*Review*

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# Tools and Methods Used for the Assessment of Body Composition in Patients With Cystic Fibrosis: A Systematic Review

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## Abstract

*Background:* Cystic fibrosis (CF) is characterized by changes in fat mass and lean body mass that may have important prognostic value. We aim to appraise the type and frequency of application of body composition (BC) methods in child and adult patients with CF. *Methods:* We used 4 databases (Embase, PubMed, Scopus, and Web of Science) to perform the literature search. The search was conducted from January 2017 to February 2017. Two independent reviewers selected articles based on titles and abstracts to check eligibility for inclusion. All study designs or types of articles (abstract, full text) were considered. *Results:* Eighty-four full-text articles and 40 studies presented only as abstracts were selected. Sixty-four studies included children and adolescents (age range of 0.1–18 years), and 41 studies recruited adults (range of 18–57 years); 13 studies included both age groups. Dual-energy X-ray absorptiometry (DXA) was used in 56 studies (33.9%), and bioelectric impedance analysis (BIA) was used in 12 studies (9.7%), whereas 38 studies (30.6%) combined different methods (up to 5 different methods) to assess BC. *Conclusions:* The results show a large variability in the application of BC methods in patients with CF that makes the comparison between studies difficult. The only methods with a sufficient body of literature are DXA and BIA. (*Nutr Clin Pract.* 2019;34:701–714)

## Keywords

bioimpedance analysis; body composition; cystic fibrosis; dual X-ray absorptiometry

## Introduction

Cystic fibrosis (CF) is a genetic disorder characterized by multi-organ failure, which primarily affects the lungs and the endocrine and reproductive systems.[1] The disease is usually diagnosed early in life, and the current median life expectancy in the United Kingdom is around 30 years.[2] Children with CF may have impaired growth trajectories for weight and height,[3] which are closely linked to disease severity and to recurrent infections and gastrointestinal malabsorption.[4]

The European Society for Parenteral and Enteral Nutrition (ESPEN) developed guidelines on nutrition care for patients with CF at different stages of life (infants, children, and adults) and considers the assessment of nutrition status as a primary step to achieve the best possible therapeutic and prognostic outcomes.[5] The assessment of the nutrition status represents a fundamental step in clinical diagnostic protocols to define the individual physiological and functional capacity, to identify nutrition deficiencies, and to establish therapeutic and monitoring strategies.[6,7] The body composition (BC) assessment plays an important role in the nutrition status evaluation, as it provides information on content and distribution of adiposity, lean body mass, bone health, and hydration status.

Different methods can be used to assess whole-body and segmental BC, including dual-energy X-ray absorptiometry (DXA), bioelectrical impedance (BIA), deuterium dilution (DD), skinfold thickness (SF), or imaging methods such as magnetic resonance imaging (MRI) or computed tomography (CT). The main BC components assessed by these methods are fat mass (FM), fat-free mass (FFM), total body water (TBW), extracellular water, intracellular water,

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bone mineral content (BMC), bone mineral density (BMD), protein mass, and body cell mass (BCM). The choice of the most appropriate BC method needs to take into consideration several factors to be investigated, such as clinical or research settings, financial and technical resources, or BC component.

In patients with CF, it is important to establish which specific BC components are independent predictors of clinical outcomes, since this could have implications for treatment plans and prognostic outcomes. Studies documented a significant association between a decrease in FFM and impaired pulmonary function or poor respiratory muscle strength in patients with CF.[8,9] Therefore, in recent years, there has been a growing research interest in comparing the accuracy of different BC methods in patients with CF and in the investigation of the relationship between BC and health outcomes.[10,11]

The aim of this systematic review is to critically appraise the existing evidence, focusing only on the BC methods used in child and adult patients with CF. Specifically, we will evaluate (1) the type of BC methods and frequency of application and (2) the heterogeneity across studies in the application of the different methods in adult and nonadult patients with CF.

