CFQ_{<6}$** n (22)
Physical	31.0614	26.4310	37.6263	49.7222
Emotion	47.2727	48.2323	45.8586	50.0000
Eat	55.5568	46.1279	51.0101	43.1818
Treatment	20.2005	17.5084	41.4141	38.3838
Body	22.7268	14.4781	14.8148	32.8283
Respiratory	28.2832	27.5253	31.7460	42.2078
Social	44.9486	45.4545	-	-
Digest	39.8986	23.2323	30.6397	39.3939
Weight	22.7264	-	15.1515	25.7576
Health	26.7664	-	46.1279	41.4141
Role	40.1527	-	-	-
Vitality	28.4095	-	33.9394	36.9697
School	-	-	45.9596	59.2593

***CFQ**: Cystic Fibrosis Questionnaire; **CFQ6-13**: patients ≥ 6 and < 14 years of age; **CFQ<6**: patients <6 years of age; and **CFQ14+**: patients ≥ 14 years of age. **a:** Values expressed as mean score. **(-)**: set for not applicable.*

Table (35) Compression between the mean scores of the CFQ_{14+} group with CFQ_{6-13} group

Ranks				
		N	Mean Rank	Sum of Ranks
Physical	Child	33	27.00	891.00
	Adults	22	29.50	649.00
	Total	55		
Emotion	Child	33	27.91	921.00
	Adults	22	28.14	619.00
	Total	55		
Eat	Child	33	24.42	806.00
	Adults	22	33.36	734.00
	Total	55		
Body	Child	33	26.85	886.00
	Adults	22	29.73	654.00
	Total	55		
Treatment	Child	33	28.82	951.00
	Adults	22	26.77	589.00
	Total	55		
Respiratory	Child	33	27.45	906.00
	Adults	22	28.82	634.00
	Total	55		
Digest	Child	33	24.91	822.00
	Adults	22	32.64	718.00
	Total	55		
Social	Child	33	27.91	921.00
	Adults	22	28.14	619.00
	Total	55		

Test Statistics								
	Physical	**Emotion**	**Eat**	**Body**	**Treatment**	**Respiratory**	**Digest**	**Social**
Mann-Whitney U	330.0	360.0	245.0	325.0	336.0	345.0	261.0	360.0
Asymp. Sig. (2-tailed)	.569	.959	.041	.492	.638	.756	.070	.959

***P <0.05**

There is a significant statistics between adult (14+) and child (6-13) in eat domain for adult quality of life.

Table (36): comparison between CFQ parent 6-13 scores and CFQ 6-13child scores

		N	Mean	Std. Deviation	Std. Error Mean
Physical	Parents	33	37.6263	14.30102	2.48949
	Child	33	26.4310	19.59418	3.41091
Emotion	Parents	33	45.8586	22.09560	3.84635
	Child	33	48.2323	15.13217	2.63417
Eat	Parents	33	51.0101	28.54680	4.96936
	Child	33	46.1279	26.94891	4.69120
Body	Parents	33	14.8148	16.35511	2.84706
	Child	33	14.4781	17.67436	3.07671
Treatment	Parents	33	41.4141	8.45865	1.47246
	Child	33	17.5084	13.61686	2.37039
Respiratory	Parents	33	31.7460	14.41738	2.50974
	Child	33	27.5253	19.92661	3.46878
Digest	Parents	33	30.6397	22.05323	3.83897
	Child	33	23.2323	26.98360	4.69724

Table (37): Level of significance between CFQ parent $_{6-13}$ score and CFQ $_{6-13}$ child version scores in physical and treatment domains

Domains	t	Sig. (2-tailed)[a]
Physical	2.651	.010
Emotion	-.509	.612
Eat	.714	.478
Body	.080	.936
Treatment	8.567	.000
Respiratory	.986	.328
Digest	1.221	.227

a: *$P < 0.05$*

Correlation between quality of life scores with demographic data.

- adult (14 years of age and more) group
    - There is a no correlation between age and QoL score for adult (14+) group as described in table (38) below:

Adult (14+)	N	Minimum	Maximum	Mean	Std. Deviation
Age	22	14	35	19.36	5.770
Valid N (listwise)	22				

Table (38): Age parameter:

Correlation Matrix			
Age		**pearson**	**sig.**
	Physical	-.009	.485
	Role	.061	.393
	Vitality	-.040	.430
	Emotion	-.181	.210
	Social	.076	.368
	Body	.021	.463
	Eat	-.137	.271
	Treatment	-.137	.272
	Health	.145	.260
	Weight	-.249	.132
	Respiratory	-.115	.305
	Digest	-.158	.241

***P < 0.05**

Table (39): Gender parameter

Ranks				
Sex of patients		**N**	**Mean Rank**	**Sum of Ranks**
Physical	Male	13	11.96	155.50
	Female	9	10.83	97.50
	Total	22		
Vitality	Male	13	12.38	161.00
	Female	9	10.22	92.00
	Total	22		
Emotion	Male	13	12.12	157.50
	Female	9	10.61	95.50
	Total	22		
Eat	Male	13	11.85	154.00
	Female	9	11.00	99.00
	Total	22		
Treatment	Male	13	14.12	183.50
	Female	9	7.72	69.50
	Total	22		
Health	Male	13	12.19	158.50
	Female	9	10.50	94.50
	Total	22		
Social	Male	13	11.54	150.00
	Female	9	11.44	103.00
	Total	22		
Body	Male	13	11.54	150.00
	Female	9	11.44	103.00
	Total	22		
Role	Male	13	12.73	165.50
	Female	9	9.72	87.50
	Total	22		
Weight	Male	13	11.88	154.50
	Female	9	10.94	98.50
	Total	22		
Respiratory	Male	13	13.08	170.00
	Female	9	9.22	83.00
	Total	22		
Digest	Male	13	11.04	143.50
	Female	9	12.17	109.50
	Total	22		

Table (40): Level of significance for QoL related to gender

Test Statistics						
	Physical	**Vitality**	**Emotion**	**Eat**	**Treatment**	**Health**
Mann-Whitney U	52.500	47.000	50.500	54.000	24.500	49.500
Exact Sig. [2*(1-tailed Sig.)]	.695	.471	.601	.794	.021	.556
	Social	**Body**	**Role**	**Weight**	**Respiratory**	**Digest**
Mann-Whitney U	58.000	58.000	42.500	53.500	38.000	52.500
Exact Sig. [2*(1-tailed Sig.)]	1.000	1.000	.292	.744	.186	.695

***P<0.05**

There are no significant differences in QoL for adult group with respect to gender with the exception of treatment (0.021) to male only.

Table (41): Vacation without disease parameter

Ranks				
Vacation without disease		**N**	**Mean Rank**	**Sum of Ranks**
Physical	Yes	9	15.44	139.00
	No	13	8.77	114.00
	Total	22		
Vitality	Yes	9	15.78	142.00
	No	13	8.54	111.00
	Total	22		
Emotion	Yes	9	13.89	125.00
	No	13	9.85	128.00
	Total	22		
Eat	Yes	9	12.28	110.50
	No	13	10.96	142.50
	Total	22		
Treatment	Yes	9	13.78	124.00
	No	13	9.92	129.00
	Total	22		
Health	Yes	9	15.11	136.00
	No	13	9.00	117.00
	Total	22		
Social	Yes	9	9.83	88.50
	No	13	12.65	164.50
	Total	22		
Body	Yes	9	15.72	141.50
	No	13	8.58	111.50
	Total	22		
Role	Yes	9	15.44	139.00
	No	13	8.77	114.00
	Total	22		
Weight	Yes	9	12.56	113.00
	No	13	10.77	140.00
	Total	22		
Respiratory	Yes	9	14.17	127.50
	No	13	9.65	125.50
	Total	22		
Digest	Yes	9	15.83	142.50
	No	13	8.50	110.50
	Total	22		

Table (42): Level of significance of QoL for adult (14+) group related to vacation without disease

Test Statistics						
	Physical	**Vitality**	**Emotion**	**Eat**	**Treatment**	**Health**
Mann-Whitney U	23.000	20.000	37.000	51.500	38.000	26.000
Exact Sig. [2*(1-tailed Sig.)]	.017	.009	.164	.647	.186	.030
	Social	**Body**	**Role**	**Weight**	**Respiratory**	**Digest**
Mann-Whitney U	43.500	20.500	23.000	49.000	34.500	19.500
Exact Sig. [2*(1-tailed Sig.)]	.324	.009	.017	.556	.110	.007

***P < 0.05**

There are statistically significant differences in physical (0.017), vitality (0.009), health (0.03), body (0.009), role (0.017) and digest (0.007) domains with respect to vacation without disease for adult (14+) group.

- Marital status parameter for adult (14+) (single/married) correlated with QoL

There is a no correlation between marital status and QOL score for adult (14 and more) group as described in table (43):

Table (43): Marital status parameter for adult (14+) correlated with QOL

Test Statistics

	Physical	**Vitality**	**Emotion**	**Eat**	**Treatment**	**Health**
Mann-Whitney U	3.000	15.500	8.500	5.000	13.000	5.000
Exact Sig. [2*(1-tailed Sig.)]	.052	.623	.216	.104	.485	.104
	Social	**Body**	**Role**	**Weight**	**Respiratory**	**Digest**
Mann-Whitney U	9.500	12.500	19.500	9.000	9.500	9.000
Exact Sig. [2*(1-tailed Sig.)]	.260	.424	.952	.260	.260	.260

***P <0.05**

- Education level of adult (14+) group related to QoL

There is a no correlation between educational level and QoL score for adult (14+) group as described in table below.

Table (44): Education level parameter

Test Statistics [a, b]						
	Physical	**Emotion**	**Vitality**	**Social**	**Eat**	**Role**
Chi-square	4.485	.358	1.908	4.298	.999	2.507
df	3	3	3	3	3	3
Asymp. Sig.	.214	.949	.592	.231	.802	.474
	Body	**Treatment**	**Health**	**Respiratory**	**Digest**	**Weight**
Chi-square	.098	1.837	3.193	3.070	.312	.975
df	3	3	3	3	3	3
Asymp. Sig.	.992	.607	.363	.381	.958	.807

a. Kruskal Wallis Test

b. Grouping Variable: Education level

*P < 0.05

- Work or school status of adult (14+) related to QoL

There is a correlation between work or school status and QoL score of physical (0.039) and role (0.016) domains for taking educational courses at home as described

Table (45): Work or school status of adult parameter

Test Statistics [a, b]						
	Physical	**Emotion**	**Vitality**	**Social**	**Eat**	**Role**
Chi-square	10.090	7.280	8.625	1.578	8.710	12.204
df	4	4	4	4	4	4
Asymp. Sig.	.039	.122	.071	.813	.069	.016
	Body	**Treatment**	**Health**	**Respiratory**	**Digest**	**Weight**
Chi-square	5.610	6.428	6.331	4.958	8.032	2.207
df	4	4	4	4	4	4
Asymp. Sig.	.230	.169	.176	.292	.090	.698

a. Kruskal Wallis Test

b. Grouping Variable: Work of patients

*P < 0.05

Child (6-13) group:

- In child (6-13) group there is no differences in QoL with respect to gender with the exception of the eat (0.03) domain related to male.

Table (46): Gender parameter effect

Test Statistics								
	Physical	**Emotion**	**Social**	**Eat**	**Treat**	**Body**	**Reparatory**	**Digest**
Mann-Whitney U	115.50	112.00	97.00	68.50	106.0	80.00	99.500	116.0
Exact Sig. [2*(1-tailed Sig.)]	.699	.618	.291	.030	.471	.089	.326	.726

***P < 0.05**

- In child (6-13) group there is no difference in QoL with respect to vacation without disease with the exception of the eat (0.049) domain related to yes answers.

Table (47): Vacation without disease parameter

Test Statistics								
	Physical	**Emotion**	**Social**	**Eat**	**Treat**	**Body**	**Respiratory**	**Digest**
Mann-Whitney U	61.00	97.00	82.00	53.5	86.50	91.00	90.000	96.000
Exact Sig. [2*(1-tailed Sig.)]	.107	.918	.470	.049	.578	.726	.696	.885

***P < 0.05**

- In child (6-13) group there is no differences in QoL with respect to education level with the exception of social (0.016) domain related to 7th grade

(Table 48): Education level parameter

Test Statistics [a, b]

	Physical	**Emotion**	**Social**	**Eat**	**Treat**	**Body**	**Respiratory**	**Digest**
Chi-square	12.182	8.299	17.293	10.138	11.291	5.226	10.348	7.671
df	7	7	7	7	7	7	7	7
Asymp. Sig.	.095	.307	.016	.181	.126	.632	.170	.363

a. Kruskal Wallis Test

b. Grouping Variable: Education level

p < 0.05

- In child (6-13) group (mean age is 9.21 years of age) there is no difference in QoL with respect to age with the exception of social (0.004) domain

(Table 49): Age parameter

Correlation Matrix			
Age		**correlation**	**sig.**
	Physical	-.047	.397
	Emotion	.008	.482
	Social	.458	.004
	Eat	.188	.147
	Body	.060	.370
	Treatment	-.187	.149
	Respiratory	.221	.108
	Digest	.057	.377

***p < 0.05**

CFQ- Parent (6-13) group correlation:

Parent's relationship (father, mother, grandfather and brother) parameter related to QoL domains.

There is no difference in QoL score with respect to relationship as shown

Table (50): Relationship effect

Test Statistics						
	Physical	**Emotion**	**Vitality**	**School**	**Eat**	
Chi-square	3.168	4.083	1.972	.610	3.870	
df	2	2	2	2	2	
Asymp. Sig.	.205	.130	.373	.737	.144	
	Body	**Treat**	**Health**	**Respiratory**	**Digest**	**Weight**
Chi-square	1.243	3.434	.898	2.500	3.601	.535
df	2	2	2	2	2	2
Asymp. Sig.	.537	.180	.638	.287	.165	.765

***p < 0.05**

- In CFQ- Parent (6-13) group there is no difference in QoL with respect to education level of the parents with the exception of emotion (0.013), vitality (0.006) and eat (0.02) domains (table 51) related to college degree.

Table 51: Education level of the parents parameter

Test Statistics						
	Physical	**Emotion**	**Vitality**	**School**	**Eat**	
Chi-square	4.471	10.846	12.300	6.086	9.795	
df	3	3	3	3	3	
Asymp. Sig.	.215	.013	.006	.108	.020	
	Body	**Treat**	**Health**	**Respiratory**	**Digest**	**Weight**
Chi-square	2.595	7.197	4.515	6.090	6.330	3.391
df	3	3	3	3	3	3
Asymp. Sig.	.458	.066	.211	.107	.097	.335

***p < 0.05**

- In CFQ- Parent (6-13) group there is no difference in QoL with respect to work status of parents with the exception of school (0.021) domain (table 52) for seeking work.

Table (52): Work status of parents parameter

Test Statistics						
	Physical	**Emotion**	**Vitality**	**School**	**Eat**	
Chi-square	3.459	4.194	5.119	9.687	5.971	
df	3	3	3	3	3	
Asymp. Sig.	.326	.241	.163	.021	.113	
	Body	**Treat**	**Health**	**Respiratory**	**Digest**	**Weight**
Chi-square	1.699	2.238	2.824	5.729	4.283	3.026
df	3	3	3	3	3	3
Asymp. Sig.	.637	.524	.419	.126	.232	.388

***p < 0.05**

- Age of parents parameter:

  There is no difference in QoL of CF patients with respect to ages of their parents with the exception of physical (0.021), digest (0.008) domains with negative correlation as described

Table (53): Ages of their parents effect

Age of parents	N	Minimum	Maximum	Mean	Std. Deviation
age	33	24	60	34.67	7.326
Valid N (list wise)	33				

Ages of parent	Correlation	Sig.
Physical	-.356	.021
Emotion	.109	.274
Vitality	-.057	.376
School	.086	.317
Eat	.240	.089
Body	.242	.088
Treatment	-.146	.209
Health	.057	.376
Respiratory	.005	.489
Digest	-.418	.008
Weight	.132	.232

***p < 0.05**

- Marital status of parents parameter (married /divorced)

There is no significant statistical relationship between the marital status of parents and QoL of their patients as described below:

Table (54): Marital status of parents and QoL of their patients correlation

Test Statistics								
	Physical	**Emotion**	**Eat**	**Body**	**Treat**	**Respiratory**	**Digest**	**Social**
Mann-Whitney U	24.500	24.000	24.000	29.000	22.000	25.000	15.000	11.500
Exact Sig. [2*(1-tailed Sig.)]	.640	.640	.640	.909	.545	.689	.273	.159

***P < 0.05**

- Monthly income parameter effect.

  There is no correlation between monthly income (NIS) and QoL score for all groups as described in table (55) below:

Table (55): Monthly income parameter effect

Test Statistics						
	Physical	**Emotion**	**Vitality**	**School**	**Eat**	**Body**
Chi-square	3.928	2.931	.671	.783	.799	1.316
df	2	2	2	2	2	2
Asymp. Sig.	.140	.231	.715	.676	.671	.518
	Treat	**Health**	**Respiratory**	**Digest**	**Weight**	
Chi-square	5.725	2.989	.296	1.113	1.941	
df	2	2	2	2	2	
Asymp. Sig.	.057	.224	.862	.573	.379	

***P < 0.05**

- Total number of family member live in the same place parameter effect on QoL.

  There is a statistically significant relationship between number of family member live in the same place and QoL score in vitality (0.032) and health (0.042) domain for all groups as described in table (56). Negative correlation: with high number of family member the vitality and the health status of CF patients decrease.

Table (56): Correlation between number of family member live in the same place and QoL score

Correlation Matrix		**Number of family member**	**Sig.**
Correlation	**Physical**	-.114	.385
	Emotion	-.119	.380
	Vitality	-.639	.032
	School	.031	.468
	Eat	-.304	.213
	Body	-.246	.262
	Treatment	.365	.167
	Health	-.604	.042
	Respiratory	.063	.436
	Digest	-.023	.477
	Weight	-.275	.237

***P < 0.05**

- Geographic distribution of CF patients results are described in table (57):

  There are 58 families:

  1. The highest number of CF patients is from the Hebron district (50 patients).
  2. Hebron families were the most in which they have more than one patients in each family (8 families contain two patients).
  3. The family that has the highest number of patients (4 patients) was from Nablus district.