## Materials and Methods

The protocol of the systematic review has been developed according to the PRISMA (Preferred Reporting Items for Systematic reviews and Meta-Analyses)[12] guidelines, and it has been registered in the PROSPERO database (International Prospective Register of Systematic Reviews; http://www.crd.york.ac.uk/prospero, registration number: CRD42017062559).

### *Literature Search*

Four databases (Embase, PubMed, Scopus, and Web of Science) were utilized to perform a comprehensive search of the literature. The search was conducted from the inception of the databases until February 2017, and the aim was to evaluate the instruments used to assess BC in patients (children and adults) affected by CF. The following keywords were used: cystic fibrosis OR cystic fibrosis transmembrane conductance regulator (CFTR) AND body composition OR nutritional status; AND anthropometry OR bioimpedance analysis OR densitometry OR dual-energy x-ray absorptiometry; AND multi-compartment model. References of eligible articles were also screened to identify additional studies that may have not been included in the primary search.

### *Study Selection and Inclusion Criteria*

The PICOS (Participants, Interventions, Comparisons, Outcomes, and Study design) criteria used to delineate the research question for this review were described in Table 1. All study designs were considered except reviews, letters, and editorials. The abstracts published by the same authors of full-text articles were included if the year of publication and the sample size were different. Articles were excluded from the review if (1) only weight, height, and body mass index (BMI) were considered as a proxy of BC and (2) the method to assess BC was not reported. Titles and abstracts were assessed by 2 independent investigators to check eligibility for inclusion. A concordant decision between the 2 investigators meant that articles were either assessed in the full-text phase or removed from the main analysis. Any disagreement in the inclusion of an article was resolved by a third investigator.

**Table 1.** Participants, Interventions, Comparisons, Outcomes, and Study Design Criteria for Inclusion and Exclusion of Studies.

| Parameter | Criteria |
|---|---|
| Participants | Children, adolescents, and adult subjects with cystic fibrosis |
| Intervention | Evaluation of body composition; studies evaluating body compartments were included and studies evaluating only body weight, body height, and body mass index were excluded |
| Comparison | How effective the different body composition evaluation methods are |
| Outcomes | The outcome was the analysis of the tools and methods used to assess body composition in people with cystic fibrosis |
| Study design | No selection considering the study design on the condition that the body composition analysis was performed |

### *Data Extraction and Quality Assessment*

The following information was retrieved from each article: (1) authors, title, and year of publication; (2) study design and research/clinical setting; (3) sample size; (4) subjects' characteristics (ie, age, gender, weight, height, pulmonary function forced expiratory volume in 1 second); (5) method used to assess BC; (6) BC components (ie, FM, FFM, TBW, BMD); and (7) summary of main findings. These data were included in an electronic database by a first investigator and cross-checked by another investigator. Considering the age range, 3 categories were created: "pediatric," including subjects from birth to 18 years; "adult" subjects older than 18 years; and "mixed ages," indicating unknown age range.

The Downs and Black instrument was used to assess the methodological quality and the risk of bias of the studies comprised in this systematic review.[13] The Downs and Black checklist consists of 27 items to assess study