Table (57) Geographic distribution of CF patients

			District								
			Jerusalem	Bethlehem	Hebron	Ramallah	Nablus	Jenin	Qalqilia	Tulkarem	Total
Number of CF patients in each family	**1**	Count	1	2	28	3	3	4	1	1	43
		% of patients answered related to region	2.3%	4.7%	65.1%	7%	7%	9.3%	2.3%	2.3%	100.0%
	2	Count	0	4	16	2	0	2	0	0	24
		% of patients answered related to region	0%	16.7%	66.7%	8.3%	0%	8.3%	0%	0%	100.0%
	3	Count	0	0	6	0	0	0	0	0	6
		% of patients answered related to region	0%	0%	100.0%	0%	0%	0%	0%	0%	100.0%
	4	Count	0	0	0	0	4	0	0	0	4
		% of patients answered related to region	0%	0%	0%	0%	100.0%	0%	0%	0%	100.0%
Total		Count	1	6	50	5	7	6	1	1	77
		% of patients answered related to region	1.3%	7.8%	64.9%	6.5%	9.1%	7.8%	1.3%	1.3%	100.0%

- **QoL domain score correlated with CF patients living regions (Jerusalem, Bethlehem, Hebron, Ramallah, Nablus, Jenin, Qalqilia and Tulkarem).**

  All our patients suffer from CF disease in the same level there is no differences between the districts as described below in table (58):
  No significant correlation.

Table (58): CF patients living regions parameter

Test Statistics

	Physical	Emotion	Vitality	School	Eat	
Exact fisher test	6.499	8.619	3.144	3.872	2.748	
df	7	7	6	3	7	
Asymp. Sig.	.483	.281	.791	.276	.907	
	Body	**Treatment**	**Health**	**Respiratory**	**Digest**	**Weight**
Exact fisher test	4.757	8.225	4.961	11.012	5.919	7.605
df	7	7	6	7	7	6
Asymp. Sig.	.690	.313	.549	.138	.549	.268

***P < 0.05**

- **QoL domain score correlated with patient kind of living (city, village or camp).**

  No significant correlation in (table 59) below.

Table (59): patient kind of living (city, village or camp)

Test Statistics						
	Physical	**Emotion**	**Vitality**	**School**	**Eat**	**Body**
Exact fisher test	2.946	2.879	.988	2.220	.590	.836
df	2	2	2	1	2	2
Asymp. Sig.	.229	.237	.610	.136	.744	.658
	Treatment	**Health**	**Respiratory**	**Digest**	**Weight**	
Exact fisher test	2.150	.285	.478	.108	.713	
df	2	2	2	2	2	
Asymp. Sig.	.341	.867	.787	.947	.700	

***P < 0.05**

Percentage of death cases due to CF disease in families and their geographic distribution

The study shows that 21% of families (12/58) having death cases related to CF disease, 58.3% (7/12) from Hebron district, two families from Ramallah (16.7%), the other two families from Jenin (16.7%) and one family from Nablus (8.3%) district as described in table (60):

Table (60): CF Death cases geographic distribution by district

			District								Total
			Jerusalem	Bethlehem	Hebron	Ramallah	Nablus	Jenin	Qalqilia	Tulkarem	
Number of death related to CF disease	**0**	Count	1	4	31	2	3	3	1	1	46
		% of families	2.17%	8.7%	67.4%	4.4%	6.5%	6.5%	2.17%	2.17%	100%
	1	Count	0	0	3	2	1	2	0	0	8
		% of families			37.5%	25%	12.5%	25%			100%
	2	Count	0	0	2	0	0	0	0	0	2
		% of families			100%						100%
	3	Count	0	0	1	0	0	0	0	0	1
		% of families			100%						100%
	4	Count	0	0	1	0	0	0	0	0	1
		% of families			100%						100%
Total		Count	1	4	38	4	4	5	1	1	58
		% of families	1.73%	6.89%	65.52%	6.89%	6.89%	8.62%	1.73%	1.73%	100%

Quality of life related to health profile parameter.

2.3.1 Quality of life scores correlated with BMI (Kg/m^2)

There is a significant statistic between physical domain (0.042) in quality of life questionnaire and BMI results of Pearson correlation coefficients (r) as described in ***Table (61): BMI results of Pearson correlation coefficients***

Correlation Matrix			
	Domain	**BMI results**	**sig.**
Correlation	Physical	.605	.042
	Emotion	.424	.128
	Vitality	.054	.446
	School	.486	.092
	Eat	.397	.145
	Body	.579	.051
	Treatment	.418	.131
	Health	.186	.315
	Respiratory	-.497	.087
	Digest	-.207	.297
	Weight	.346	.181

***P < 0.05**

Quality of life scores correlated with FEV_1

For child and adult groups there is no statistical significant between quality of life domain score and FEV_1level measured as described in tables below:

Table (62): FEV_1 for child 6-13 years of age correlated with QoL domain

Test Statistics [a, b]

	Physical	**Emotion**	**Eat**	**Body**	**Treatment**	**Respiratory**	**Digest**	**Social**
Chi-square	.191	.102	1.455	.667	5.133	1.813	.648	1.444
df	2	2	2	2	2	2	2	2
Asymp. Sig.*	.909	.950	.483	.716	.077	.404	.723	.486

a. Kruskal Wallis Test

b. Grouping Variable: Section V. Health Profile FEV_1 for child (6-13)

*** P < 0.05**

Table (63): FEV_1 for adult 14 years of age and more correlated with QoL domain

Test Statistics [a, b]

	Physical	Vitality	Emotion	Eat	Treatment	Health
Chi-square	3.599	2.061	.694	.492	1.564	3.573
df	3	3	3	3	3	3
Asymp. Sig.	.308	.560	.875	.921	.668	.311
	Social	**Body**	**Role**	**Weight**	**Respiratory**	**Digest**
Chi-square	2.248	1.998	4.992	2.034	.598	3.150
df	3	3	3	3	3	3
Asymp. Sig.	.523	.573	.172	.565	.897	.369

a. Kruskal Wallis Test

b. Grouping Variable: Section V. Health Profile FEV_1

* P < 0.05

There is no statistical significant correlation between quality of life domain scores and FEV_1 level measured.

Quality of life scores correlated with age of diagnoses

There is a correlation between diagnostic age and CFQ-R score in social domain (0.03) with negative relation as the patient diagnose earlier in their life have good CFQ-R score in sociality as described in table (64) below:

Table (64): Pearson correlation between diagnostic age and CFQ-R score

Correlation Matrix			
		Diagnostic age	**sig**
Correlation	Physical	-.225	.157
	Emotion	-.041	.428
	Vitality	-.063	.390
	Eat	-.327	.069
	Body	-.021	.464
	Treatment	-.011	.481
	Health	-.129	.284
	Respiratory	-.134	.276
	Digest	-.029	.450
	Weight	-.170	.224
	Social	-.407	.030

***P<0.05**

Correlation between quality of life domain scores and willingness to pay

There is no statistical significant correlation between quality of life domain score and WTP as measured in table (65).

Table (65): WTP correlation

Ranks

	Willingness to pay	N	Mean Rank	Sum of Ranks
Physical	Yes	71	39.23	2785.50
	No	5	28.10	140.50
	Total	76		
Emotion	Yes	72	39.95	2876.50
	No	5	25.30	126.50
	Total	77		
Vitality	Yes	41	22.93	940.00
	No	3	16.67	50.00
	Total	44		
Eat	Yes	72	38.83	2795.50
	No	5	41.50	207.50
	Total	77		
Body	Yes	72	39.42	2838.50
	No	5	32.90	164.50
	Total	77		
Treatment	Yes	72	38.35	2761.00
	No	5	48.40	242.00
	Total	77		
Health	Yes	41	22.76	933.00
	No	3	19.00	57.00
	Total	44		
Respiratory	Yes	72	39.03	2810.50
	No	5	38.50	192.50
	Total	77		
Digest	Yes	72	39.87	2870.50

	No	5	26.50	132.50
	Total	77		
Weight	Yes	41	22.41	919.00
	No	3	23.67	71.00
	Total	44		
Social	Yes	52	27.29	1419.00
	No	3	40.33	121.00
	Total	55		

Table (66): level of significance between QoL and WTP

	Physical	**Emotion**	**Vitality**	**Eat**	**Body**	
Mann-Whitney U	125.500	111.500	44.000	167.500	149.500	
Exact Sig. [2*(1-tailed Sig.)]	.285	.161	.448	.802	.539	
	Treatment	**Health**	**Respiratory**	**Digest**	**Weight**	**Social**
Mann-Whitney U	133.000	51.000	177.500	117.500	58.000	41.000
Exact Sig. [2*(1-tailed Sig.)]	.347	.659	.960	.203	.895	.186

***P < 0.05**

There is no significant statistical correlation between QoL domains and WTP

Relationship between taking influenza vaccine and QoL domain scores.

There is no correlation between quality of life domain scores and taking influenza vaccine in CF cases as described in table (67).

Table (67): Effect of taking influenza vaccine

	Physical	Emotion	Vitality	School	Eat	Body
Mann-Whitney U	674.000	621.000	186.500	5.000	579.000	721.500
Asymp. Sig. (2-tailed)	.649	.232	.205	.539	.102	.861
	Treat	**Health**	**Respiratory**	**Digest**	**Weight**	**Social**
Mann-Whitney U	667.000	224.500	695.000	646.500	204.000	364.500
Asymp. Sig. (2-tailed)	.464	.713	.660	.341	.362	.952

P < 0.05

- 41 of patient took influenza vaccine. 9.8% patients didn't enter hospital and 2.4% enter hospital 8 times yearly. And 36 patients who did not take influenza vaccine 2.8% enter the hospital 15 times yearly as described below in table (68).

Table (68): Taking influenza vaccine related to number of hospitalization

Taking influenza vaccine * Number of hospitalization Cross tabulation

			Number of hospitalization									
			0	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**15**	Total
Taking influenza vaccine	**Yes**	Count	4	7	11	7	5	1	2	3	1	0	41
		% answered	9.8%	17.1%	26.8%	17.1%	12.2%	2.4%	4.9%	7.3%	2.4%	.0%	100.0%
	No	Count	1	9	10	7	1	0	4	3	0	1	36
		% answered	2.8%	25.0%	27.8%	19.4%	2.8%	.0%	11.1%	8.3%	.0%	2.8%	100.0%
Total		Count	5	16	21	14	6	1	6	6	1	1	77
		% answered	6.5%	20.8%	27.3%	18.2%	7.8%	1.3%	7.8%	7.8%	1.3%	1.3%	100.0%

Exact fisher test

	Value	df	Asymp. Sig. (2-sided)
Pearson fisher test	8.141[a]	9	.520
Likelihood Ratio	9.650	9	.380
Linear-by-Linear Association	.361	1	.548
N of Valid Cases	77		

a. 14 cells (70.0%) have expected count less than 5. The minimum expected count is .47.

2.6 Comparison between quality of life domain score for our CF patients to normative CF international data

There is a huge difference between our CF quality of life domain scores and US international data scoring [53], with our patients the scores were less than 50% of all domains for all patients group version which indicated sever status of our patients relative to data for US sample in table (69).

Table (69): CFQ-R domains by version for a national, US sample [53].

CFQ-R scale	Teen/adult	Child	Parent [a]
	Mean ± SD	Mean ± SD	Mean ± SD
	n = 4,679	n = 2,068	n = 2,728
Physical functioning	71.7 ± 27.4	77.3 ± 21.1	83.8 ± 19.1
Role functioning	80.1 ± 20.2	NA	NA
Vitality	59.5 ± 20.6	NA	69.7 ± 15.5
Emotional functioning	76.4 ± 20.0	73.9 ± 14.8	82.7 ± 15.3
Social functioning	72.4 ± 17.9	67.9 ± 18.0	NA
Body image	70.6 ± 26.7	77.8 ± 26.2	71.7 ± 28.0
Eating problems	89.7 ± 18.2	82.8 ± 22.2	78.4 ± 27.6
Treatment burden	61.5 ± 21.0	68.8 ± 22.1	63.5 ± 23.1
Health perceptions	67.2 ± 24.1	NA	77.1 ± 19.3
Weight	66.5 ± 37.2	NA	60.3 ± 37.2
Respiratory symptoms	62.9 ± 22.6	73.6 ± 20.0	75.4 ± 19.2
Digestive symptoms	80.3 ± 19.1	71.8 ± 27.1	71.4 ± 19.2
School functioning	NA	NA	76.9 ± 23.2

CFQ-R: *Cystic Fibrosis Questionnaire-Revised.* ***NA****: not applicable.* ***SD****: standard deviation.*

a*: Data from the children for whom the parents are reporting*

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Other quality of life assessment in patients with cystic fibrosis by means of the cystic fibrosis questionnaire carried out at the State University at Campinas school of medical sciences, Campinas, Brazil [54]. This study indicated that our patients with CF disease have poor quality of life compared with patients followed at the Brazilian center as described in table (74):

Table (70): Quality of life scores from the questionnaires related to cystic fibrosis patients at Brazilian center, by group [54].

Domain	**Group** [a]				
	CFQ_{6-11}	**CFQ_{12-13}**	**CFQ_{14+}**	**Parent $_{6-11}$**	**Parent $_{12-13}$**
	(n = 39)	**(n = 12)**	**(n = 24)**	**(n=39)**	**(n=12)**
Physical	71.4 ± 25.3	66.2 ± 28.1	72.4 ± 24.9	85.3 ± 19.5	79.3 ± 23.2
Body image	77.5 ± 25.9	63.0 ± 23.4	78.7 ± 20.7	81.5 ± 26.7	74.1 ± 29.3
Digestive	78.6 ± 22.3	75.0 ± 20.7	88.4 ± 14.5	77.2 ± 20.4	74.1 ± 18.6
Respiratory	74.4 ± 16.0	69.4 ± 25.0	68.7 ± 15.4	78.5 ± 15.9	80.6 ± 13.9
Emotional	79.4 ± 11.5	71.5 ± 19.0	82.8 ± 15.2	86.2 ± 14.3	73.9 ± 22.6
Social	73.0 ± 16.5	59.5 ± 22.3	68.1 ± 16.1	83.4 ± 18.3	77.8 ± 28.8
Eat	79.8 ± 22.1	75.0 ± 28.5	89.3 ± 16.2	79.9 ± 28.7	70.8 ± 28.5
Treatment	83.5 ± 14.4	70.4 ± 24.3	64.8 ± 19.0	78.1 ± 19.8	82.4 ± 20.4
Vitality			76.7 ± 16.7	74.4 ± 15.9	71.1 ± 20.4
Health			65.3 ± 26.1	80.3 ± 22.4	73.1 ± 27.0
Role			77.4 ± 20.5	NA	NA
Weight			63.9 ± 38.0	60.7 ± 37.4	50.0 ± 43.8

CFQ: *Cystic Fibrosis Questionnaire;* ***CFQ6-11****: patients ≥ 6 and < 12 years of age;* ***CFQ12-13****: patients ≥ 12 and < 14 years of age; and* ***CFQ14+****: patients ≥ 14 years of age.*
a: *Values expressed as mean ± SD.*

Part 3

Economic evaluation of using new medications for cystic fibrosis patients in our countries.

Costs of a disease as described in table (71) are divided in direct and indirect costs. For CF the clinical visit, hospital admission, outpatient drug costs (antibiotics, hypertonic saline, Creon, etc.) and laboratory tests are seen as direct costs. Direct non-medical costs include out of pocket expenses for dietary recommendations and travel costs to receive care. The indirect costs include for example productivity losses. Detailed description of direct medical and non-medical cost is described below in Tables 72 to 74. Direct costs appear to account for most expenses of health care in CF patients. Total costs for patient with the mean age of our sample 10.7 years of age were estimated to be around 35650.2 NIS per patient per year.

Table (71): Mean (S.D) medical consumption per patient over 1 year, stratified by outpatient and inpatient (hospital) care and costs.

Type	Health care resources	Mean (S.D)
Direct medical costs	- Inhaled antibiotics therapy (months) - Hospital admission [No.] - IV-antibiotic therapy [days] - Clinic visits [No.] - Sputum culture test [No.] - Blood tests [No.] - Radiographs [No.]	5.58 (3.833) 2.99 (2.458) 7.51 (6.752) 3.52 (3.633) 4.39 (2.537) 1.16 (0.365) 1.04 (0.195)
Direct non-medical costs	- Travel costs to receive care	81.033 NIS
Indirect costs	- Productivity loss [No. per month]	4.88 (6.909)

Direct medical costs burden

Table (72) described the payment expenses for CF patients services

Service Branch	Description	Price (NIS)
Laboratory tests	Sputum Culture / Gram Stain	40
	CBC	20
	BUN (Blood Urea Nitrogen)	16
	Creatinine (Serum)	16
	Electrolytes (Na/K - Serum)	20
	CRP (C-Reactive Protein Titer)	25
	Alkaline Phosphatase	16
	GPT/ALT (Alanine Aminotransferase)	15
	GOT/AST (Aspartate transaminase)	15
	PTT (Partial Thromboplastin Time)	24
	PT (Prothrombin Time) / INR	24
	Protein Total (Serum)	16
	Albumin (Serum)	16
	Glucose (Serum)	10
	HbA1C	35
	Vitamin D (Total)	100
	Vitamin E Level	350
	Vitamin K Level	550
	Acid Fast Bacilli test	40
	IgE Level test	60
	Sweat Chloride test	50
	Genetic Analysis (CF Mutations)	2500
Radiology exams		
	Chest-STANDARD FRONTAL VIEW	20
	Chest-Frontal + lateral	30
Pulmonology clinic services		
	Pulmonology Clinic - New Visit	70
	Pulmonary function test	800
Inpatient night fees	Pediatrics hospitalization night	170
	ICU hospitalization night	450
	*The escort pays 20 NIS per night	20

Inpatient services for CF disease

Total inpatient hospital services
- **Chest Therapy Session (cost 25 NIS for each session).** - **All laboratory tests and radiology exams previously discussed.** - **Most commonly inpatient medications.** Creon 10000 IU Capsules Hypertonic saline 3%, 7% solution for Inhalation Vitamin K 2 mg Oral - I.M. - I.V. (Konakion®) Salbutamol 5mg/1ml solution (Ventoline®) Tocopherol 100, 200 or 400mg Tabs. (Evitol®) Vitamin A 10.000 I.U. + Vitamin D3 4000 I.U.) / 1 ml "Adol" Azithromycin 250 mg Cap Ciprofloxacin 500 mg Tabs Gentamycin-NaCl- 0.8mg/ml-0.09%-100ml (80mg/BAG) Ceftazidime 1 g Vial. (Fortum®) Amikacin 500mg/2ml Vial Vancomycin 500mg vial Meropenem (Meronem 1gm IV vial) **Average hospitalization days: 7.51 days** **Average hospitalization admission numbers: 2.99** **Daily Average Real Cost around 300 NIS** **The real cost of the stay around 2400 NIS** **Average cost per patient per year <u>around 7200 NIS</u>**

Health related economical endpoint for CF patients

Table (73): Total Economical endpoint costs per patient per year in NIS

Main Cost Items	Mean	Cost/Unit	Total Cost	Notes
- Inhaled antibiotics therapy [months]	5.58	5.4 (BID)	± 1900	Gentamycin 80 mg / 2 ml Ampoule
- Clinic visits [No.]	3.52	70	± 280	Can be obtained free from MOH.
- Sputum culture test [No.]	4.39	40	± 176	
- Blood tests [No.]	1.16	1408	± 1634	
- Radiographs [No.]	1.04	30	± 31.2	
- Hospital admission [No.]	2.99	170	± 7200	300*7.51*2.99 = 7200
- Total hospital services [days]	7.51	300 per night		
- Travel costs to receive care	82		±1200	For total 7 times back and forth.
- **Drugs:**	**Cost/Unit**		**Total cost**	**Notes**
1. Adol® drops 10ml (Vitamin A 500 IU & D_3 200 IU).	10 NIS		360	Can be obtained free from MOH
2. Tocopherol (Evitol®) 400 mg tablet.	46 NIS		552	Unit of 200 mg form used = 23 NIS
3. Vitamin K 2 mg / 0.2 ml oral - I.M.- I.V. (Konakion®).	7 NIS		2520	Must obtained free from MOH Obtained free from MOH
4. Creon 10000 IU (100 capsule).	145 NIS		12528	Free from Caritas baby hospital only
5. Hypertonic saline 3% prepared from 23.4% HTS 230ml.	20 NIS		375.7	Free from Caritas baby hospital only
6. Hypertonic saline 7% solution (180ml).	46.8 NIS		1123	Can be obtained free from MOH
7. Salbutamol (5mg/ml) respiratory solution (Ventolin® solution 20ml).	20 NIS		720	Can be obtained free from MOH
8. Azithromycin 250 mg EOD (box of 6 caps).	25 NIS		900	Can be obtained free from MOH
9. Other oral antibiotic:				
a. Augmentin® syrup ES (600mg/5ml).	30 NIS		360	
b. Ciprofloxacin 500mg (15 tablets).	35 NIS		420	
c. Trimethoprim 40mg with Sulphamethoxazole 200mg/5ml (Sulprim® suspension 100ml).	16 NIS		192	
d. Cefuroxime axetil Suspension 250mg/5ml (Zinnat® 100ml)	44 NIS		792	

No.: number; BID: twice daily; NIS: new Israel shekel; EOD: every other day; MOH: ministry of health.

- **Total costs for CF patient 10.7 years of age**

Table (74): Total costs per year

Main Cost Items	**Total Cost (NIS) per year**
- Inhaled antibiotics therapy	1900
- Clinic visits	280
- Sputum culture test	176
- Blood tests	1634
- Radiographs	31.2
- Sweat Chloride test	50
- Genetic Analysis (CF Mutations)	2500
- Total hospital services	7200
- Pulmonary function test	800
- Travel costs to receive care	1200
- Oral antibiotics medications	1782
- Vitamins and enzymes	15960
- Airway clearance medications	1123
- Bronchodilators	720
- Other medications	294
Total cost = 35650.2 NIS	

- According to pharmaco-economic analysis of aerosol Dornase alfa (rhDNase) drug the reduced costs of RTI-related care are expected to be about 33% (18.3-37.5%) of the total costs [3, 22, 55]. A significant impact on our total health care budget will be seen when introducing this medication to our CF patients, preliminary estimate from this study indicates that if rhDNase could be used, a reduction in the cost-effectiveness ratio can be obtained and costs reduction by 11765 NIS can be estimated. This added value can help in part of the cost for making aerosol Dornase alfa available for CF patients.

- Economic evaluation of Tobramycin nebulizer solution in cystic fibrosis showed that cost offsets may occur through changes in overall patient management with a reduction in the use of other healthcare resources to be about 25.5% of the total costs [38, 56]. A significant impact on our total health care budget will be seen when introducing this medication to our CF patients with costs reduction by 9269.1 NIS can be estimated. This added value can help in part of the cost for making Tobramycin nebulizer solution available for CF patients.

Chapter 5: Discussion

We described the clinical characteristics and outcomes of the 77 patients included in the Caritas baby hospital who visited pediatric pulmonology clinic. Our data indicate that the patients with CF followed under study have poor QoL, this has been confirmed by the death of two participant one month after we finished the study, a boy at 16 years of age and a girl didn't complete the seven months of her life, they died from their respiratory complication.

Our sample was the population sample of CF disease as we took the available CF patients in West Bank. There were nine other CF patients that Caritas was aware of, but three of them refused to participate as they do not acknowledge the existence of the disease and three others cannot be reached because they traveled to other countries for treatment and the other three have not been confirmed as CF yet.

Regarding patients' characteristics, mean age at diagnosis was **4.16** years of age, ranging from <1 to 30 years, and the main clinical manifestations were pulmonary infections, malnutrition and pancreatic insufficiency, as in other studies; as already known, the late diagnosis results in worse prognosis of CF lung disease. Fortunately, improvements in age at diagnosis has been observed in recent years [57].

In this study, CF patients were divided into age groups according to the original protocol of the CFQ-R [58]. The formal inclusion of CFQ-R questionnaires as a clinical outcome was essential, as it detected the impact of treatment over QoL, from the perspective of patients and their families. It allowed the identification of baseline reference values for QoL in the different age groups, and the progression of the QoL domains scores over time. The present study was an attempt to rescue the outcomes of distinct age groups. Thus, it would be possible to make comparisons between these groups, to evaluate individual patients in relation to the baseline characteristics of their respective age groups, and to plan future strategies.

At Caritas baby hospital, disease severity and its impact in patients with CF on the respiratory tract is determined by spirometery (FEV_1), body mass index (BMI, Kg/m^2) from their health profile and cystic fibrosis clinical score are also used. However, these methods cannot translate the patient perception of what it is like to live with a fatal chronic illness and therefore tell us little about the daily routine of patients and how they live.

Our results show that the QoL of all patients is dissatisfactory in all domains (health, physical functioning, psychosocial functioning, and treatment burden), This is possibly due to the fact of poor health care services of medical and diagnostic procedure given to our patients relative to other population. In addition, self-perceived QoL varies from individual to individual and as values, beliefs, cultural context, and social context change their views over the years [54].

Comparison of mean scores of the CFQ_{14+} group with CFQ_{6-13}, no statistically significant difference between them was observed but in general the scores for adult (14+) are slightly higher than child (6-13) scores except for emotion and social domain This is possibly due to the fact that children are less anxious, less depressed but stubborn and refuse permanent treatment and they are distracted because they are in a transitional school stage of their life. There is a significant statistic between adult and child in eat domain as adult cares about the nature of his/her eating more than child. Although the score for patients less than 6 years of age is much higher than both as parents take care of their food needs.

Symptoms of anxiety and depression in child, adolescents and adults correlate with low scores on instruments designed to quantify QoL and have been described as risk factors for poor treatment compliance, increased morbidity, and increased health care use in chronic diseases in many studies [59].

Regarding the questionnaires completed by the parents, we observe good agreement between the mean scores on the CFQ Parents 6-13 and the information obtained by means of the questionnaires applied to the patients. As determined in the score result of the parents the lowest scores were observed for the weight and body domains, suggesting parental dissatisfaction with the gastrointestinal functioning of their children. And statistical significance was seen in physical and treatment domain only.

Some studies have shown differences between parent and child reporting of QoL, especially regarding physical and emotional aspects [60]. This is probably due to the high level of emotional distress experienced by parents. The health problems of children with CF limit their participation in physical activities, as well as in school and family activities, causing caregivers anxiety and depression [61].

In addition, concerns about the life expectancy, together with the expensive and demanding treatment regimens, contribute to the onset of depressive symptoms in caregivers, directly affecting activities of daily living and treatment compliance [61].

Illness severity as measured by FEV1 ranged from 33 to 111 percent predicted with mean value of 69.6 percent, was done for only 26 patients as the rest of patients (29) unable to pay due to poverty with high test price (800 NIS) and other 22 patients were less than 6 years of age and can't do the test. For child and adult groups there is no correlation between quality of life domain score and FEV_1level measured as shown in other study FEV1 percent predicted may not improve substantially in patients whose lung function is > 75% predicted; however, these patients may report improvement in respiratory symptoms after treatment with antibiotics. Thus, in some cases, the patient reported outcomes may be more sensitive to change in symptoms than traditional pulmonary function indexes [62-65].

In three studies conducted in the 2000s, the correlation between QOL and FEV1 in individuals with CF was assessed by the Child Health Questionnaire, with conflicting results. In two of the studies, no such correlation was found. However, the authors of

the third study observed that adolescents and adults with abnormal FEV1 reported a poor perception of their physical health [54, 66, 67].

There is a correlation between BMI results for 72 patients sample with mean value 15.9978 Kg/m^2 ranged from 9.60-23.12 and physical domain in quality of life questionnaire only, as described in the literature as an important factor for the onset of physical stress in individuals with CF, since it correlates with higher morbidity and mortality, requiring treatments that are even more demanding.

The assessment of QoL in individuals with CF is important because it reveals the patient perception of what it is like to live with a fatal chronic illness and can improve treatment compliance [54, 68] In addition, it provides information for economic planning and make it possible to determine the impact of new treatments, as shown in a recent studies [69].

Most studies suggest that self-perceived health is directly related to age and to respiratory system impairment, becoming more evident in adolescents and adults with greater lung injury [70, 71].

In our study, as we compared quality of life score with demographic data we conclude that there is no correlation between age and QoL score for adult (14 and more) group as described. There are no differences in QoL with respect to gender with the exception of treatment to male as male compliance to treatment may be more than female because of different female concerns (body image, and weight). Specifically, social pressures to be thin were expected to affect females differentially. As detected in many studies with women experiencing greater declines in lung function than men [72].

However in many studies, women reported better functioning on scales that measured body image and weight, which could be related to a societal preference for thinness in women, regardless of the health consequences of low body weight in CF [53].

For adult group, there are differences in physical, vitality, health, body, role and digest domains with respect to vacation without disease. There is no statistical difference with marital status as they were single or married all of them suffered from the disease with the same level. There are no differences between the levels of education for quality of life domains as all of patients are educated there is no uneducated patients. There is a correlation between quality of life physical and role domains related with work or school status for patients taking educational courses at home as they feel good and are more active and keep up their duties more than others status.

In child (6-13) group there is no differences in QoL with respect to gender just in the eat domain related to male as males with no problem with eating more than female. There are no differences in QoL with respect to vacation without disease just in the eat domain related to yes answers as they eat well during vacation when they are

without disease problem. There is no difference in QoL with respect to education level just in social domain related to 7th grade as they more mature than other and deal with their friends as easily as they can. In child (6-13) group (mean age is 9.21 years of age) there are no differences in QoL with respect to age with the exception of social domain as we said as they grow up they are better in dealing with people.

In Parents (6-13) group, in the correlation between relationship (father, mother, grandfather and brother) parameter with QoL domains there is no differences in QoL score with respect to relationship. And there are no differences in QoL with respect to education level of the parents just in emotion, vitality and eat domains related to college degree. As the level of education for parents increase their knowledge about the disease and their ability to control increases. There is no differences in QoL with respect to work status of parents just in school domain for seeking work status as they able to educate their children and teach them well and feel the importance of science and keeping up with studying. There are differences in QoL of CF patients with respect to ages of their parents in physical, digest domains with negative correlation as they get older the quality of life of their children decreased. There is no correlation between marital status of the parents (married or divorced) and quality of life of their children.

There is no correlation between monthly income (NIS) and QoL score for all groups in contrast to many studies indicate that as the income increase the QoL increase. There is a significant statistic between number of family member live in the same place and QoL score in vitality and health domain for all groups with negative correlation, with high number of family members the vitality and the health status of CF patients decrease.

With geographic distribution of CF patients results as described for 58 families, Hebron is the district with most patients suffering from CF disease (50 patients from Hebron) and it was the highest in which they have more than one patient in each family (8 families contain two patients). The reason for this is the high rate of marriage between relatives as indicated in many studies the rate of consanguineous marriages in Palestine was found to be 45% in 2004 [41]. The family that has the highest number of patients (4 patients) was from Nablus district. In all districts studied, patients suffer from CF disease in the same level there is no differences in quality of life between the districts and there is no significant correlation between QoL domain score and patient kind of living (city, village and camp) this indicates that all Palestinian CF patients live in the same conditions, whether in a village, town or camp from north to south.

In our study, 21% of families (12/58) reported death cases related to CF disease, one family from Hebron has four CF death cases, this high rate of diagnosed CF death cases related to poor management strategies, therapies, and lack of earlier diagnostic procedures.

46.8% of CF patients don't take influenza vaccine yearly to prevent them from recurrent infections as confirmed in many studies [73, 74]. There are many reasons for this clarified when we asked the patients. One of reasons given is the lack of knowledge about the benefit from vaccination and they should take it, or for not being able to buy it or get it from Ministry of Health, or some patients said that they used it without any benefit.

As we measured in the willingness to pay section, 93.5% answered yes for paying and 6.5% answered no for that. Of patients who said yes 51.4% willing to pay are able to give 100 NIS out of pocket each month to get these new drugs, 37.5% are able to pay 50 NIS, 8.3% able to pay 500 NIS and 2.8% able to pay 2000 NIS or more to get these new drugs. This mean that our patients looking for a solution to their current situation.

In our study, 40.3% of patients chose among the things that were presented to them the most important thing they needed is to facilitate the mechanism of treatment by providing modern equipment for treatment and 33.3% of patients chose to pay in return for new medicines that reduce disease symptom and improve general health in different ways.

One might anticipate that patients who are willing to pay may have the worse QoL but in our study there is no statistical significant correlation between willingness to pay and quality of life domains as all CF patient in our country have poor quality of life scores as they suffer from the disease in the same level without differences and most of them willing to pay and the main reason for patients who don't want to pay is poor financial situation and poverty. The amount of money they are willing to pay is related to their monthly income not to the severity of the disease status.

In our study we compared our CF patient’s quality of life scores to normative CF international data, US sample and Brazilian sample. As we see Palestinian CF patients have poor quality of life, this is related to that our treatment regimen for CF is highly complex and time consuming, requiring 2–4 h of treatment every day. The treatment regimen includes multiple inhaled therapies, airway clearance two times per day, oral medications, and boosting calories to 110–200% of the recommended daily allowance. The challenges of adhering to this regimen include the time required, the complexity of using and cleaning the equipment, and its considerable cost. In addition, patients experience frequent pulmonary exacerbations, hospitalizations, and segregation from peers due to multi-resistant bacteria. High rates of depression and anxiety have also been reported by both patients and caregivers.

After economic evaluation of health care resources use and costs, the total costs of care for CF patient 10.7 years of age were estimated to be around 35650.2 NIS per patient per year as the treatment burden of this disease in the West Bank is very huge and expensive as we discussed. This total cost can be reduced by 33% and 25.5% with administration of Dornase-alpha mucolytic drug and Tobramycin antibiotic drug

respectively [22, 38]. According to literature review studies which indicated that by using these drugs, cost offsets may occur through changes in overall patient management with a reduction in the use of total health care resources. The savings obtained from using recommended drug may help offset the cost of adding them to the health care of CF patients.

Limitation

These results should be interpreted in light of some limitations. First, as a result of the lack of special centers that monitor and deal with CF patients and clarify many clinical aspects and outcomes of CF patients, we had difficulty in obtaining the full number of patients in West Bank and Gaza strip. As well, the sample size, although reasonable for this rare disease, was relatively small for the analyses that were conducted. Thus, this study was likely underpowered to detect some of the predicted relationships.

Second, the lack of a comparison group between our CF patients treated with new medication that we discussed in this study as Dornase-alpha or Tobramycin inhalation solution is a limitation that impairs a complete investigation about the benefits of these new drugs in the West Bank. In view of the current recommendations regarding the use of Dornase alpha or Tobramycin, it was decided to base our data on the literature studies due to high cost price for these medication and lack of financial and human resources to apply these drugs in the West Bank. Nevertheless, in our study, subjects served as their own controls as clinical information for our CF patients were compared to normative CF international data.

Chapter 6: Conclusion

CF places a large treatment burden on patients and their families with complex, time-intensive therapies and multiple medications administered throughout the day. Recent studies of adults with CF found that perceived treatment burden was highly associated with the number of nebulized medications prescribed. In addition, lengthy hospitalizations, which are commonplace in treatment plans, are disruptive to families, schooling, work, and extracurricular activities.

In summary, We reported that CF patients and their families in the West Bank face many barriers including large treatment burden that may make adherence difficult, financial challenges, late diagnosis on their life with poor diagnostic procedure and lack of resources needed to ensure optimal care for patients with CF. These resources include adequate clinic space and a dedicated CF team with nurses, a nutritionist, social workers, pharmacists, and respiratory therapists, as well as ancillary support from psychology, clinical laboratories (microbiology, chemistry and molecular diagnostics), radiology, and pulmonary function testing. Confronted with complex medical care, it may not be possible to adequately address all issues in the time allotted, and assessing patient compliance is difficult, as self-reported adherence typically represents an overestimation.

We have observed that our CF patients have significant disease morbidity and mortality despite all routine therapies that they receive. There is a significant decrease in the CFQ-R scores of the respiratory symptoms, emotional functioning, body image, and treatment burden domains in the subgroup of patients with cystic fibrosis. And quality of life for patients with CF is poor relative to international standards, the medications used including hypertonic saline and gentamycin are not first line therapies around the world, patients and their families demand better treatment and are willing to pay to get better treatment.

So continued research and work are needed to identify optimal outcome measures, In order to provide everything new, advanced and useful in management of our CF patients specially by the role of pharmacist as pivotal to the medicines management program to support the optimization of medicines for patients. The benefits of a dedicated CF pharmacist have previously been described, including benefits in terms of financial savings, improvements in patient care and efficient use of resources. This role of the pharmacist in pharmaceutical care model needs to be enlarged to improve efficiency and safety of drug therapy, to guard compliance to medication, to improve patients quality of life, and to ameliorate patient satisfaction.

Future Directions and recommendations

This study highlighted several possible future directions related to CF disease in the West Bank. Based on the findings from the current study, we can give an objective proof for the need of new therapies for CF patients in Palestine to Ministry of Health and government in order to improve their QoL, health status and longevity.

Recommendations to Policy Makers and Health Providers:

Establish a center for cystic fibrosis under supervision of Ministry of Health which includes specialists, trained nurses, dietitians, pharmacists, physiotherapists and psychologists with full equipment to follow up patients, note growth and development and give instructions, this could also expand to allocating special hospital departments for CF or even special clinics distributed in various localities to be able to better manage CF patients and assist them, this would enhance the trust in the medical body thus improving complicate from the patients side.

Specific criteria should be followed by physicians in the diagnosis of CF patients. The criteria for CF diagnosis must not relay on symptoms and sweat test only. Screening tests should be performed especially for families with CF history as we will ask for early medical screening program for the disease before marriage which are commonly applied in other countries. Training and counseling concerning the effects of consanguineous marriage involving religious and community leaders. Make neonatal screening program of CF for early diagnosis and to avoid complications of the disease. A comprehensive database must be established to hereditary diseases commonly found among Palestinian population including CF.

Recommendations for Researchers

Extensive mutation analysis to determine the relationship between the CFTR gene mutations and the course of the disease should be evaluated in order to provide better management and treatment for the CF patients. To concentrate on extra research projects on CF disease would benefit from an increase in the number of participants in future studies.