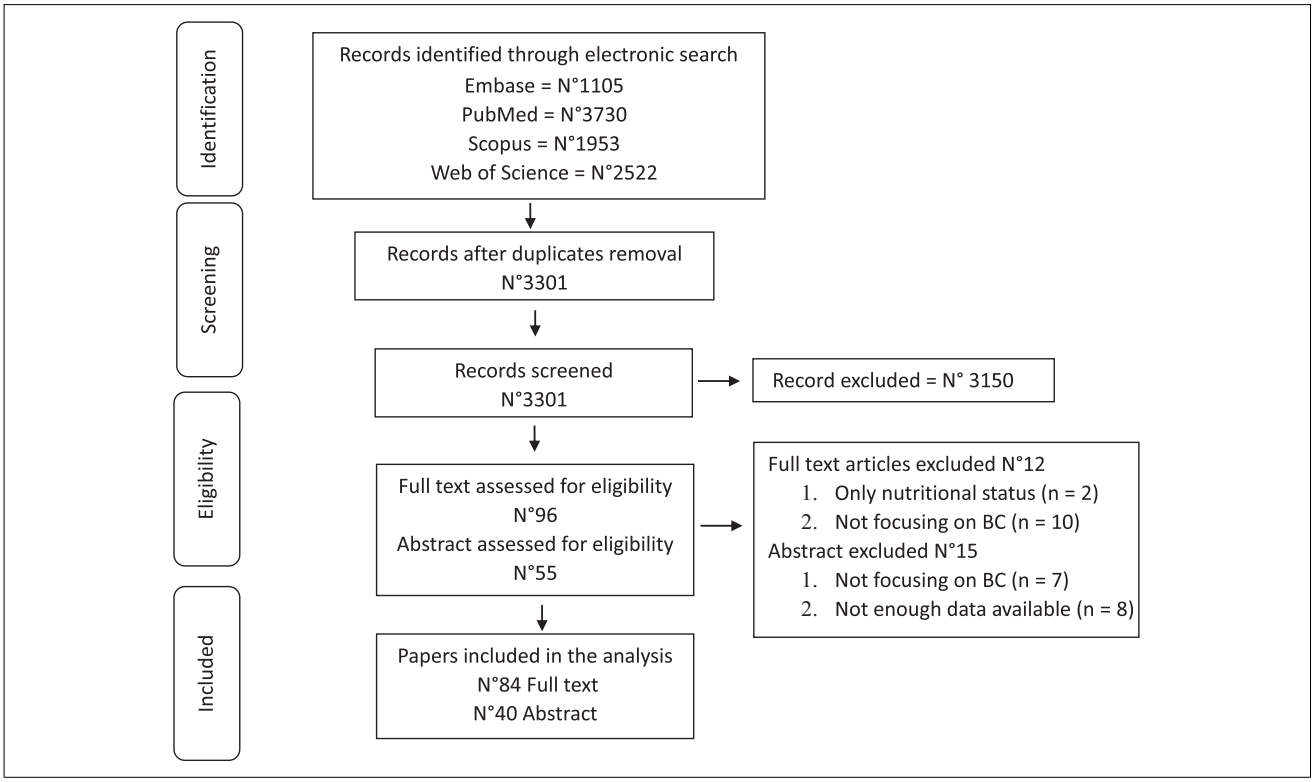


**Figure 1.** Flow diagram of the search strategy.

quality, including reporting, external validity, and internal validity bias. The checklist for this study was modified by removing 8 questions (4, 8, 14, 15, 19, 23, 24, and 27) of the 27 original items that were not relevant to the aim of this study. Furthermore, 3 items (9, 17, and 26) focusing on the follow-up were excluded for cross-sectional studies. Therefore, the final checklist consisted of 19 items for longitudinal studies and 16 items for cross-sectional studies, with a maximum score of 20 or 17 points, respectively. High or low quality was determined using the median split of the scores. The quality assessment was carried out by 2 independent authors, and when disagreements between assessors occurred, consensus was achieved through a third assessor's opinion.

## Results

### *Selection of Eligible Articles*

Three thousand three hundred one studies were identified by searching Embase, Pubmed, Scopus, and Web of Science databases after the removal of 6009 duplicates. During the title and abstract screening phase, 3150 were excluded because of missing data on BC. Some of the eligible studies were published as abstract only (mainly contributions to conferences on CF), and therefore a full manuscript was not available. However, the decision of the research team was to include the abstracts in the systematic review as long as they met the inclusion and exclusion criteria considering that abstracts usually are pilot studies using emerging techniques. In total, 84 full texts and 40 abstracts were included and evaluated in the systematic review. The selection and screening process is summarized in Figure 1.

### *Sample Size and Study Design*

The 40 abstracts selected in the review included 2438 patients with CF; 6 studies included a control group, giving a total number of 594 controls.[14-19] One study compared the BC of patients with CF to existing reference values obtained from a healthy age-matched and gender-matched population.[20] A longitudinal study had the smallest sample size (6 patients),[21] whereas a cross-sectional study included the largest number of patients with CF (138).[22] The number of participants with CF included in the 84 full-text articles ranged from 8 to 226 for a total of 4699 patients; 41 studies also had a control group as part of the study design (see Table 2) and included a total of 2261 controls ranging from a minimum of 8 to a maximum of 322 participants. The sample size of the full-text studies ranged from 8 to 226 participants with CF. Multiple studies were conducted by the same authors, but it is not clear if they studied a separate population; although not so accurate, it

**Table 2.** Characteristics of the 40 Abstracts Included in the Systematic Review.

| Reference | Country | Study Design | Sample Size | Age (in Years) | Methods Used for the Body Composition Analysis |
|---|---|---|---|---|---|
| Alicandro et al (2012)[22] | Italy | CS | 138 | 8–47[a] | BIA-DXA-SF |
| Almajan-Guta et al (2012)[60] | Romania | CS | 20 | 14–18[a] | BIA |
| Bianchi et al (2009)[14] | Italy | CS | 136/136 | 3–24[a] | DXA |
| Bisogno et al (2013)[46] | Italy | L | 85 | 19–27[a] | DXA |
| Bosnak-Guclu et al (2012)[15] | Turkey | CS | 36/35 | NR | BIA |
| Brookes et al (2011)[16] | Australia | CS | 53/53 | 7–18[a] | pQCT |
| Chirita-Emandi et al (2014)[125] | Romania | L | 101 | 8–18[a] | DXA |
| Cordioli et al. (2010)[126] | Italy | CS | 27 | 5–17[a] | DXA |
| De Waele et al (2009)[81] | Belgium | CS | 62 | 12–38[a] | DXA-pQCT-ULT |
| De Waele et al (2007)[70] | Belgium | CS | 51 | 2.3–20.5[a] | ULT |
| Djeddi et al (2010)[57] | France | CS | 29 | 15.2 ± 1.5[b] | BIA |
| Dusser et al (2013)[75] | France | CS | 46 | 13[c] | BIA-DXA |
| Gornicka et al (2010)[127] | Poland | CS | 20 | 5.9–19.1[a] | DXA |
| Hatziagorou et al (2010)[77] | Greece | CS | 30 | 15.4 ± 4.9[b] | DXA-ULT |
| Hatziagorou et al (2013)[61] | Greece | CS | 64 | 0.1–18 [a] | BIA |
| Hilton et al (2015)[41] | UK | CS | 17 | NR | BIA |
| Jaksic et al (2016)[49] | New Zealand | L | 60 | 5.9–18.8 [a] | DXA |
| Junge et al (2012)[59] | Germany | CS | 156 | 11.3 ± 3.4[b] | BIA |
| King et al (2014)[64] | Australia | CS | 59 | 31.0 ± 9.2[b] | SF |
| Mailhot et al (2014)[17] | Canada | CS | 16/13 | 30 ± 9[b] | DXA |
| Marostica et al (2015)[18] | Brazil | CS | 35/35 | 6–18[a] | ULT |
| Mead et al (2015)[128] | UK | CS | 172 | 28.5[c] | DXA |
| Mielus et al (2013)[129] | Poland | CS | 72 | 8–18[a] | DXA |
| Murphy et al (2015)[45] | Australia | CS | 82 | NR | TBK |
| Nadeem (2010)[48] | Ireland | L | 51 | 8–19[a] | DXA |
| O'Driscoll et al (2015)[29] | UK | CS | 150 | 16–66[a] | DXA |
| Oldroyd et al (2009)[21] | UK | L | 6 | 8.1–11.8[a] | DXA |
| Prais et al (2010)[33] | Israel | CS | 77 | 4–59[a] | ULT |
| Proud et al (2012)[20] | UK | CS | 117/4463 | 17–53[a] | BIA |
| Proud et al (2016)[63] | UK | CS | 89 | 29.1[c] | BIA |
| Proud et al (2016)[34] | UK | L | 8 | 20–46 [a] | BIA |
| Roddy et al (2012)[47] | Ireland | L | 50 | 12.8 ± 2.1[b] | DXA |
| Rousseau-Nepton et al (2012)[130] | Canada | CS | 19 | 6–16[a] | DXA |
| Scott et al (2012)[58] | USA | CS | 15 | 13.9[b] | BIA |
| Sheikh et al (2012)[19] | USA | CS | 98/322 | 5–18[a] | DXA |
| Simovik et al (2011)[131] | New Zealand | CS | 35 | 10–18.8[a] | DXA |
| Solarino et al (2015)[42] | Italy | CS | 44 | NR | DXA |
| Svekusova et al (2011)[62] | Slovakia | CS | 36 | 5–18[a] | BIA |
| Tierney et al (2015)[43] | Australia | L | 20 | NR | DXA |
| Williams et al (2010)[44] | UK | L | 56 | NR | DXA |