Although the results of economic evaluation that has been done in this study could not be used specifically since they mirror some distortions and limitations, however, this study has succeeded in identifying the major trends of the QoL for cystic fibrosis patients in addition to pin pointing the relative importance of new therapeutic options in their lives and its specific attributes. It is however, important to have effective awareness campaigns about cystic fibrosis in society in order to further decrease the incidence levels of cystic fibrosis.

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Appendix A: Informed consent form

أقرُّ أنا الموقع إسمي أدناه بأنه قد تم إعلامي بفحوى هذه الدراسة (**تقييم نوعية حياة مرضى التليف الكيسي في الضفة الغربية والخيارات العلاجية الجديدة**) وأنني قد وافقت بمحض إرادتي على أن أشارك فيها لما فيها من خدمة للعلم والمعرفة.

وأقرُّ أيضاً أنه تم إعلامي بجميع أهداف الدراسة وهي:

- دراسة الوضع الصحي لمرضى التليف الكيسي في فلسطين.
- دراسة العبء الاقتصادي وتكاليف العلاج الحالية وتأثيرها على المرضى.
- معرفة رغبة المرضى في المساهمة المالية مقابل الحصول على علاج جديد يحسن من الوضع الصحي ويقلل من اعراض المرض ودراسة العوامل التي ستأثر على اجابتهم.
- لفت النظر إلى الحاجة الى علاج جديد لمرض التليف الكيسي (بالاعتماد على النتائج).

كما وأعلمت أن المعلومات التي يتحصل عليها منّي سوف تعامل بسرية وسيتم تداولها في المحافل العلمية دون ذكر إسمي.

كما وأقرّ أنه تم الإجابة بشكل مرضي عن جميع أسئلتي الأخرى حول الدراسة.

لقد قرأت المعلومات السابق ذكرها أو تم قراءتها لي وأوافق على المشاركة في الدراسة.

اسم المشارك :
توقيع المشارك:
التاريخ:

اسم الباحث:
توقيع الباحث:

Appendix B: Cystic Fibrosis Questionnaire – Revised (CFQ-R) form

1. Child (6-11) years of age version

بالرغم من ان هذه الأسئلة كتبت بلسان الذكر فانها تنطبق على الذكر والأنثى.

تم تصميم هذا الاستبيان لكي يستعمله المُحاور. من فضلك استعمل هذه الصيغة مع الأطفال الأصغر سناً. استعمل هذا الاستبيان بصيغة التقرير الذاتي مع الأطفال القادرين على قراءة الأسئلة والإجابة عنها بأنفسهم. مثلاً: أطفال أعمارهم 12 و 13 سنة.

هناك إرشادات للمحاور بخصوص كل فصل من فصول الاستبيان. الإرشادات التي عليك *تلاوتها* على الطفل موجودة داخل علامتي اقتباس. الإرشادات التي عليك *إتباعها* مؤشرة بخطٍ تحتي وكتابة مائلة.

المُحاور: *الرجاء طرح الأسئلة التالية.*

أ. ما هو تاريخ ولادتك ؟

التاريخ ☐☐ ☐☐ ☐☐☐☐
اليوم الشهر السنة

ب. هل أنت؟

☐ ولد ☐ بنت

ت. هل خرجت **خلال آخر أسبوعين** في عطلة أو تغيبت عن المدرسة لأسباب **لا** تتعلق بصحتك؟

☐ نعم ☐ لا

ث. في أي صف أنت الآن؟
(الصيف: أي صف أنهيت)

☐ الروضة (البستان)
☐ الصف الأول
☐ الصف الثاني
☐ الصف الثالث
☐ الصف الرابع
☐ الصف الخامس
☐ الصف السادس
☐ الصف السابع
☐ لا أذهب إلى المدرسة

أطفال من سن 6 إلى 11 سنة (صيغة المُحاور)

CYSTIC FIBROSIS QUESTIONNAIRE-REVISED

المحاور *: من فضلك اقرأ ما يلي للطفل:*

"هذه الأسئلة هي لأطفال مثلك الذين عندهم مرض التليف الكيسي. إجاباتك ستساعدنا على فهم هذا المرض وكيف تساعدك علاجاتك. لهذا فإن إجابتك على هذه الأسئلة, ستساعدك وتساعد الآخرين مثلك في المستقبل."

" اجب عن كل سؤال أطرحه عليك بواسطة اختيار بطاقة واحدة من البطاقات التي سأريك إياها".

□□□□□ □□□□□□□□□□ □□□□□□□ □□□□

"انظر على هذه البطاقة واقرأ معي ما تقول **صحيحاً جدا/ صحيحاً أكثر ألوقت / صحيحاً إلى حد ما/ليس صحيحاً بالمرة.**

"إليك أحد الأمثلة: لو سألتك إذا كان **صحيحاً جداً** أو **صحيحاً أكثر ألوقت** أو **صحيحاً إلى حد ما** أو **ليس صحيحاً بالمرة** أن الفيلة تستطيع الطيران، فأي إجابة من أربع الإجابات الموجودة على البطاقة تختار؟"

اعرض البطاقة الزرقاء للطفل.

"الآن انظر إلى هذه البطاقة واقرأ معي ما تقول: **دائماً / كثيراً من ألوقت/ أحياناً / ابدا لا.**"

"إليك مثال آخر: لو سألتك إذا كنت تذهب إلى القمر **دائماً، كثيراً من ألوقت ، أحياناً أو أبدا لاً**، فأي إجابة من البطاقة تختار؟"

اعرض البطاقة البرتقالية للطفل.

"الآن, سوف أسألك بعض الأسئلة عن حياتك اليومية."

"قل لي إن كانت الجمل التي أقرأها لك **صحيحة جداً** أو **صحيحة أكثر الوقت** أو **صحيحة إلى حدّ ما** أو **ليست صحيحة بالمرة**".

من فضلك ضع علامة في المربع الذي يشير إلى إجابة الطفل.

"خلال آخر **أسبوعين** ":	صحيحاً جدا	صحيحاً أكثر الأوقات	صحيحاً إلى حد ما	ليس صحيحاً بالمرة
1. استطعت أن تمشي بنفس السرعة مثل الآخرين	☐	☐	☐	☐
2. استطعت أن تصعد الدرج بنفس ألسرعة مثل الآخرين.....	☐	☐	☐	☐
3. استطعت أن تركض, تقفز, وتتسلق كما تشاء.....	☐	☐	☐	☐
4. استطعت أن تركض بنفس السرعة ولنفس المسافات كما يفعل الأخرين	☐	☐	☐	☐
5. كنت قادراً على ممارسة الرياضة التي تحبها (مثلاً السباحة، كرة القدم، الرقص أو غيرها)	☐	☐	☐	☐
6. وجدت صعوبة في حمل أو رفع أشياء ثقيلة مثل الكتب أو الحقيبة المدرسية أو حقيبة الظهر	☐	☐	☐	☐

أطفال من سن 6 إلى 11 سنة (صيغة المُحاوِر)

CYSTIC FIBROSIS QUESTIONNAIRE-REVISED

المحاور: *اعرض البطاقة الزرقاء للطفل.*

من فضلك ضع علامة في المربع الذي يشير إلى إجابة الطفل.

"خلال آخر **أسبوعين**، قل لي كم مرة ":	دائما	كثيراً من الوقت	أحيانا	أبدا لا
7. شعرت أنك تعبان.....	☐	☐	☐	☐
8. شعرت أنك زعلان	☐	☐	☐	☐
9. شعرت انك منزعج.....	☐	☐	☐	☐
10. شعرت بالقلق	☐	☐	☐	☐
11. شعرت بالحزن	☐	☐	☐	☐
12. كانت عندك مشكلة في أن ترقد للنوم.....	☐	☐	☐	☐
13. حلمت أحلاماً سيئة أو رأيت الكوابيس في منامك	☐	☐	☐	☐
14. شعرت بشكل جيد مع نفسك	☐	☐	☐	☐
15. كانت لديك مشكلة في الأكل	☐	☐	☐	☐
16. كان عليك أن تتوقف عن ممارسة الأنشطة المرحة لكي تقوم بعلاجاتك	☐	☐	☐	☐
17. تم دفعك للأكل	☐	☐	☐	☐

المحاور: *اعرض البطاقة البرتقالية للطفل.*

"والآن قل لي إن كنت تعتقد أن الجمل التي أقرأها لك **صحيحة جداً، صحيحة أكثر الوقت ، صحيحة إلى حد ما أو غير صحيحة بالمرة**".

من فضلك ضع علامة في المربع الذي يشير إلى إجابة الطفل.

"خلال آخر **أسبوعين** ":	صحيحاً جدا	صحيحاً أكثر الأوقات	صحيحاً إلى حد ما	ليس صحيحاً بالمرة
18. استطعت القيام بكل علاجاتك.....	☐	☐	☐	☐
19. استمتعت في تناول الأكل.....	☐	☐	☐	☐
20. التقيت كثيرا مع أصدقاء.....	☐	☐	☐	☐
21. بقيت في البيت أكثر مما أردت.....	☐	☐	☐	☐
22. شعرت براحة في النوم بعيداً عن البيت (لدى صديق أو في بيوت أقرباء العائلة أو في أي مكان آخر).....	☐	☐	☐	☐

"خلال آخر أسبوعين ":	صحيحاً جدا	صحيحاً أكثر الأوقات	صحيحاً إلى حد ما	ليس صحيحاً بالمرة
23. شعرت أنك مُهمَل	☐	☐	☐	☐
24. غالباً ما دعوت أصدقائك لزيارة بيتك.....	☐	☐	☐	☐
25. تعرضت لمضايقة أطفال آخرين.....	☐	☐	☐	☐
26. شعرت براحة بالحديث عن مرضك مع الآخرين (أصدقاء, معلمين).....	☐	☐	☐	☐
27. اعتقدت انك قصير جدا.....	☐	☐	☐	☐
28. اعتقدت انك ضعيف جدا	☐	☐	☐	☐
29. اعتقدت انك مختلف جسميا عن أولاد آخرين في عمرك.....	☐	☐	☐	☐
30. انزعجت من القيام بعلاجاتك	☐	☐	☐	☐

المُحاور: *اعرض البطاقة الزرقاء للطفل مرة أخرى*

من فضلك ضع علامة في المربع الذي يشير إلى إجابة الطفل.

"قل لي كم مرة في آخر **أسبوعين**":	دائما	كثيراً من ألوقت	أحيانا	أبدا لا
31. سعلت في ساعات النهار	☐	☐	☐	☐
32. استيقظت في الليل بسبب السعال.....	☐	☐	☐	☐
33. سعلت بوجود بلغم	☐	☐	☐	☐
34. كانت عندك مشكلة في التنفس	☐	☐	☐	☐
35 . اوجعتك بطنك.....	☐	☐	☐	☐

*تأكد من فضلك أنه تمت الإجابة على **كل** الأسئلة.*

شكراً على تعاونك!

2.Child (12-13) years of age version

أطفال أعمارهم 12 و 13 سنة (صيغة التقرير الذاتي)

CYSTIC FIBROSIS QUESTIONNAIRE-REVISED

بالرغم من ان هذه الأسئلة كتبت بلسان الذكر فانها تنطبق على الذكر والأنثى.

هذه الأسئلة موجهة لأطفال مثلك الذين عندهم مرض التليف الكيسي. ستساعدنا إجاباتك على فهم هذا المرض وكيف تساعدك العلاجات التي تتلقاها. لذا، فإن الإجابة عن هذه الأسئلة ستساعدك وتساعد الآخرين مثلك في المستقبل.

الرجاء الإجابة عن كل الأسئلة. ليست هناك إجابات صحيحة أو إجابات غير صحيحة! إذا لم تكن متأكداً من الإجابة، فاختر الإجابة الأقرب إلى حالتك.

الرجاء كتابة الإجابة أو أشر في المربع المناسب لإجابتك عن هذه الأسئلة.

أ. ما هو تاريخ ولادتك ؟

التاريخ ☐☐ ☐☐ ☐☐☐☐

اليوم الشهر السنة

ب. هل أنت؟

☐ ولد ☐ بنت

ت. هل خرجت **خلال آخر أسبوعين** في عطلة أو تغيبت عن المدرسة لأسباب **لا** تتعلق بصحتك؟

☐ نعم ☐ لا

ث. في أي صف أنت الآن :
(في الصيف: أي صف أنهيت)

☐ الصف الخامس

☐ الصف السادس

☐ الصف السابع

☐ الصف الثامن

☐ الصف التاسع

☐ لا أذهب إلى المدرسة

أطفال أعمارهم 12 و 13 سنة (صيغة التقرير الذاتي)

CYSTIC FIBROSIS QUESTIONNAIRE-REVISED

من فضلك اشر في المربع المناسب لإجابتك .

خلال الأسبوعين الماضيين:	صحيحاً جدا	صحيحاً أكثر الأوقات	صحيحاً إلى حد ما	ليس صحيحاً بالمرة
1. استطعت أن تمشي بنفس السرعة مثل الآخرين	☐	☐	☐	☐
2.استطعت أن تصعد الدرج بنفس السرعة مثل الآخرين	☐	☐	☐	☐
3. استطعت أن تركض, تقفز, وتتسلق كما تشاء	☐	☐	☐	☐
4. استطعت أن تركض بنفس السرعة ولنفس المسافات كما يفعل الآخرين	☐	☐	☐	☐
5. كنت قادراً على ممارسة الرياضة التي تحبها (مثلاً السباحة، كرة القدم، الرقص أو غيرها)	☐	☐	☐	☐
6. وجدت صعوبة في حمل أو رفع أشياء ثقيلة مثل الكتب أو الحقيبة المدرسية أو حقيبة الظهر	☐	☐	☐	☐

من فضلك اشر في المربع المناسب لإجابتك .

وخلال **آخر أسبوعين** أشر كم مرة:	دائماً	غالباً	أحياناً	أبداً لا
7. شعرت أنك تعبان.....	☐	☐	☐	☐
8. شعرت أنك زعلان	☐	☐	☐	☐
9. شعرت انك منزعج.....	☐	☐	☐	☐
10. شعرت بالقلق	☐	☐	☐	☐
11. شعرت بالحزن	☐	☐	☐	☐
12. كانت عندك مشكلة في أن ترقد للنوم.....	☐	☐	☐	☐
13. حلمت أحلاماً سيئة أو رأيت الكوابيس في منامك	☐	☐	☐	☐
14. شعرت بشكل جيد مع نفسك	☐	☐	☐	☐

من فضلك اشر في المربع المناسب لإجابتك .

وخلال **آخر أسبوعين** أشر كم مرة:	دائما	كثير من ألوقت	أحيانا	أبداً لا
15. كانت لديك مشكلة في الأكل	☐	☐	☐	☐
16. كان عليك أن تتوقف عن ممارسة الأنشطة المرحة لكي تقوم بعلاجاتك	☐	☐	☐	☐
17. تم دفعك للأكل	☐	☐	☐	☐

من فضلك اشر في المربع المناسب لإجابتك .

خلال آخر **أسبوعين** :	صحيحاً جدا	صحيحاً أكثر الأوقات	صحيحاً إلى حد ما	ليس صحيحاً بالمرة
18. استطعت القيام بكل علاجاتك.....	☐	☐	☐	☐
19. استمتعت في تناول الأكل.....	☐	☐	☐	☐
20. التقيت كثيرا مع أصدقاء.....	☐	☐	☐	☐
21. بقيت في البيت أكثر مما أردت.....	☐	☐	☐	☐
22. شعرت براحة في النوم بعيداً عن البيت (لدى صديق أو في بيوت أقرباء العائلة أو في أي مكان آخر).....	☐	☐	☐	☐
23. شعرت أنك مُهمَل	☐	☐	☐	☐
24. غالباً ما دعوت أصدقائك لزيارة بيتك.....	☐	☐	☐	☐
25. تعرضت لمضايقة أطفال آخرين.....	☐	☐	☐	☐
26. شعرت براحة بالحديث عن مرضك مع الآخرين (أصدقاء, معلمين).....	☐	☐	☐	☐
27. اعتقدت انك قصير جدا.....	☐	☐	☐	☐
28. اعتقدت انك نحيف جدا	☐	☐	☐	☐
29. اعتقدت انك مختلف جسميا عن أولاد آخرين في عمرك...	☐	☐	☐	☐

خلال آخر أسبوعين :	صحيحاً جدا	صحيحاً أكثر الأوقات	صحيحاً إلى حد ما	ليس صحيحاً بالمرة
30. انزعجت من القيام بعلاجاتك	☐	☐	☐	☐

من فضلك اشر في المربع المناسب لإجابتك.

دعنا نعلم كم مرة خلال آخر أسبوعين:	دائما	غالباً	أحياناً	أبداً لا
31. سعلت في ساعات النهار	☐	☐	☐	☐
32. استيقظت في الليل بسبب السعال.....	☐	☐	☐	☐
33. سعلت بلغم	☐	☐	☐	☐
34. كانت عندك مشكلة في التنفس	☐	☐	☐	☐
35. آوجعتك بطنك.....	☐	☐	☐	☐

تأكد من فضلك أنه تمت الإجابة على كل الأسئلة.

شكراً على تعاونك!

3.Adult 14 years and more version

المراهقين والبالغين (مرضى من سن 14 سنة وما فوق)

CFQ-R

CYSTIC FIBROSIS QUESTIONNAIRE-REVISED

بالرغم من ان هذه الأسئلة كتبت بلسان الذكر فانها تنطبق على الذكر والأنثى.

إن فهم تأثير مرضك وعلاجاتك على حياتك اليومية من شأنه مساعدة الفريق الطبي على متابعة حالتك الصحية وملائمة علاجاتك. ولهذا السبب تم تصميم هذا الاستبيان خاصة للأشخاص الذين يعانون من مرض التليف الكيسي. شكراً لتعاونك معنا في تعبئة هذه الاستمارة.

تعليمات : تتعلق الأسئلة التالية بوضعك الصحي الحالي كما تفهمه أنت. ستساعدنا هذه المعلومات أن نفهم أفضل كيف تشعر في حياتك اليومية.

الرجاء الإجابة عن كل الأسئلة. ليست هناك إجابات صحيحة أو إجابات غير صحيحة! إذا لم تكن متأكداً من الإجابة، فاختر الإجابة الأقرب إلى حالتك.

الفصل 1. معطيات ديموغرافية

من فضلك أملئ المعلومات أو اشر في المربع المناسب لإجابتك على هذه الأسئلة.