BIA, bioelectric impedance analysis; CS, cross-sectional; DXA, dual-energy X-ray absorptiometry; L, longitudinal; NR, not reported; pQCT, peripheral quantitative computed tomography; SF, skinfold; TBK, total body potassium; ULT, ultrasound.
[a]Age range.
[b]Age media.
[c]Age median.

could be useful to get an overview of the total number of participants.

Sixty-four (51.6%) of the total number of studies included a pediatric population with an age range between 0.1 and 18 years and a total number of 3890 children and adolescents with CF. Two of these studies assessed BC in toddlers (<2 years) with CF.[23,24] Forty-one studies (33.1%) recruited adult patients aged between 18 and 57 years and a total number of 1983 patients with CF. Only 15 studies included patients older than 40 years.[20,22,25-37] Ten studies (8.1%) included both children and adults[20,22,28-30,33,35,38-40] (range: 4–66 years, N = 768). Six studies (published as abstracts) did not report information on the age of the patients[15,41-45] (Tables 2, 3, and 4). Thirty-one studies

**Table 3.** Characteristics of the 84 Full-Text Studies Included in the Systematic Review.

| Reference | Country | Study Design | Sample Size | Age (in Years) | Methods Used for the Body Composition Analysis |
|---|---|---|---|---|---|
| Alicandro et al (2014)[25] | Italy | CS | 85 | 18–44[a] | DXA |
| Alicandro et al (2015)[96] | Italy | CS | 142 | 17.25 ± 3.5[b] | BIA-DXA-SF |
| Alvarez et al (2016)[73] | USA | CS | 32/20 | CF: 26.1 ± 8.9; C: 30.9 ± 8.8[b] | ADP |
| Azcue et al (1992)[76] | Canada | CS | 20/21 | CF: 21.2 ± 9.1; C: 21.5 ± 8.6[b] | BIA-$H_2{}^{18}O$ |
| Bai et al (2016)[71] | USA | CS | 12/24 | CF: 11.8 ± 0.9; C: 12.4 ± 0.9[b] | pQCT |
| Baker et al (2016)[26] | USA | L | 63 | 18–57[a] | BIA-DXA |
| Beaumesnil et al (2011)[38] | France | CS | 55 | 4–29[a] | BIA-DXA-SF |
| Bianchi et al (2005)[50] | Italy | L | 136 | 14 ± 5.2[b] | DXA |
| Boguszewski et al (2007)[132] | Brazil | CS | 26/33 | 5–15.5[a] | DXA |
| Borovnicar et al (2000)[87] | Australia | CS | 19 | 10.4 ± 0.4[b] | DD-TBCl-TBK |
| Borowitz et al (1994)[27] | USA | CS | 10/10 | CF: 18–39; C: 15–43 | BIA-DD |
| Brookes et al (2015)[72] | Australia | CS | 53/53 | CF: 12.5 ± 1.6; C: 11.8 ± 1.6[b] | pQCT |
| Buntain et al (2003)[133] | Australia | CS | 153/149 | 5 and older[a] | DXA |
| Cemlyn-Jones et al (2008)[28] | Portugal | CS | 22 | 14–45[a] | DXA |
| Charatsi et al (2016)[10] | France | CS | 54 | 5–21[a] | BIA-DXA |
| Chaves et al (2015)[108] | Brazil | CS | 56 | 12.2 ± 2.5[b] | DXA |
| Conway et al (2008)[134] | UK | CS | 107 | 11.9 ± 1.64[b] | DXA |
| De Meer et al (1999)[51] | Netherlands | L | 26/13 | CF: 14.7 ± 2; C: 15.2 ± 1.9[b] | SF |