أ. ما هو تاريخ ولادتك ؟

التاريخ ☐☐ ☐☐ ☐☐☐☐

اليوم الشهر السنة

ب. ما هو جنسك؟

☐ ذكر ☐ أنثى

ت. هل خرجت خلال اخر أسبوعين في عطلة أو تغيبت عن المدرسة أو العمل لأسباب **لا** تتعلق بصحتك؟

☐ نعم ☐ لا

ث. ما هي حالتك الاجتماعية الحالية؟

☐ أعزب/ لم أتزوج أبداً
☐ متزوج
☐ أرمل
☐ مطلق
☐ منفصل

ج. ما هو أعلى صف أنهيته في المدرسة؟

☐ دراسة ثانوية جزئية أو أقل
☐ شهادة ثانوية
☐ مدرسة صناعية
☐ تعليم جامعي جزئي
☐ شهادة جامعية
☐ شهادة مهنية أو شهادة تخرج

خ. أي من الخيارات التالية هي الافضل لوصف شكل عملك الحالي أو وضعك المدرسي؟

☐ أذهب إلى مدرسة خارج البيت
☐ أتعلم دورات تثقيفية في البيت
☐ أبحث عن عمل
☐ أعمل بوظيفة كاملة أو جزئية (إما خارج البيت أو في عمل أقوم به من البيت)
☐ ربة بيت وقت كامل
☐ لا أتعلم في المدرسة ولا أعمل بسبب حالتي الصحية
☐ لا أعمل لأسباب أخرى

المراهقين والبالغين (مرضى من سن 14 سنة وما فوق)

CFQ-R

CYSTIC FIBROSIS QUESTIONNAIRE-REVISED

الفصل 2. جودة الحياة

من فضلك اشر في المربع المناسب لإجابتك عن هذه الأسئلة.

*خلال آخر **أسبوعين**, إلى أي حد وجدت صعوبة في :*	كثيراً من الصعوبة	بعض الصعوبة	قليلاً من الصعوبة	بدون صعوبة
1. ممارسة أنشطة قوية كالركض أو ممارسة الألعاب الرياضية.....	☐	☐	☐	☐
2. المشي بنفس السرعة مثل الآخرين.....	☐	☐	☐	☐
3. حمل أو رفع أغراض ثقيلة كالكتب والمشتريات أو الحقائب المدرسية	☐	☐	☐	☐
4. صعود دور واحد من الدرج.....	☐	☐	☐	☐
5. صعود الدرج بنفس السرعة مثل الآخرين	☐	☐	☐	☐

***خلال آخر أسبوعين** , اشر كم مرة:*	دائماً	غالباً	أحياناً	أبداً لا
6. شعرت جيدا.....	☐	☐	☐	☐
7. شعرت بالقلق.....	☐	☐	☐	☐
8. شعرت بأنك عديم الفائدة.....	☐	☐	☐	☐
9. شعرت أنك تعبان.....	☐	☐	☐	☐
10. شعرت أنك مفعم بالحيوية.....	☐	☐	☐	☐
11. شعرت مرهقا.....	☐	☐	☐	☐
12. شعرت بالحزن	☐	☐	☐	☐

ضع من فضلك دائرة حول الرقم المناسب لإجابتك . اختر من فضلك جواباً واحداً فقط لكل سؤال.

*حين تفكر في وضعك / لصحي خلال **آخر أسبوعين**:*

13. إلى أي مدى تواجه صعوبة في المشي؟
1. بوسعك المشي لمدة طويلة دون أن تتعب
2. يمكنك المشي لمدة طويلة لكنك تتعب
3. ليس بوسعك المشي لمدة طويلة لأنك تتعب بسرعة
4. أنت تتجنب المشي قدر الامكان لأنه أمر متعب للغاية بالنسبة لك

14. ما هو شعورك بالنسبة للأكل؟
1. مجرد التفكير بالأكل يجعلك تشعر بالغثيان
2. أنت لا تتمتع بالأكل أبداً
3. بوسعك أحياناً أن تتمتع بالأكل
4. بوسعك دائماً التمتع بالأكل

15. .إلى أي مدى علاجاتك تصعب حياتك اليومية ؟
1. قطعاً لا.
2. قليلاً.
3. إلى حد ما
4. كثيراً

16. كم من الوقت تقضي حاليا كل يوم لتلقي علاجاتك ؟
1. كثيراً
2. بعض الوقت
3. قليلاً
4. ليس كثيراً جدا

17. كم يصعب عليك أن تقوم بعلاجاتك (بما فيه الأدوية) كل يوم؟
1. قطعا لا
2. قليلاً
3. إلى حد ما
4. جداً

18. كيف ترى صحتك الآن؟
1. ممتازة
2. جيدة
3. مقبولة
4. سيئة

الرجاء اختيار المربع المناسب لإجابتك.

عند التفكير في صحتك خلال آخر أسبوعين, اشر إلى أي مدى كل جملة هي صحيحة أو خطا بالنسبة لك.	صحيحاً جداً	صحيحاً نوعاً ما	خاطئاً نوعاً ما	خاطئاً جداً
19. أجد صعوبة في استعادة عافيتي بعد المجهود البدني	☐	☐	☐	☐
20. أضطر للحد من ممارسة الأنشطة القوية مثل الركض أو ممارسة الألعاب الرياضية.....	☐	☐	☐	☐
21. أضطر لإرغام نفسي على الأكل.....	☐	☐	☐	☐
22. اضطر أن أبقى في البيت أكثر مما أريد.....	☐	☐	☐	☐
23. اشعر براحة عندما أتحدث عن مرضي مع الآخرين	☐	☐	☐	☐
24. أعتقد أنني نحيف جداً.....	☐	☐	☐	☐
25. أعتقد أني أبدو مختلفاً عن سائر أبناء جيلي.....	☐	☐	☐	☐
26. اشعر بسوء من مظهري الخارجي	☐	☐	☐	☐
27. يخشى الناس من الاحتمال أنني معدي	☐	☐	☐	☐
28. ألتقي مع أصحابي أحيانا كثيرةً	☐	☐	☐	☐
29. اعتقد أن الآخرين ينزعجون من سعالي	☐	☐	☐	☐
30. اشعر بالراحة عند خروجي في الليل	☐	☐	☐	☐
31. غالبا أشعر بالوحدة	☐	☐	☐	☐
32. أشعر أني معافى	☐	☐	☐	☐
33. من الصعب التخطيط للمستقبل (مثلا الذهاب للدراسة في الكلية أو التخطيط للزواج أو الترقي في العمل وما إلى ذلك).....	☐	☐	☐	☐

عند التفكير في صحتك خلال آخر **أسبوعين**, اشر إلى أي مدى كل جملة هي صحيحة أو خطا بالنسبة لك.	صحيحاً جداً	صحيحاً نوعاً ما	خاطئاً نوعاً ما	خاطئاً جداً
34. أمارس حياة طبيعية	☐	☐	☐	☐

الفصل 3: المدرسة، العمل أو النشاطات اليومية

الأسئلة 35 إلى 38 حول المدرسه والعمل أو مهمات يوميه أخرى .

35. إلى أي مدى كانت عندك مشكله في مواظبتك مع واجباتك في المدرسة , عملك المحترف , أو فعاليات يومية أخرى خلال آخر **أسبوعين؟**
1. لم تكن عندك مشكلة في المواظبة
2. استطعت أن تواظب لكن كان صعبا
3. لقد تخلفت
4. لم يكن بوسعك القيام بتلك النشاطات على الإطلاق

36. بأي وتيرة تغيبت عن المدرسة, العمل, أو لم تستطع أن تكمل فعالياتك اليومية خلال آخر أسبوعين بسبب مرضك أو علاجاتك؟

☐ دائماً ☐ غالباً ☐ أحيانا ☐ أبداً لا

37. بأي وتيرة يعترض مرض ألسيستيك فيبروزيس طريقك في التقيد بمدرستك أو بعملك أو بأهدافك الشخصية؟

☐ دائماً ☐ غالباً ☐ أحيانا ☐ أبداً لا

38. كيف يتعارض مرض ألسيستيك فيبروزيس مع الخروج من البيت لأداء مهام مثل القيام بمشتريات أو زيارة البنك؟

☐ دائماً ☐ غالباً ☐ أحيانا ☐ أبداً لا

الفصل 4. صعوبات الأعراض المرضية

الرجاء اختيار المربع المناسب لإجابتك.

*اشر كيف شعرت في آخر **أسبوعين**.*	كثير جداً	إلى حد ما	قليلاً	لا على الإطلاق
39. هل كانت عندك صعوبة في الزيادة في الوزن؟	☐	☐	☐	☐
40. هل كان أنفك و صدرك مليئين بالبلغم؟.....	☐	☐	☐	☐
41. هل كنت تسعل خلال اليوم؟.....	☐	☐	☐	☐
42. هل كنت تضطر للسعال لإخراج البلغم؟	☐	☐	☐	☐ انتقل إلى السؤال رقم 44

43. هل كان البلغم على الأغلب: ☐ صافياً ☐ صافياً يميل إلى الصفرة ☐ أصفر-اخضر ☐ أخضر مع آثار دم ☐ لا أدري

*خلال آخر **أسبوعين** ، بأي وتيرة :*	دائماً	غالباً	أحياناً	أبداً لا
44. صفرت في التنفس؟	☐	☐	☐	☐
45. واجهت مشكلة في التنفس؟.....	☐	☐	☐	☐
46. استيقظت في الليل لأنك كنت تسعل؟	☐	☐	☐	☐
47. كنت تعاني من مشكلة غازات؟	☐	☐	☐	☐

خلال آخر **أسبوعين** ، بأي وتيرة:	دائماً	غالباً	أحياناً	أبداً لا
48. كان عندك إسهال؟	☐	☐	☐	☐
49. كان عندك وجع في البطن ؟	☐	☐	☐	☐
50. كان عندك مشاكل في تناول الطعام؟	☐	☐	☐	☐

تأكد من فضلك أنه تمت الإجابة على كل الأسئلة.

شكراً على تعاونك!

4.Parent for child (6-13) years of age version

CFQ-R

ألوالدين/ القائمين على العناية (أطفال من سن 6 إلى 13 سنة)

CYSTIC FIBROSIS QUESTIONNAIRE-REVISED

بالرغم من ان هذه الأسئلة كتبت بلسان الذكر فانها تنطبق على الذكر والأنثى.

إن فهم تأثير مرض طفلك وعلاجاته على حياتها اليومية يمكن أن يساعد الطاقم الطبي على متابعة صحة طفلك وملائمة العلاج له. ولهذا السبب فقد طورنا استبيان جودة الحياة خصيصاً لوالدي الأطفال المصابين بمرض التليف الكيسي. نشكرك على استعدادك لتعبئة هذا الاستبيان.

تعليمات : الأسئلة التالية تتعلق بالوضع الصحي الحالي لطفلكم كما يفهمه هو. ستسمح لنا هذه المعلومات بأن نفهم بشكل أفضل كيف يشعر في حياته اليومية.

الرجاء الإجابة عن كل الأسئلة. ليست هناك إجابات صحيحة أو إجابات غير صحيحة! إذا لم تتأكدوا من الجواب، فاختاروا الإجابة التي تبدو الأقرب إلى وضع طفلكم.

الفصل 1. معطيات ديموغرافية

من فضلك أملئ المعلومات أو اشر في المربع المناسب لإجابتك على هذه الأسئلة.

أ. ما هو تاريخ ولادة **طفلك؟**

التاريخ ☐☐ ☐☐ ☐☐☐☐

اليوم الشهر السنة

ب. ما هي علاقتك بالطفل؟

- ☐ أم
- ☐ أب
- ☐ جدة
- ☐ جد
- ☐ قريب عائلة آخر
- ☐ أم بالتبني
- ☐ أب بالتبني
- ☐ آخر (اشرح من فضلك) _____

ت. خلال **آخر أسبوعين**، هل كان طفلك في عطلة أو خارج المدرسة لأسباب **لا** علاقة لها بصحته ؟

☐ نعم ☐ لا

ث. ما هو تاريخ ولادتك ؟

التاريخ ☐☐ ☐☐ ☐☐☐☐

اليوم الشهر السنة

ج . ما هي حالتك الاجتماعية الحالية؟

- ☐ أعزب/ لم أتزوج أبداً
- ☐ متزوج
- ☐ أرمل
- ☐ مُطلق
- ☐ منفصل

د. ما هو أعلى صف أنهيته في المدرسة؟

- ☐ دراسة ثانوية جزئية أو أقل
- ☐ شهادة ثانوية
- ☐ مدرسة صناعية
- ☐ تعليم جامعي جزئ
- ☐ شهادة جامعية
- ☐ شهادة مهنية أو شهادة تخرج

ذ. أي من الخيارات التالية مي الأفضل لوصف وضعك الحالي بالنسبة للعمل؟

- ☐ أبحث عن عمل
- ☐ أعمل بوظيفة كاملة أو جزئية (إما خارج البيت أو عمل أقوم به من داخل البيت)
- ☐ ربة بيت وقت كامل
- ☐ لا أعمل بسبب صحتي
- ☐ لا أعمل لأسباب أخرى

ألوالدين/ القائمين على العناية (أطفال من سن 6 إلى 13 سنة)

CFQ-R

CYSTIC FIBROSIS QUESTIONNAIRE-REVISED

الفصل 2. جودة الحياة

أشر من فضلك: كيف كان شعور طفلك خلال آخر أسبوعين من خلال الإشارة إلى المربع المناسب لإجابتك.

إلى أي مدى كان طفلك يواجه صعوبة في:	كثير من الصعوبة	بعض الصعوبة	قليل من الصعوبة	بدون صعوبة
1. ممارسة أنشطة قوية كالركض أو ممارسة الألعاب الرياضية.....	☐	☐	☐	☐
2. المشي بنفس السرعة مثل الآخرين.....	☐	☐	☐	☐
3.صعود الدرج بنفس ألسرعة مثل الآخرين	☐	☐	☐	☐
4. حمل أو رفع الأغراض الثقيلة كالكتب أو الحقيبة المدرسية أو حقيبة الظهر...	☐	☐	☐	☐
5. صعود عدة أدوار من الدرج.....	☐	☐	☐	☐

يرجى أن تؤشر في المربع المناسب لإجابتك.

*خلال آخر **أسبوعين**, اشر في أي وتيرة كان طفلك:*	دائماً	غالباً	أحياناً	أبداً لا
6. يبدو سعيداً.....	☐	☐	☐	☐
7. يبدو قلقاً.....	☐	☐	☐	☐
8. يبدو متعباً.....	☐	☐	☐	☐
9. يبدو سريع الغضب.....	☐	☐	☐	☐
10. يبدو جيدا	☐	☐	☐	☐
11. يبدو منزعجاً.....	☐	☐	☐	☐
12. يبدو نشيطاً.....	☐	☐	☐	☐
13. . تغيب عن المدرسة أو تأخر بالذهاب إلى المدرسة أو إلى فعاليات أخرى بسبب مرضه أو بسبب العلاجات	☐	☐	☐	☐

ضع من فضلك دائرة حول الرقم المناسب لإجابتك. اختر من فضلك إجابة واحدة فقط عن كل سؤال.

*حين تفكر في وضع طفلك الصحي خلال آخر **أسبوعين**, اشر:*

14. إلى أي مدى كان طفلك يشارك في الأنشطة الرياضية وغيرها من الأنشطة البدنية، مثل درس الرياضة
1. لم يشارك في الأنشطة البدنية
2. شارك في الأنشطة الرياضية أقل من المعتاد
3. شارك كالمعتاد لكن مع بعض الصعوبة
4. كان بوسعه المشاركة في الأنشطة البدنية دون أي صعوبة

15. ما هو مدى الصعوبة التي كان يواجهها طفلك في المشي
1. بوسعه المشي لمدة طويلة دون تعب
2. بوسعه المشي لمدة طويلة لكنه يتعب
3. ليس بوسعه المشي لمدة طويلة لأنه يتعب بسرعة.
4. إنه يتفادى المشي قدر الامكان لأنه أمر متعب جداً بالنسبة له

يرجى وضع إشارة في المربع المناسب لإجابتك عن هذه الأسئلة.

حين تفكر في وضع طفلك الصحي خلال آخر ***أسبوعين****, اشر ما مدى صحة أو عدم صحة هذه الجمل بالنسبة لطفلك:*

	صحيحاً جداً	صحيحاً أكثر الأوقات	خاطئاً نوعاً ما	خاطئاً جداً
16. كان لطفلي صعوبة في الانتعاش بعد الجهد البدني	☐	☐	☐	☐
17. أوقات تناول وجبات الطعام فيها صعوبة	☐	☐	☐	☐
18. العلاجات التي يتلقاها طفلي تعرقل قيامه بأنشطته	☐	☐	☐	☐
19. يشعر طفلي أنه صغير بالمقارنة مع أطفال آخرين من جيله.....	☐	☐	☐	☐
20. يشعر طفلي بأنه مختلف بدنيا عن باقي الأطفال في جيله.....	☐	☐	☐	☐
21. يعتقد طفلي أنه نحيف جداً.....	☐	☐	☐	☐
22. يشعر طفلي أنه بصحة جيدة	☐	☐	☐	☐
23. يميل طفلي إلى الانطواء على نفسه.....	☐	☐	☐	☐
24. يمارس طفلي حياة عادية.....	☐	☐	☐	☐
25. يتسلى طفلي اقل من العادة.....	☐	☐	☐	☐
26. يجد طفلي صعوبة في التدبر مع الأخرين	☐	☐	☐	☐
27. يجد طفلي صعوبة في التركيز	☐	☐	☐	☐
28. يستطيع طفلي المواظبة على واجباته المدرسية وفعالياته الصيفية (مثال المخيم الصيفي)	☐	☐	☐	☐
29. لا يبدو أداء طفلي حسناً كالمعتاد في المدرسة أو في الفعاليات الصيفية (مثال المخيم الصيفي).	☐	☐	☐	☐
30. يمضي طفلي الكثير من الوقت في علاجاته كل يوم.	☐	☐	☐	☐

ضع من فضلك دائرة حول الرقم المناسب لإجابتك. يرجى أن تختار جواب واحد فقط لكل سؤال.

31. ما هي الصعوبة التي يواجهها طفلك في اقامة علاجاته (بما فيها الأدوية) كل يوم؟
1. قطعاً لا
2. قليلا
3. إلى حد ما
4. جداً

32. كيف تعتقد أن حالة طفلك الصحية الآن؟
1. ممتازة
2. جيدة
3. مقبولة
4. سيئة

الفصل 3. صعوبات الأعراض المرضية

تم تصميم مجموعة الأسئلة التالية لتحديد وتيرة معاناة طفلك من صعوبات تنفسية معينة كالسعال أو قصر النفس.

أشر من فضلك كيف كان يشعر طفلك خلال آخر أسبوعين.	كثيراً جداً	إلى حد ما	قليلاً	لا على الإطلاق
33. كان لطفلى صعوبة في الزيادة في الوزن	☐	☐	☐	☐
34. كان أنف و صدر طفلك مليئين بالبلغم.....	☐	☐	☐	☐
35. كان طفلي يسعل خلال النهار.....	☐	☐	☐	☐
36. كان طفلي يضطر للسعال لإخراج البلغم.....	☐	☐	☐	☐ ↓ انتقل إلى السؤال رقم 38

37. كان بلغم طفلي على الأغلب : ☐ صافيا ☐ صافيا يميل إلى الصفرة ☐ أصفر-اخضر
☐ أخضر مع آثار دم ☐ لا أدري

خلال آخر أسبوعين:	دائماً	غالباً	أحياناً	أبداً لا
38. طفلى يصفر عند التنفس	☐	☐	☐	☐
39. لطفلي كانت مشكلة في التنفس.....	☐	☐	☐	☐
40. طفلي استيقظ من نومه في الليل لأنه كان يسعل.....	☐	☐	☐	☐
41. كان عند طفلي غازات.....	☐	☐	☐	☐
42. **كان عند طفلي** إسهال	☐	☐	☐	☐
43. شعر طفلي بوجع في البطن	☐	☐	☐	☐
44. واجه طفلي مشاكل في تناول الطعام	☐	☐	☐	☐

من فضلك تأكد من انك قد أجبت عن كل الأسئلة.