| Donovan et al (1998)[135] | USA | CS | 30/30 | CF: 30 ± 2; C: 32 ± 2[b] | DXA |
| Duveau et al (1999)[136] | France | CS | 45 | 13 ± 5.5[b] | DXA |
| Elkin et al (2000)[137] | UK | CS | 25/25 | CF: 28 ± 8; C: 28 ± 7[b] | DXA |
| Elkin et al (2001)[138] | UK | CS | 107 | 28 ± 8[b] | DXA |
| Engelen et al (2012)[105] | USA | CS | 77 | 14.8 ± 2.9[b] | DXA |
| Enright et al (2007)[139] | UK | CS | 40/30 | CF: 18–32; C: 18–33[a] | DXA |
| Flohr et al (2002)[140] | Germany | CS | 75 | 25.3 ± 6.92[b] | DXA |
| Forte et al (2012)[65] | Brazil | CS | 69 | 5.4–16.5[a] | SF |
| Frangolias et al (2003)[141] | Canada | CS | 68 | 18–55[a] | DXA |
| Giróna et al (2004)[142] | Spain | CS | 33 | 23.06 ± 6.12[b] | DXA |
| Gordon et al (2007)[88] | USA | CS | 64 | 31.4 ± 9.1[b] | BIA-SF |
| Greer et al (1991)[23] | Australia | L | 25 | Birth to 1–2 years[a] | SF-TBK |
| Grey et al (1993)[143] | New Zealand | CS | 22/65 | CF: 23 ± 8; C: 26 ± 6[b] | DXA |
| Groeneweg et al (2002)[89] | Netherlands | CS | 58 | 4–18[a] | BIA-SF |
| Gronowitz et al (2003)[30] | Sweden | CS | 70 | 6–49[a] | DXA |
| Gruet et al (2015)[74] | France | CS | 15/15 | CF: 28 ± 6; C: 28 ± 5[b] | MRI |
| Hardin et al (2001)[39] | USA | CS | 41 | 10–30[a] | DXA |
| Hauschild et al (2016)[90] | Brazil | CS | 46/24 | 8.5[c] | BIA-SF |
| Henderson et al (1996)[92] | USA | CS | 62 | 10.7 ± 3.6[b] | DXA-SF |
| Henderson et al (1999)[91] | USA | CS | 47/40 | 5.7–20.3[a] | DXA-SF |
| Hollander et al (2005)[31] | Netherlands | CS | 35 | 18–46[a] | BIA-SF |
| Ionescu et al (1998)[66] | UK | CS | 49/25 | 23.7 ± 4.4[b] | SF |
| Ionescu et al (2000)[144] | UK | CS | 22/22 | CF: 23.6; C: 23.8[b] | DXA |
| Ionescu et al (2002)[145] | UK | CS | 40/22 | CF: 23.1; C: 23.8[b] | DXA |
| Ionescu et al (2003)[82] | UK | CS | 56/20 | 17–38[a] | BIA-DXA |
| Kelly et al (2008)[146] | USA | CS | 82/322 | CF: 13.2 ± 2.9; C: 12.9 ± 2.9[b] | DXA |
| King et al (2013)[52] | Australia | L | 58 | 33.9 ± 7.7[b] | DXA |
| King et al (2005)[32] | Australia | CS | 76 | 19–59[a] | BIA-DXA-SF |
| King et al (2010)[9] | Australia | CS | 86/156 | 30.0 ± 7.7[b] | DXA |
| Lucidi et al (2009)[147] | Italy | CS | 82/82 | CF: 13.5 ± 5.6; C: 12.9 ± 5.9[b] | DXA |
| Marin et al (2004)[95] | Chile | CS | 15/15 | CF: 8.2 ± 3.8; C: 7.9 ± 3.2[b] | DD-SF |
| McNaughton et al (2000)[68] | Australia | CS | 226/140 | CF: 8.76 ± 5.54[b] | TBK |
| Miller et al (1982)[67] | Australia | CS | 9/8 | 5.6–13.2[a] | SF |
| Moriconi et al (2006)[148] | USA | CS | 24/24 | CF: 30.4 ± 9.4; C: 30.5 ± 8.8[b] | DXA |
| Newby et al (1990)[97] | USA | CS | 8/8 | CF: 27.3 ± 3.4; C: 28.4 ± 3.5[b] | BIA-DD-TOBEC-SF-U |