شكراً على تعاونك!

Appendix C: Health status, socio-economic and willingness to pay form

الحالة الصحية

أ. ما هي الادوية التي تتناولها وكيف تأخذها : _____

_____

_____

ب. ما هو نوع مرضك:

- ○ خفيف ($70 \leq FEV_1 < 89$)
- ○ متوسط ($40 \leq FEV_1 < 70$)
- ○ حاد ($FEV_1 < 40$)

ت. كم وزنك (كغم) وكم طولك (متر) ؟

_____

ث. هل حصلت على توعية بخصوص مرض التليف الكيسي؟

- ○ لا
- ○ نعم ؛ أين ؟ ..... متى ؟ .....

الوضع الاجتماعي والاقتصادي

أ. عدد افراد الاسرة (الاب/الام/الابناء): _____

ب. كم فرد يسكن في البيت: _____

ت. مكان السكن : □ مدينة □ قرية □ مخيم

□ محافظة القدس □ محافظة بيت لحم □ محافظة الخليل □ محافظة رام الله والبيرة
□ محافظة طوباس □ محافظة نابلس □ محافظة جنين □ محافظة أريحا
□ محافظة قلقيلية □ محافظة سلفيت □ محافظة طولكرم

ث. السكن : □ ملك □ ايجار

ج. كم تكلفة مواصلاتك للوصول الى مراكز العلاج؟ _____

ح. ما هو معدل الدخل الشهري للأسرة (بالشيكل) ؟

○ 1500 >

○ 3000 - 1500

○ 5000 - 3001

○ 5000 <

خ. هل تحصل على اية مساعدة / دعم خارجي (جمعيات، اقارب وغيرها):

○ لا

○ نعم ؛ من أين؟ _____

الوضع الاقتصادي بما يتعلق بصحة المريض

1. **كم شهر بالسنة تأخذ تبخيرات المضاد الحيوي:** _____
2. **كم مره تدخل المستشفى بالسنة:** _____
3. **كم هي المدة التي تتلقى فيها المضادات الحيوية عن طريق الوريد عند دخولك للمستشفى:** _____
4. **كم مره تتواصل فيها مع الطبيب لأسباب تتعلق بمرض التليف الكيسي سنوياً:** _____
5. **كم مرة بالسنة تقوم بالفحوصات التالية:**

أ. فحص البلغم: _____

ب. فحوصات الدم: _____

ت. فحوصات اشعة: _____

6. **ما هو معدل تغيبك عن الدراسة او العمل لأسباب تتعلق بمرض التليف الكيسي شهرياً:** _____
7. **هل تتلقى تطعيم الانفلونزا سنوياً :**

○ نعم

○ لا، لماذا؟ _____

8. **هل هنالك ادوية اضافية تتناولها :**

○ لا

○ نعم ؛ ما هي وكم تكلفتها ؟ _____

الرجاء اختيار المربع المناسب لإجابتك.

	دائماً	غالباً	احياناً	ابداً لا
	☐	☐	☐	☐

1. **هل تفكر في وضعك المادي؟.....**
2. **هل لديك الثقة بأن علاجك سوف يكون متوفراً في جميع الأوقات؟.....**
3. **هل انت مقتنع بحصولك على كامل احتياجاتك الصحية والعلاجية؟ .....**

4. **هل تؤثر طرق العلاج الحالية على حياتك الاجتماعية؟.....**

5. **هل لديك الموارد المالية الكافية لتلقي العلاج؟ .....**

6. **هل تشعر بأن طرق علاجك الحالية يجب ان تتغير؟.....**

الاستعداد لدفع مبلغ من المال مقابل الحصول على علاج جديد

اذا توفر لديك بعض الادوية التي تساعد على التقليل من اعراض المرض والتحسين من الحالة الصحية من خلال التخفيف من الاعراض والمفاقمات الرئوية التي تصيبك ، وتمنحك فرصة علاجية تقلل من الحاجة للعناية الصحية لكل ما يتعلق بالالتهابات الرئوية الحادة وما يرافقها من خلال الاستخدام اليومي والمتواصل للدواء دون الحاجة للعلاج عن طريق الوريد او دخول المستشفى .

هل عندك استعداد لدفع مبلغ اكبر من الذي تدفعه حاليا مقابل الحصول على تلك الادوية:

- **نعم**
- **لا**

اذا كانت الاجابة ب نعم:

ضع باعتبارك دخلك الشهري وميزانية الأسرة ، ما هو أكبر مبلغ من المال <u>بالشيكل</u> مستعد ان تدفعه شهرياً مقابل الحصول على تلك الادوية:

- 50
- 100
- 500
- 1000
- 1500
- 2000 أو أكثر

ما هي العوامل / الأمور التي تريد تحقيقها من خلال مساهمتك بالدفع:

	الصفة	نعم	لا
1	توفير أدوية جديدة تقلل من الأعراض وتحسن الحالة الصحية التي تحتاج الى المضادات الحيوية الوريدية		
2	تسهيل آلية العلاج من خلال توفير اجهزة حديثة للعلاج		
3	تقليل الوقت الذي تستغرقه أثناء تلقيك العلاج بالتبخيرة		
4	التقليل من تكاليف العلاج الشهرية من خلال تقليل عدد زيارات/دخول المستشفى		
5	تحسين القدرة على ممارسة الحياة اليومية بشكل طبيعي		
6	أمور اخرى، اكتبها:		

مما سبق ما هو أهم شيء يجعلك مستعدا لدفع المال مقابله بالنسبة لك: _____

اذا كانت الاجابة ب لا:

ما هي الأمور التي دفعتك للإجابة ب لا:

	الصفة	نعم	لا
1	الحالة المادية سيئة		
2	عدم الرغبة في التغيير		
3	أرى الوضع مناسب		
4	الاعتياد على استخدام الأدوية المتوفرة لدي		
5	عدم الرغبة في العلاج بشكل مطلق سواء بما هو متوفر من أدوية قديمة أو جديدة		
6	غير ذلك، اكتبه:		

Appendix D: Medical Research Agreement of Principles in Caritas baby hospital

P.O. Box : 6[illegible]
Phone +972 2 275 65 00, Fx +972 2 275 63 01
info@arb-mail.org, www.childrens-relief-bethlehem.org
Arab Bank, Bethlehem, Acct. 702200

Medical Research Agreement of Principles HEC_FO_003

Date: 17/12/2016

This is to certify that Caritas Baby Hospital represented by: Dr. Nisreen Rumman will be collaborating with Al-Quds University represented by: Dr. Hussein hallak to conduct a Medical Research Project entitled: Assessing the need of new therapeutic options for Cystic fibrosis patients in Palestine. The research project will be conducted by: Samya Salah.

The above research project was reviewed by members of Caritas Medical Research Committee and was approved on 22/12/16 and given MRC-Project Number MRC-21.

After the fruitful accomplishment of the project both parties agree to publish the work in a peer reviewed journal and the authorship location in the manuscript will be as follows:

First author: Samya Salah
Second author: Nisreen Rumman
Third author: Amal Nassar
Fourth author: Mohammed Zwahra
Before last author: Hussein hallak
Last author: Maher Khdour.

Principal Investigator
Hallak

Caritas Baby Hospital
MRC Representative
22/12/16

Collaborating Institution
Hussein Hallak PHD
Faculty of Medicine
Al-Quds University
Associate Professor

Appendix E: Data for results

- Domain scored for each item of adult 14 years of age and more version

Descriptive Statistics					
	N	Minimum	Maximum	Mean	Std. Deviation
Section II. Quality of Life q1	22	1.00	4.00	37.878788	.83355
Section II. Quality of Life q2	22	1.00	4.00	37.878788	.88884
Section II. Quality of Life q3	22	1.00	4.00	28.787879	1.03719
Section II. Quality of Life q4	22	1.00	4.00	31.818182	.95005
Section II. Quality of Life q5	22	1.00	3.00	22.727273	.77989
Section II. Quality of Life q13	22	1.00	4.00	62.121212	.88884
Section II. Quality of Life q19	22	1.00	4.00	25.757576	.75162
Section II. Quality of Life q20	22	1.00	4.00	25.757576	.92231
Physical	22	.00	91.67	31.0614	24.42242
Section III. School, Work, or Daily Activities q 35	22	1.00	4.00	43.939394	.94548
Section III. School, Work, or Daily Activities q 36	22	1.00	3.00	36.363636	.68376
Section III. School, Work, or Daily Activities q 37	22	1.00	4.00	34.848485	.72225

Section III. School, Work, or Daily Activities q 38	22	1.00	4.00	33.333333	.69007
Role	22	.00	91.67	40.1527	21.76737
Section II. Quality of Life q6	22	1.00	4.00	71.212121	.83355
Section II. Quality of Life q9	22	1.00	3.00	30.30303	.81118
Section II. Quality of Life q10	22	1.00	4.00	13.636364	.79637
Section II. Quality of Life q11	22	1.00	4.00	40.909091	.92231
Vitality	22	.00	91.67		22.95386
Section II. Quality of Life q7	22	1.00	4.00	43.939394	.94548
Section II. Quality of Life q8	22	1.00	4.00	56.060606	1.17053
Section II. Quality of Life q12	22	1.00	4.00	53.030303	1.00755
Section II. Quality of Life q31	22	1.00	4.00	53.030303	.73414
Section II. Quality of Life q33	22	1.00	4.00	30.30303	1.01929
Emotion	22	6.67	100.00		24.85114
Section II. Quality of Life q22	22	1.00	4.00	43.939394	.94548
Section II. Quality of Life q23	22	1.00	3.00	40.909091	.75162
Section II. Quality of Life q27	22	1.00	4.00	57.575758	.98473
Section II. Quality of Life q28	22	1.00	4.00	53.030303	.73414
Section II. Quality of Life q29	22	1.00	3.00	31.818182	.57547
Section II. Quality of Life q30	22	1.00	4.00	40.909091	.81251
Social	22	11.11	66.67		12.70508

Section II. Quality of Life q24	22	1.00	4.00	18.181818	.85786
Section II. Quality of Life q25	22	1.00	44.00	83.333333	9.08557
Section II. Quality of Life q26	22	1.00	4.00	31.818182	.95005
Body	22	.00	88.89	22.7268	27.32017
Section II. Quality of Life q14	22	1.00	4.00	40.909091	.68534
Section II. Quality of Life q21	22	1.00	4.00	51.515152	.85786
Section IV. Symptom Difficulties q 50	22	1.00	4.00	56.060606	.77989
Eat	22	11.11	100.00		22.48673
Section II. Quality of Life q15	22	1.00	4.00	78.787879	.72673
Section II. Quality of Life q16	22	1.00	4.00	78.787879	.78954
Section II. Quality of Life q17	22	3.00	4.00	81.818182	.50965
Treatment	22	.00	66.67	20.2005	17.69651
Section II. Quality of Life q18	22	1.00	4.00	66.666667	.69007
Section II. Quality of Life q32	22	1.00	4.00	25.757576	.97257
Section II. Quality of Life q34	22	1.00	4.00	21.212121	.78954
Health	22	.00	100.00	26.7664	23.67253
Section IV. Symptom Difficulties q 40	22	1.00	3.00	25.757576	.86914
Section IV. Symptom Difficulties q 41	22	1.00	4.00	21.212121	.84771
Section IV. Symptom Difficulties q 42	22	1.00	3.00	19.69697	.73414

Section IV. Symptom Difficulties q 43	22	1.00	4.00	65.151515	.72225
Section IV. Symptom Difficulties q 44	22	1.00	4.00	37.878788	.83355
Section IV. Symptom Difficulties q 45	22	1.00	4.00	33.333333	.87287
Section IV. Symptom Difficulties q 46	22	1.00	3.00	31.818182	.84387
Respiratory	22	.00	77.78		22.73846
Section IV. Symptom Difficulties q 47	22	1.00	4.00	36.363636	1.01929
Section IV. Symptom Difficulties q 48	22	1.00	4.00	46.969697	1.05375
Section IV. Symptom Difficulties q 49	22	1.00	4.00	36.363636	1.01929
Digest	22	.00	100.00	39.8986	28.20616

- Quality of life domain scores for adult (14+) correlated with their marital status (single or married).

Ranks

Marital status of adult		N	Mean Rank	Sum of Ranks
Physical	single	20	12.35	247.00
	married	2	3.00	6.00
	Total	22		
Vitality	single	20	11.73	234.50
	married	2	9.25	18.50
	Total	22		
Emotion	single	20	12.08	241.50
	married	2	5.75	11.50
	Total	22		
Eat	single	20	12.25	245.00
	married	2	4.00	8.00
	Total	22		
Treatment	single	20	11.85	237.00

	married	2	8.00	16.00
	Total	22		
Health	single	20	12.25	245.00
	married	2	4.00	8.00
	Total	22		
Social	single	20	12.03	240.50
	married	2	6.25	12.50
	Total	22		
Body	single	20	11.88	237.50
	married	2	7.75	15.50
	Total	22		
Role	single	20	11.48	229.50
	married	2	11.75	23.50
	Total	22		
Weight	single	20	12.05	241.00
	married	2	6.00	12.00
	Total	22		
Respiratory	single	20	12.03	240.50
	married	2	6.25	12.50
	Total	22		
Digest	single	20	12.05	241.00
	married	2	6.00	12.00
	Total	22		

- Quality of life domain scores for adult (14+) correlated with level of education.

Ranks			
	Education level of adult	N	Mean Rank
Physical	Some high school or less	15	10.50
	High school diploma/GED	2	12.00
	College degree	4	16.88
	Professional or graduate degree	1	4.00
	Total	22	
Vitality	Some high school or less	15	10.30
	High school diploma/GED	2	12.50
	College degree	4	14.50
	Professional or graduate degree	1	15.50

	Total	22	
Emotion	Some high school or less	15	11.13
	High school diploma/GED	2	11.75
	College degree	4	13.13
	Professional or graduate degree	1	10.00
	Total	22	
Eat	Some high school or less	15	11.33
	High school diploma/GED	2	11.50
	College degree	4	13.38
	Professional or graduate degree	1	6.50
	Total	22	
Treatment	Some high school or less	15	10.33
	High school diploma/GED	2	12.75
	College degree	4	15.00
	Professional or graduate degree	1	12.50
	Total	22	
Health	Some high school or less	15	10.57
	High school diploma/GED	2	12.00
	College degree	4	16.13
	Professional or graduate degree	1	6.00
	Total	22	
Social	Some high school or less	15	11.53
	High school diploma/GED	2	7.75
	College degree	4	15.50
	Professional or graduate degree	1	2.50
	Total	22	
Body	Some high school or less	15	11.33
	High school diploma/GED	2	12.75
	College degree	4	11.63
	Professional or graduate degree	1	11.00
	Total	22	
Role	Some high school or less	15	10.57
	High school diploma/GED	2	12.50
	College degree	4	12.25

	Professional or graduate degree	1	20.50
	Total	22	
Weight	Some high school or less	15	11.83
	High school diploma/GED	2	10.75
	College degree	4	12.00
	Professional or graduate degree	1	6.00
	Total	22	
Respiratory	Some high school or less	15	10.73
	High school diploma/GED	2	15.25
	College degree	4	14.38
	Professional or graduate degree	1	4.00
	Total	22	
Digest	Some high school or less	15	11.23
	High school diploma/GED	2	11.75
	College degree	4	12.88
	Professional or graduate degree	1	9.50
	Total	22	

- Quality of life domain scores for adult (14+) correlated with work status.

Ranks			
	Work status of adult	N	Mean Rank
Physical	Attending school outside the home	12	12.17
	Taking educational courses at home	1	22.00
	Seeking work	1	2.00
	Working full or part time (either outside the home or at a home-based business)	5	14.30
	Not attending school or working due to my health	3	3.83
	Total	22	
Vitality	Attending school outside the home	12	11.50

	Taking educational courses at home	1	22.00
	Seeking work	1	3.00
	Working full or part time (either outside the home or at a home-based business)	5	14.70
	Not attending school or working due to my health	3	5.50
	Total	22	
Emotion	Attending school outside the home	12	12.33
	Taking educational courses at home	1	22.00
	Seeking work	1	1.50
	Working full or part time (either outside the home or at a home-based business)	5	12.50
	Not attending school or working due to my health	3	6.33
	Total	22	
Eat	Attending school outside the home	12	12.88
	Taking educational courses at home	1	21.50
	Seeking work	1	1.50
	Working full or part time (either outside the home or at a home-based business)	5	12.00
	Not attending school or working due to my health	3	5.17
	Total	22	
Treatment	Attending school outside the home	12	10.88
	Taking educational courses at home	1	22.00
	Seeking work	1	3.50
	Working full or part time (either outside the home or at a home-based business)	5	14.50
	Not attending school or working due to my health	3	8.17

	Total	22	
Health	Attending school outside the home	12	10.96
	Taking educational courses at home	1	22.00
	Seeking work	1	2.00
	Working full or part time (either outside the home or at a home-based business)	5	14.10
	Not attending school or working due to my health	3	9.00
	Total	22	
Social	Attending school outside the home	12	12.04
	Taking educational courses at home	1	5.50
	Seeking work	1	10.00
	Working full or part time (either outside the home or at a home-based business)	5	12.90
	Not attending school or working due to my health	3	9.50
	Total	22	
Body	Attending school outside the home	12	12.50
	Taking educational courses at home	1	21.00
	Seeking work	1	4.50
	Working full or part time (either outside the home or at a home-based business)	5	11.50
	Not attending school or working due to my health	3	6.67
	Total	22	
Role	Attending school outside the home	12	12.63
	Taking educational courses at home	1	22.00
	Seeking work	1	3.00

	Working full or part time (either outside the home or at a home-based business)	5	13.90
	Not attending school or working due to my health	3	2.33
	Total	22	
Weight	Attending school outside the home	12	12.50
	Taking educational courses at home	1	15.50
	Seeking work	1	6.00
	Working full or part time (either outside the home or at a home-based business)	5	10.80
	Not attending school or working due to my health	3	9.17
	Total	22	
Respiratory	Attending school outside the home	12	11.83
	Taking educational courses at home	1	22.00
	Seeking work	1	8.50
	Working full or part time (either outside the home or at a home-based business)	5	12.30
	Not attending school or working due to my health	3	6.33
	Total	22	
Digest	Attending school outside the home	12	12.83
	Taking educational courses at home	1	21.00
	Seeking work	1	2.50
	Working full or part time (either outside the home or at a home-based business)	5	12.20
	Not attending school or working due to my health	3	4.83
	Total	22	

- Domain scores for each item of Child (6-13) years of age version

Descriptive Statistics

	N	Minimum	Maximum	Mean	Std. Deviation
Q.1	33	1.00	3.00	34.3434	.58549
Q.2	33	1.00	3.00	25.2525	.75126
Q.3	33	1.00	3.00	24.2424	.67420
Q.4	33	1.00	3.00	24.2424	.62614
Q.5	33	1.00	3.00	19.1919	.61392
Q.6	33	1.00	4.00	31.3131	.86384
Q.7	33	1.00	4.00	33.3333	.79057
Q.8	33	1.00	4.00	46.4646	.82687
Q.9	33	1.00	3.00	38.3838	.71244
Q.10	33	1.00	4.00	52.5253	.79177
Q.11	33	2.00	4.00	69.6970	.63066
Q.12	33	2.00	4.00	65.6566	.30464
Q.13	33	2.00	4.00	64.6465	.34816
Q.14	33	1.00	3.00	15.1515	.71111
Q.15	33	1.00	4.00	54.5455	.89506
Q.16	33	1.00	3.00	30.3030	.52223
Q.17	33	1.00	4.00	51.5152	.90453
Q.18	33	1.00	3.00	13.1313	.55562
Q.19	33	1.00	4.00	32.3232	.84723
Q.20	33	1.00	3.00	28.2828	.61853
Q.21	33	2.00	4.00	51.5152	.71111
Q.22	33	1.00	2.00	10.1010	.46669
Q.23	33	2.00	4.00	91.9192	.50189
Q.24	33	1.00	3.00	35.3535	.49620
Q.25	33	2.00	4.00	74.7475	.61392
Q.26	33	1.00	3.00	26.2626	.59987
Q.27	33	1.00	3.00	16.1616	.61853
Q.28	33	1.00	3.00	13.1313	.60927
Q.29	33	1.00	3.00	14.1414	.56071
Q.30	33	1.00	3.00	9.0909	.57406
Q.31	33	1.00	3.00	19.1919	.75126
Q.32	33	1.00	3.00	36.3636	.80482
Q.33	33	1.00	3.00	16.1616	.71244
Q.34	33	1.00	3.00	38.3838	.83371
Q.35	33	1.00	3.00	23.2323	.80951
Valid N (list wise)	33				

- Correlation between child (6-13) years domain scores and their gender

Ranks				
	Gender of patients	N	Mean Rank	Sum of Ranks
physical	male	12	17.88	214.50
	female	21	16.50	346.50
	Total	33		
Emotion	male	12	18.17	218.00
	female	21	16.33	343.00
	Total	33		
Social	male	12	19.42	233.00
	female	21	15.62	328.00
	Total	33		
Eat	male	12	21.79	261.50
	female	21	14.26	299.50
	Total	33		
Treatment	male	12	18.67	224.00
	female	21	16.05	337.00
	Total	33		
Body	male	12	20.83	250.00
	female	21	14.81	311.00
	Total	33		
Respiratory	male	12	19.21	230.50
	female	21	15.74	330.50
	Total	33		
Digest	male	12	16.17	194.00
	female	21	17.48	367.00
	Total	33		

- Correlation between child (6-13) years of age domain scores and taking vacation without disease.

Ranks				
	Vacation from school	N	Mean Rank	Sum of Ranks
Physical	yes	8	21.88	175.00
	no	25	15.44	386.00

	Total	33		
Emotion	yes	8	17.38	139.00
	no	25	16.88	422.00
	Total	33		
Social	yes	8	19.25	154.00
	no	25	16.28	407.00
	Total	33		
Eat	yes	8	22.81	182.50
	no	25	15.14	378.50
	Total	33		
Treatment	yes	8	18.69	149.50
	no	25	16.46	411.50
	Total	33		
Body	yes	8	18.13	145.00
	no	25	16.64	416.00
	Total	33		
Respiratory	yes	8	18.25	146.00
	no	25	16.60	415.00
	Total	33		
Digest	yes	8	16.50	132.00
	no	25	17.16	429.00
	Total	33		

- Correlation between child (6-13) years of age domain scores and level of education.

Ranks			
	Education level	N	Mean Rank
Physical	Kindergarten	3	15.33
	1st grade	6	23.33
	2nd grade	1	1.50
	3rd grade	6	13.17
	4th grade	3	6.67
	5th grade	7	20.57
	6th grade	4	15.50
	7th grade	3	22.83
	Total	33	

Emotion	Kindergarten	3	22.83
	1st grade	6	20.42
	2nd grade	1	2.50
	3rd grade	6	12.92
	4th grade	3	15.33
	5th grade	7	14.43
	6th grade	4	16.50
	7th grade	3	25.67
	Total	33	
Social	Kindergarten	3	12.33
	1st grade	6	15.33
	2nd grade	1	1.50
	3rd grade	6	14.58
	4th grade	3	5.83
	5th grade	7	19.57
	6th grade	4	23.50
	7th grade	3	31.50
	Total	33	
Eat	Kindergarten	3	11.50
	1st grade	6	16.58
	2nd grade	1	19.50
	3rd grade	6	15.92
	4th grade	3	5.67
	5th grade	7	24.14
	6th grade	4	15.50
	7th grade	3	21.33
	Total	33	
Treatment	Kindergarten	3	21.67
	1st grade	6	15.92
	2nd grade	1	3.00
	3rd grade	6	18.25
	4th grade	3	6.17
	5th grade	7	22.07
	6th grade	4	12.50
	7th grade	3	21.67
	Total	33	
Body	Kindergarten	3	20.83
	1st grade	6	18.92
	2nd grade	1	9.00
	3rd grade	6	16.67

	4th grade	3	19.50
	5th grade	7	18.07
	6th grade	4	9.00
	7th grade	3	18.33
	Total	33	
Respiratory	Kindergarten	3	10.50
	1st grade	6	14.67
	2nd grade	1	2.50
	3rd grade	6	15.17
	4th grade	3	23.33
	5th grade	7	24.07
	6th grade	4	12.88
	7th grade	3	19.33
	Total	33	
Digest	Kindergarten	3	23.00
	1st grade	6	14.67
	2nd grade	1	22.00
	3rd grade	6	15.50
	4th grade	3	9.00
	5th grade	7	18.71
	6th grade	4	14.25
	7th grade	3	24.67
	Total	33	

- Domain score for each item of parent (6-13) version

Descriptive Statistics

	N	Minimum	Maximum	Mean	Std. Deviation
Section II. Quality of Life q1	33	1	4	32.32	.883
Section II. Quality of Life q2	33	1.00	4.00	31.3131	.65857
Section II. Quality of Life q3	33	1.00	4.00	30.3030	.76500
Section II. Quality of Life q4	33	1.00	4.00	28.2828	.83371

Section II. Quality of Life q5	33	1.00	4.00	27.2727	.76871
Section II.Quality of Life q6	33	1.00	4.00	35.3535	.99810
Section II.Quality of Life q7	33	1.00	4.00	46.4646	.82687
Section II.Quality of Life q8	33	1.00	3.00	31.3131	.78817
Section II. Quality of Life q9	33	1.00	4.00	33.3333	1.06066
Section II.Quality of Life q10	33	1.00	4.00	35.3535	.89928
Section II.Quality of Life q11	33	1.00	4.00	34.3434	.84723
Section II.Quality of Life q12	33	1.00	4.00	35.3535	.74747
Section II. Quality of Life q13	33	1.00	4.00	48.4848	.75378
Section II. Quality of Life q14	33	1.00	4.00	57.5758	.87581
Section II. Quality of Life q15	33	2.00	4.00	61.6162	.66714
Section II. Quality of Life q16	33	1.00	3.00	32.3232	.68396
Section II.Quality of Life q17	33	1.00	4.00	48.4848	.93845
Section II. Quality of Life q18	33	1.00	3.00	31.3131	.70442
Section II.Quality of Life q19	33	1.00	4.00	18.1818	.75378
Section II. Quality of Life q20	33	1.00	3.00	15.1515	.56408
Section II.Quality of Life q21	33	1.00	3.00	11.1111	.59512
Section II.Quality of Life q22	33	1.00	4.00	31.3131	.82687
Section II. Quality of Life q23	33	1.00	4.00	52.5253	1.00095

Section II.Quality of Life q24	33	1.00	4.00	39.3939	1.04447
Section II.Quality of Life q25	33	1.00	4.00	44.4444	.88976
Section II.Quality of Life q26	33	1.00	4.00	50.5051	.90558
Section II.Quality of Life q27	33	1.00	4.00	49.4949	.83371
Section II. Quality of Life q28	33	1.00	4.00	45.4545	.89506
Section II. Quality of Life q29	33	1.00	4.00	40.4040	.85723
Section II.Quality of Life q30	33	1.00	3.00	19.1919	.61392
Section II.Quality of Life q31	33	2.00	4.00	73.7374	.69631
Section II.Quality of Life q32	33	2.00	4.00	67.6768	.58549
Section III. Symptom Difficulties q33	33	1.00	4.00	15.1515	.71111
Section III. Symptom Difficulties q34	33	1.00	3.00	14.1414	.56071
Section III. Symptom Difficulties q35	33	1.00	3.00	20.2020	.74747
Section III. Symptom Difficulties q36	33	1.00	3.00	12.1212	.65279
Section III. Symptom Difficulties q37	33	2.00	5.00	61.6162	.71244
Section III. Symptom Difficulties q38	33	1.00	4.00	41.4141	.96922
Section III. Symptom Difficulties q39	33	1.00	4.00	39.3939	.88227

Section III. Symptom Difficulties q40	33	1.00	3.00	33.3333	.82916
Section III. Symptom Difficulties q41	33	1.00	3.00	31.3131	.82687
Section III. Symptom Difficulties q42	33	1.00	4.00	36.3636	.91391
Section III. Symptom Difficulties q43	33	1.00	3.00	24.2424	.80128
Section III. Symptom Difficulties q44	33	1.00	4.00	53.5354	.93339

- Correlation between quality of life domain score and monthly income.

Ranks

Section V. Socio-economic status q9		N	Mean Rank
Physical	1500>	20	44.10
	1500-3000	50	35.00
	3001-5000	6	49.00
	Total	76	
Emotion	1500>	20	43.60
	1500-3000	51	36.03
	3001-5000	6	48.92
	Total	77	
Vitality	1500>	9	23.72
	1500-3000	32	21.69
	3001-5000	3	27.50
	Total	44	
School	1500>	3	4.33
	1500-3000	5	5.00
	3001-5000	1	7.00
	Total	9	
Eat	1500>	20	40.95
	1500-3000	51	37.54
	3001-5000	6	44.92
	Total	77	

Body	1500>	20	43.43
	1500-3000	51	37.04
	3001-5000	6	40.92
	Total	77	
Treatment	1500>	20	48.35
	1500-3000	51	34.75
	3001-5000	6	43.92
	Total	77	
Health	1500>	9	24.61
	1500-3000	32	20.88
	3001-5000	3	33.50
	Total	44	
Respiratory	1500>	20	41.33
	1500-3000	51	38.25
	3001-5000	6	37.67
	Total	77	
Digest	1500>	20	36.55
	1500-3000	51	38.98
	3001-5000	6	47.33
	Total	77	
Weight	1500>	9	27.28
	1500-3000	32	21.05
	3001-5000	3	23.67
	Total	44	

- Correlation between quality of life domain scores and relationship with patients (father, mother, grandfather and brother).

Ranks

	Relationship	N	Mean Rank
Physical	mother	28	16.05
	father	3	24.00
	Grandfather	1	6.50
	Total	32	
Emotion	mother	28	17.70
	father	3	9.83
	Grandfather	1	3.00
	Total	32	
Vitality	mother	28	17.09
	father	3	15.17

	Grandfather	1	4.00
	Total	32	
School	mother	28	16.64
	father	3	13.50
	Grandfather	1	21.50
	Total	32	
Eat	mother	28	17.70
	father	3	9.00
	Grandfather	1	5.50
	Total	32	
Body	mother	28	17.05
	father	3	14.17
	Grandfather	1	8.00
	Total	32	
Treatment	mother	28	17.18
	father	3	15.17
	Grandfather	1	1.50
	Total	32	
Health	mother	28	16.71
	father	3	17.33
	Grandfather	1	8.00
	Total	32	
Respiratory	mother	28	17.02
	father	3	16.50
	Grandfather	1	2.00
	Total	32	
Digest	mother	28	15.63
	father	3	26.00
	Grandfather	1	12.50
	Total	32	
Weight	mother	28	16.75
	father	3	16.00
	Grandfather	1	11.00
	Total	32	

- Correlation between quality of life domain scores and level of education for parent.

Ranks

	School grade completed for parents	N	Mean Rank
Physical	Some high school or less	17	15.74
	High school diploma/GED	9	15.78
	Some college	3	15.17
	College degree	4	26.50
	Total	33	
Emotion	Some high school or less	17	15.24
	High school diploma/GED	9	13.56
	Some college	3	18.00
	College degree	4	31.50
	Total	33	
Vitality	Some high school or less	17	13.35
	High school diploma/GED	9	15.72
	Some college	3	22.67
	College degree	4	31.13
	Total	33	
School	Some high school or less	17	15.24
	High school diploma/GED	9	18.61
	Some college	3	10.00
	College degree	4	26.13
	Total	33	
Eat	Some high school or less	17	16.09
	High school diploma/GED	9	15.67
	Some college	3	9.00
	College degree	4	29.88
	Total	33	
Body	Some high school or less	17	15.24
	High school diploma/GED	9	16.61
	Some college	3	22.50
	College degree	4	21.25
	Total	33	
Treatment	Some high school or less	17	17.65
	High school diploma/GED	9	12.11
	Some college	3	16.00
	College degree	4	26.00

	Total	33	
Health	Some high school or less	17	16.00
	High school diploma/GED	9	17.00
	Some college	3	11.33
	College degree	4	25.50
	Total	33	
Respiratory	Some high school or less	17	14.21
	High school diploma/GED	9	18.28
	Some college	3	15.50
	College degree	4	27.13
	Total	33	
Digest	Some high school or less	17	19.26
	High school diploma/GED	9	10.22
	Some college	3	20.83
	College degree	4	19.75
	Total	33	
Weight	Some high school or less	17	18.09
	High school diploma/GED	9	16.17
	Some college	3	21.33
	College degree	4	11.00
	Total	33	

- Correlation between quality of life domain scores and work status of parent.

Ranks			
	Work status for parents	N	Mean Rank
Physical	Seeking Work	1	17.00
	Working full or part time	9	21.11
	Full time homemaker	22	14.93
	Not working due to my health	1	25.50
	Total	33	
Emotion	Seeking Work	1	21.50
	Working full or part time	9	21.83
	Full time homemaker	22	15.25
	Not working due to my health	1	7.50
	Total	33	
Vitality	Seeking Work	1	14.50
	Working full or part time	9	22.28

	Full time homemaker	22	15.55
	Not working due to my health	1	4.00
	Total	33	
School	Seeking Work	1	28.00
	Working full or part time	9	23.72
	Full time homemaker	22	14.41
	Not working due to my health	1	2.50
	Total	33	
Eat	Seeking Work	1	23.50
	Working full or part time	9	21.89
	Full time homemaker	22	15.39
	Not working due to my health	1	2.00
	Total	33	
Body	Seeking Work	1	22.50
	Working full or part time	9	18.67
	Full time homemaker	22	16.48
	Not working due to my health	1	8.00
	Total	33	
Treatment	Seeking Work	1	7.00
	Working full or part time	9	19.33
	Full time homemaker	22	16.34
	Not working due to my health	1	20.50
	Total	33	
Health	Seeking Work	1	15.50
	Working full or part time	9	20.94
	Full time homemaker	22	15.86
	Not working due to my health	1	8.00
	Total	33	
Respiratory	Seeking Work	1	33.00
	Working full or part time	9	19.33
	Full time homemaker	22	14.82
	Not working due to my health	1	28.00
	Total	33	

Digest	Seeking Work	1	18.00
	Working full or part time	9	20.33
	Full time homemaker	22	14.95
	Not working due to my health	1	31.00
	Total	33	
Weight	Seeking Work	1	26.50
	Working full or part time	9	14.44
	Full time homemaker	22	17.89
	Not working due to my health	1	11.00
	Total	33	

- Correlation between quality of life domain scores and marital status of parent (married or divorced).

Ranks

Marital status for parents		N	Mean Rank	Sum of Ranks
Physical	married	31	17.21	533.50
	Divorced	2	13.75	27.50
	Total	33		
Emotion	married	31	16.77	520.00
	Divorced	2	20.50	41.00
	Total	33		
Eat	married	31	17.23	534.00
	Divorced	2	13.50	27.00
	Total	33		
Body	married	31	16.94	525.00
	Divorced	2	18.00	36.00
	Total	33		
Treatment	married	31	17.29	536.00
	Divorced	2	12.50	25.00
	Total	33		
Respiratory	married	31	16.81	521.00
	Divorced	2	20.00	40.00
	Total	33		
Digest	married	31	17.52	543.00
	Divorced	2	9.00	18.00
	Total	33		

Social	married	31	17.63	546.50
	Divorced	2	7.25	14.50
	Total	33		

- Domain score for each item of children under 6 years of age version.