(*continued*)

**Table 3. (continued)**

| Reference | Country | Study Design | Sample Size | Age (in Years) | Methods Used for the Body Composition Analysis |
|---|---|---|---|---|---|
| Panagopoulou et al (2008)[93] | Greece | CS | 43/27 | CF: 20.2 ± 8.4; C: 19.9 ± 9.4[b] | BIA-CT |
| Pedreira et al (2005)[149] | Australia | CS | 50 | 12.7 ± 2.4[b] | DXA |
| Puiman et al (2004)[56] | Netherlands | CS | 56 | 4–18[a] | BIA |
| Putman et al (2015)[150] | USA | CS | 32/32 | 27.5[b] | DXA |
| Quirk et al (1995)[78] | Australia | CS | 28 | 4.2–16.3[a] | BIA-SF-TBK |
| Quirk et al (1997)[83] | Australia | CS | 31 | 10.1 ± 3.3[b] | BIA-SF-TBK |
| Reix et al (2010)[151] | France | CS | 161 | 10 ± 4.8[b] | DXA |
| Richards et al (2003)[116] | Australia | CS | 36/42 | CF: 25.5 ± 5.6; C: 25.4 ± 4.8[b] | BIA-DD |
| Rochat et al (1994)[152] | Switzerland | CS | 12 | 23.25 ± 2.90[b] | DXA |
| Rossini et al (2007)[153] | Italy | CS | 172 | 27.6 ± 5.7[b] | DXA |
| Salamoni et al (1996)[84] | Switzerland | CS | 14/14 | CF: 12.2 ± 3.5; C: 12.3 ± 3.5[b] | BIA-DXA-SF |
| Schepper et al (2012)[154] | Belgium | CS | 64 | 20.6 ± 5.9[b] | DXA |
| Sheikh et al (2014)[155] | USA | CS | 208/390 | 5–21[a] | DXA |
| Sheikh et al (2015)[35] | USA | CS | 103 | 16–53[a] | DXA |
| Shepherd et al (1988)[24] | Australia | CS | 140 | 2–17[a] | TBK |
| | | L | 12 | Birth to 2 years[a] | TBK |
| Shepherd et al (2001)[94] | Australia | CS | 30/18 | CF: 13.1 ± 0.6; C: 12.6 ± 1.3[b] | SF-TBK |
| Slosman et al (1992)[79] | Switzerland | CS | 10/60 | CF: 23.2 ± 1.0; C: 26.8 ± 1.4[b] | DXA-TBK |
| Spicher et al (1993)[85] | Switzerland | CS | 39/39 | CF: 12.9 ± 4.4; C: 12.1 ± 4.3[b] | BIA-SF |
| Stalvey et al (2012)[156] | USA | CS | 62 | 9.4 ± 2.1[b] | DXA |
| Stettler et al (2000)[53] | USA | CS | 25/26 | 5–10[a] | SF-DD-TOBEC |
| | | L | 25/26 | CF: 7.8 ± 1.3; C: 7.7 ± 1.3[b] | SF-DD-TOBEC |
| Street et al (2006)[157] | Italy | CS | 17 | 19–39[a] | DXA |
| Swisher et al (2003)[40] | US | CS | 10/10 | 14 and older[a] | ADP-NIR-SF |
| Tejero et al (2015)[36] | Spain | CS | 50 | 16–46[a] | TBK |
| Thomson et al (1995)[69] | Australia | CS | 144 | 0.3–17[a] | TBK |
| Tomezsko et al (1994)[86] | USA | CS | 23/24 | CF: 7.8 ± 1.3; C: 7.7 ± 1.1[b] | DD-SF-TOBEC |
| Ujhelyi et al (2004)[54] | Hungary | L | 38 | 16.5[c] | DXA |
| Wells et al (2008)[80] | Canada | CS | 55 | 13.2 ± 2.4[b] | DXA-MRI-SF |
| Williams et al (2006)[11] | UK | CS | 26/88 | 5–21[a] | ADP-DD-DXA |
| Williams et al (2010)[98] | UK | CS | 85/85 | 6–12[a] | DXA-ADP-SF-DD |
| Williams et al (2013)[55] | UK | L | 69 | 9.31 ± 1.46[b] | DXA-ADP-SF-DD |
| Ziai et al (2014)[37] | Canada | CS | 34 | 20–54[a] | BIA-DXA |