Descriptive Statistics

	N	Minimum	Maximum	Mean	Std. Deviation
Section II. Quality of Life q1	21	1	4	46.03	.921
Section II. Quality of Life q2	21	1.00	4.00	47.6190	.92582
Section II. Quality of Life q3	20	1.00	4.00	46.6667	1.04630
Section II. Quality of Life q4	20	1.00	4.00	38.3333	1.03999
Section II. Quality of Life q5	20	1.00	4.00	36.6667	1.07115
Section II.Quality of Life q6	22	1.00	4.00	39.3939	.95799
Section II.Quality of Life q7	22	1.00	4.00	51.5152	.67098
Section II.Quality of Life q8	22	1.00	4.00	45.4545	.72673
Section II. Quality of Life q9	22	1.00	3.00	22.7273	.71623
Section II.Quality of Life q10	22	1.00	4.00	34.8485	.84387
Section II.Quality of Life q11	22	1.00	3.00	39.3939	.73266
Section II.Quality of Life q12	22	1.00	4.00	42.4242	.98473
Section II. Quality of Life q13	9	2.00	4.00	59.2593	.66667
Section II. Quality of Life q14	22	1.00	4.00	90.9091	.70250

Section II. Quality of Life q15	22	2.00	3.00	48.4848	.50965
Section II. Quality of Life q16	22	1.00	4.00	45.4545	.72673
Section II.Quality of Life q17	22	1.00	4.00	45.4545	.84771
Section II. Quality of Life q18	22	1.00	4.00	31.8182	.95005
Section II.Quality of Life q19	22	1.00	4.00	30.3030	.97145
Section II. Quality of Life q20	22	1.00	4.00	33.3333	1.06904
Section II.Quality of Life q21	22	1.00	4.00	34.8485	1.09010
Section II.Quality of Life q22	22	1.00	4.00	27.2727	.90692
Section II. Quality of Life q23	22	1.00	4.00	62.1212	.83355
Section II.Quality of Life q24	22	1.00	3.00	34.8485	.72225
Section II.Quality of Life q25	22	2.00	3.00	54.5455	.49237
Section II.Quality of Life q26	22	1.00	3.00	42.4242	.82703
Section II.Quality of Life q27	22	1.00	4.00	56.0606	.64633
Section II. Quality of Life q28	5	2.00	4.00	53.3333	.89443
Section II. Quality of Life q29	5	2.00	4.00	53.3333	.89443
Section II.Quality of Life q30	22	1.00	2.00	15.1515	.50965
Section II.Quality of Life q31	22	2.00	4.00	68.1818	.65300
Section II.Quality of Life q32	22	2.00	4.00	62.1212	.46756

Section III. Symptom Difficulties q33	22	1.00	3.00	25.7576	.86914
Section III. Symptom Difficulties q34	22	1.00	4.00	28.7879	.77432
Section III. Symptom Difficulties q35	22	1.00	4.00	30.3030	.75018
Section III. Symptom Difficulties q36	22	1.00	4.00	30.3030	.81118
Section III. Symptom Difficulties q37	22	2.00	3.00	50.0000	.51177
Section III. Symptom Difficulties q38	22	1.00	4.00	56.0606	.83873
Section III. Symptom Difficulties q39	22	1.00	4.00	46.9697	.79637
Section III. Symptom Difficulties q40	22	1.00	4.00	53.0303	.66613
Section III. Symptom Difficulties q41	22	1.00	4.00	34.8485	1.17422
Section III. Symptom Difficulties q42	22	1.00	4.00	45.4545	.95346
Section III. Symptom Difficulties q43	22	1.00	4.00	37.8788	.94089
Section III. Symptom Difficulties q44	22	1.00	4.00	40.9091	1.02036

- Correlation between child (6-13) quality of life domain score and health status FEV_1 level.

Ranks			
Child (6-13) years of age			
	Health Profile FEV_1	N	Mean

				Rank
Physical		mild(89>FEV>=70)	8	16.56
		moderate(70>FEV>=40)	5	18.70
		Not available	20	16.75
		Total	33	
Emotion		mild(89>FEV>=70)	8	16.50
		moderate(70>FEV>=40)	5	18.20
		Not available	20	16.90
		Total	33	
Eat		mild(89>FEV>=70)	8	20.44
		moderate(70>FEV>=40)	5	14.90
		Not available	20	16.15
		Total	33	
Body		mild(89>FEV>=70)	8	18.75
		moderate(70>FEV>=40)	5	14.60
		Not available	20	16.90
		Total	33	
Treatment		mild(89>FEV>=70)	8	21.63
		moderate(70>FEV>=40)	5	21.30
		Not available	20	14.08
		Total	33	
Respiratory		mild(89>FEV>=70)	8	17.19
		moderate(70>FEV>=40)	5	11.80
		Not available	20	18.23
		Total	33	
Digest		mild(89>FEV>=70)	8	18.13
		moderate(70>FEV>=40)	5	14.20
		Not available	20	17.25
		Total	33	
Social		mild(89>FEV>=70)	8	17.25
		moderate(70>FEV>=40)	5	21.50
		Not available	20	15.78
		Total	33	

- Correlation between adult (14+) quality of life domain scores and health status FEV_1 level.

Ranks

	Health Profile FEV_1 for adult (14+)	N	Mean Rank
Physical	mild(89>FEV>=70)	2	16.75
	moderate(70>FEV>=40)	9	12.11
	sever	2	4.75
	Not available	9	11.22
	Total	22	
Vitality	mild(89>FEV>=70)	2	15.00
	moderate(70>FEV>=40)	9	12.44
	sever	2	6.75
	Not available	9	10.83
	Total	22	
Emotion	mild(89>FEV>=70)	2	13.75
	moderate(70>FEV>=40)	9	11.39
	sever	2	8.50
	Not available	9	11.78
	Total	22	
Eat	mild(89>FEV>=70)	2	10.00
	moderate(70>FEV>=40)	9	11.06
	sever	2	10.25
	Not available	9	12.56
	Total	22	
Treatment	mild(89>FEV>=70)	2	15.00
	moderate(70>FEV>=40)	9	12.61
	sever	2	10.50
	Not available	9	9.83
Health	mild(89>FEV>=70)	2	18.75
	moderate(70>FEV>=40)	9	12.06
	sever	2	8.75
	Not available	9	9.94
	Total	22	
Social	mild(89>FEV>=70)	2	7.00
	moderate(70>FEV>=40)	9	10.72
	sever	2	10.00
	Not available	9	13.61
	Total	22	
Body	mild(89>FEV>=70)	2	16.50
	moderate(70>FEV>=40)	9	10.22
	sever	2	9.25

	Not available	9	12.17
	Total	22	
Role	mild(89>FEV>=70)	2	17.75
	moderate(70>FEV>=40)	9	13.33
	sever	2	6.75
	Not available	9	9.33
	Total	22	
Weight	mild(89>FEV>=70)	2	10.75
	moderate(70>FEV>=40)	9	12.39
	sever	2	6.00
	Not available	9	12.00
	Total	22	
Respiratory	mild(89>FEV>=70)	2	11.50
	moderate(70>FEV>=40)	9	11.61
	sever	2	8.25
	Not available	9	12.11
	Total	22	
Digest	mild(89>FEV>=70)	2	19.00
	moderate(70>FEV>=40)	9	10.22
	sever	2	10.75
	Not available	9	11.28
	Total	22	

- Correlation between quality of life domain scores and geographic distribution of patients.

Ranks			
	District	N	Mean Rank
Physical	Jerusalem	1	26.00
	Bethlehem	6	34.50
	Hebron	49	38.72
	Ramallah	5	48.10
	Nablus	7	31.79
	Jenin	6	32.42
	Qalqilia	1	65.00
	Tulkarm	1	73.00
	Total	76	
Emotion	Jerusalem	1	13.50
	Bethlehem	6	43.50

	Hebron	50	39.12
	Ramallah	5	48.10
	Nablus	7	31.21
	Jenin	6	28.67
	Qalqilia	1	75.00
	Tulkarm	1	66.50
	Total	77	
Vitality	Bethlehem	4	22.38
	Hebron	26	22.65
	Ramallah	4	26.75
	Nablus	4	17.13
	Jenin	4	17.50
	Qalqilia	1	31.50
	Tulkarm	1	34.50
	Total	44	
School	Hebron	5	6.00
	Ramallah	2	2.25
	Nablus	1	3.50
	Jenin	1	7.00
	Total	9	
Eat	Jerusalem	1	38.50
	Bethlehem	6	33.33
	Hebron	50	40.88
	Ramallah	5	41.50
	Nablus	7	27.79
	Jenin	6	38.08
	Qalqilia	1	45.00
	Tulkarm	1	45.00
	Total	77	
Body	Jerusalem	1	46.00
	Bethlehem	6	26.25
	Hebron	50	41.53
	Ramallah	5	39.90
	Nablus	7	33.93
	Jenin	6	36.50
	Qalqilia	1	16.50
	Tulkarm	1	50.50
	Total	77	
Treatment	Jerusalem	1	23.00
	Bethlehem	6	27.67
	Hebron	50	41.45
	Ramallah	5	51.60
	Nablus	7	26.14
	Jenin	6	42.42
	Qalqilia	1	13.50

	Tulkarm	1	32.50
	Total	77	
Health	Bethlehem	4	19.13
	Hebron	26	23.65
	Ramallah	4	25.38
	Nablus	4	16.25
	Jenin	4	17.13
	Qalqilia	1	20.50
	Tulkarm	1	43.00
	Total	44	
Respiratory	Jerusalem	1	49.50
	Bethlehem	6	35.33
	Hebron	50	38.11
	Ramallah	5	64.40
	Nablus	7	45.64
	Jenin	6	24.58
	Qalqilia	1	23.50
	Tulkarm	1	23.50
	Total	77	
Digestion	Jerusalem	1	46.50
	Bethlehem	6	26.75
	Hebron	50	40.30
	Ramallah	5	41.10
	Nablus	7	39.21
	Jenin	6	31.00
	Qalqilia	1	38.50
	Tulkarm	1	76.50
	Total	77	
Weight	Bethlehem	4	11.50
	Hebron	26	23.00
	Ramallah	4	26.38
	Nablus	4	24.38
	Jenin	4	22.25
	Qalqilia	1	42.50
	Tulkarm	1	11.50
	Total	44	

- Correlation between quality of life domain scores and kind of living (city, village and camp).

Ranks			
	Kind of living	N	Mean Rank
Physical	City	23	32.04
	village	46	41.68
	camp	7	38.79

	Total	76	
Emotion	City	23	32.52
	village	47	42.17
	camp	7	39.00
	Total	77	
Vitality	City	13	22.38
	village	27	23.43
	camp	4	16.63
	Total	44	
School	City	3	6.83
	village	6	4.08
	Total	9	
Eat	City	23	41.35
	village	47	38.55
	camp	7	34.29
	Total	77	
Body	City	23	36.78
	village	47	40.73
	camp	7	34.64
	Total	77	
Treatment	City	23	36.87
	village	47	41.49
	camp	7	29.29
	Total	77	
Health	City	13	22.85
	village	27	22.81
	camp	4	19.25
	Total	44	
Respiratory	City	23	40.98
	village	47	37.61
	camp	7	41.86
	Total	77	
Digest	City	23	37.87
	village	47	39.65
	camp	7	38.36
	Total	77	
Weight	City	13	24.00
	village	27	22.41
	camp	4	18.25

	Total	44	

- Relationship between influenza vaccine and QoL domain scores.

Ranks				
	Taking influenza vaccine	**N**	**Mean Rank**	**Sum of Ranks**
Physical	Yes	41	39.56	1622.00
	No	35	37.26	1304.00
	Total	76		
Emotion	Yes	41	41.85	1716.00
	No	36	35.75	1287.00
	Total	77		
Vitality	Yes	20	25.18	503.50
	No	24	20.27	486.50
	Total	44		
School	Yes	2	4.00	8.00
	No	7	5.29	37.00
	Total	9		
Eat	Yes	41	35.12	1440.00
	No	36	43.42	1563.00
	Total	77		
Body	Yes	41	38.60	1582.50
	No	36	39.46	1420.50
	Total	77		
Treatment	Yes	41	37.27	1528.00
	No	36	40.97	1475.00
	Total	77		
Health	Yes	20	23.28	465.50
	No	24	21.85	524.50
	Total	44		
Respiratory	Yes	41	40.05	1642.00
	No	36	37.81	1361.00
	Total	77		

Digest	Yes	41	36.77	1507.50
	No	36	41.54	1495.50
	Total	77		
Weight	Yes	20	20.70	414.00
	No	24	24.00	576.00
	Total	44		
Social	Yes	32	28.11	899.50
	No	23	27.85	640.50
	Total	55		

تقييم نوعية حياة مرضى التليف الكيسي في الضفة الغربية والخيارات العلاجية الجديدة

اعداد: سامية عزت محمد صلاح

اشراف: الدكتور ماهر خضور والدكتور حسين حلاق

الملخص

أعداد مرضى التليف الكيسي تتزايد في جميع أنحاء العالم، أحدث التوقعات التي نشرت في مجلة الجهاز التنفسي الأوروبي تشير إلى زيادة حوالي 50٪ بحلول عام 2025 (20٪ من الأطفال، و 75٪ من البالغين).

لا توجد بيانات وبائية دقيقة عن مرض التليف الكيسي في فلسطين. وكان الانطباع العام أن المرض نادر الحدوث، ولكن يعود هذا على الأرجح نتيجة ضعف طرق التشخيص أو خطأ في التشخيص بسبب الوعي المحدود عن المرض في المنطقة.

مرض التليف الكيسي يحمل المرضى عبئاً كبيراً في العلاج بسبب العدد المتزايد من الأدوية المتاحة والحاجة إلى إجراءات مطولة كل يوم لتناول هذه الأدوية. التكنولوجيا الجديدة المستخدمة في تناول الادوية هي مفيدة للغاية لأنها قد تخفف عبء المرض عن طريق تقليل وقت العلاج وتقديم المزيد من الفعالية والسلامة. هذه الخيارات غير متاحة لمرضى التليف الكيسي في فلسطين فقط العلاجات التقليدية البدائية متوفرة ومن هنا تكمن المشكلة الأساسية.

تقييم وجهة نظر المريض من تحسن الأعراض ونوعية الحياة المرتبطة بالصحية والرضا يجب أن تكون جزءا من اتخاذ القرار العلاجي. معظم دراسات نوعية الحياة لمرضى التليف الكيسي تمت في الدول المتقدمة وعدد قليل منها في الدول النامية. ولكن لم تجرى أية منها في فلسطين.

الهدف من الدراسة

وكان الغرض من هذا المشروع دراسة الوضع الصحي لمرضى التليف الكيسي في فلسطين باستخدام عدة محاور للمقارنة تشمل؛ قضايا جودة الحياة لمرضى التليف الكيسي الذين يتلقون العلاج في مستشفى كاريتاس للأطفال وحالتهم الصحية، دراسة العبء الاقتصادي وتكاليف العلاج الحالية وتأثيرها على المرضى، معرفة رغبة المرضى في المساهمة المالية مقابل الحصول على علاج جديد يحسن من الوضع الصحي ويقلل من اعراض المرض ودراسة العوامل التي ستأثر على اجابتهم، لفت النظر الى الحاجة الى علاج جديد لمرض التليف الكيسي بالاعتماد على النتائج.

اجراءات الدراسة

دراسة مسحية وصفية أجريت للمرضى الذين يعانون من مرض التليف الكيسي في الضفة الغربية. يستخدم هؤلاء المرضى العلاجات الأساسية ويتلقون العلاج في عيادة أمراض الرئة لدى الأطفال في مستشفى كاريتاس للأطفال. أكمل حوالي 77 مشاركاً أربعة محاور للتقييم وقدموا معلومات ديمغرافية. تم دراسة حالة مرضى التليف الكيسي في فلسطين باستخدام جوانب مختلفة. وتم قياس جودة حياتهم باستخدام الاستبيان المعتمد لقياس جودة الحياة لمرضى التليف الكيسي والمترجم للغة العربية. وتم فحص حالتهم الصحية عن طريق قياس معايير مختلفة تشمل: فحص وظائف الرئة، مؤشر كتلة الجسم، عمر التشخيص وعدد الوفيات في كل اسرة. وقد تم حساب التكاليف المتعلقة بالعلاج والاستعداد لدفع مبلغ من المال مقابل الحصول على علاج جديد لتحسين الوضع الصحي. تم الحصول على موافقة لجنة أخلاق البحث العلمي في مستشفى الكاريتاس للأطفال لعمل الدراسة، والموافقة المكتوبة من المرضى ووالديهم قبل تعبئة الاستبيان. تم تحليل النتائج باستخدام البرامج المتاحة للتحليل وبرنامج SPSS.

النتائج والتوصيات

إن متوسطات قيم نوعية الحياة لمرضى التليف الكيسي في الضفة الغربية أقل من 60٪ تراوحت من 14.5 الى 55.6 مما يدل على نوعية حياة رديئة مقارنة بالدول الأخرى. أدنى درجة كانت للمجال الذي يقيم الصحة الجسمية (14.5) وطريقة العلاج (17.5) وصحة الجهاز التنفسي (27.5). ويبدو أن أعلى قيمة كانت للمجال الذي يقيم طبيعة الأكل (55) والحالة النفسية والعاطفية للمرضى (50). ومتوسط شدة المرض بالاعتماد على فحص وظائف الرئة والذي يقيس FEV_1 في المئة كانت بمعدل 69.6٪. ومتوسط سجل مؤشر كتلة الجسم كان يعادل 15.998 (كغم/متر مربع). مع متوسط العمر الإجمالي للتشخيص في العينة كان 4.16 سنة. وأظهرت الدراسة أن 58.3٪ (12/7) من محافظة الخليل كان لديهم حالات وفاة تتعلق بمرض التليف الكيسي.

وكشفت النتائج أن نوعية الحياة لمرضى التليف الكيسي تتأثر بالعمر والجنس وأخذ عطلة بدون مرض والعمل أو الوضع الدراسي والمستوى التعليمي، ومقاييس مؤشر كتلة الجسم، وسن التشخيص للمرضى، ومعايير تتعلق بالوالدين والتي شملت: العمر والمستوى التعليمي والعمل للوالدين. وتأثرت أيضا من العدد الإجمالي لمرضى التليف الكيسي في كل عائلة.

كما اظهرت الدراسة أن نوعية الحياة لمرضي التليف لا تتأثر بالحالة الاجتماعية والتوزيع الجغرافي ومكان الإقامة (مدينة، قرية أو مخيم)، والتدابير التي تتخذ في FEV_1، والاستعداد لدفع مبلغ من المال مقابل الحصول على علاج جديد، والعلاقة بالوالدين (الأب أو الأم)، والدخل الشهري للأسرة، وتأثير أخذ لقاح الأنفلونزا سنوياً.

93.5٪ من المرضى قالوا نعم وهم على استعداد لدفع مبلغ من المال مقابل الحصول على علاج جديد و6.5٪ قالوا لا نتيجة الحالية المادية السيئة. 51.4% منهم على استعداد لدفع 100 شيكل الى2.7٪ على استعداد لدفع 2000 شيكل أو أكثر. مع التقييم الاقتصادي لمرضى التليف الكيسي، فإن التكاليف الإجمالية لمريض يبلغ

من العمر 10.7 سنين والذي يمثل متوسط اعمار العينة قدرت بنحو 35650.2 شيكل للمريض سنوياً. وقد تم تقدير تخفيض التكاليف الصحية بعد تزويدهم ب Dornase-alfa كدواء مفكك للبلغم وتبخيرات محلول المضاد الحيوي Tobramycin بمبالغ كبيرة التي من شأنها أن تساعد في التحفيز على توفير هذه الأدوية المتاحة للمرضى التليف الكيسي.

وأخيراً أظهرت الدراسة أن لدينا نوعية حياة رديئة بالنسبة للمعايير الدولية، والأدوية المستخدمة بما في ذلك Hypertonic saline و Gentamycin nebulizer solution ليست الادوية المتطورة والمعتمدة في العالم، وكذلك المرضى وأسرهم يطالبون بحياة افضل وعلاجات جديدة ، وعلى استعداد للمشاركة بمبلغ من المال مقابل الحصول على علاج أفضل. لذلك فان لدينا دليل شامل يثبت الحاجة إلى علاجات جديدة لمرضى التليف الكيسي في فلسطين من أجل تحسين نوعية حياتهم، حالتهم الصحية، وزيادة متوسط اعمارهم.