ADP, air displacement plethysmography; BIA, bioelectric impedance analysis; C, control group; CF, cystic fibrosis; CS, cross-sectional; CT, computed tomography; DD, deuterium dilution; DXA, dual-energy X-ray absorptiometry; $H_2{}^{18}O$, water isotope; L, longitudinal; MRI, magnetic resonance imaging; NIR, near-infrared interactance; NR, not reported; pQCT, peripheral quantitative computed tomography; SF, skinfolds; TBCl, total body chloride; TBK, total body potassium; TOBEC, total body electrical conductivity; ULT, ultrasound; U, densitometry by underwater weighing.
[a]Age range.
[b]Age media.
[c]Age median

(published as abstracts) had a cross-sectional design, whereas 9 studies[16,21,34,43,44,46-49] were longitudinal with a follow-up duration between 3 months and 10 years. The 84 articles (full texts) included only 9 studies with a longitudinal design with a follow-up duration between 1 and 4 years[23,24,26,50-55] (Tables 2 and 3).

*Quality assessment.* According to the modified Downs and Black tool, the quality assessment indicated that 44% (4/9) of longitudinal studies (Table S2) and 37% (28/75) of the cross-sectional studies (Table S3) had lower quality (based on a median split count of <15/20 and <11/17, respectively). Considering the total number of studies, 38% (32/84) had low quality.

## *Methods for BC Assessment*

DXA was used in 56 studies (33.9%, see Tables 2 and 3 for details), whereas 12 studies (9.7%) used only BIA[15,20,34,41,56-63]; 5 studies (4%) applied SF,[51,64-67] and 5 other studies used the total body potassium counting method (TBK).[24,36,45,68,69] Three studies used ultrasound

**Table 4.** Number and Percentage of Studies Using Single or Multiple Methods to Assess BC in CF Subjects Stratified by Age Groups.

| | Abstract and Full Text | | | | |
|---|---|---|---|---|---|
| Methods | Pediatric, n (%) | Adults, n (%) | Mixed Age Group, n (%) | Age Not Reported, n (%) | Total Number of Studies, N (%) |
| Single BC methods | 42 (33.9) | 30 (24.2) | 8 (6.5) | 6 (4.8) | 86 (69.4) |
| DXA | 25 (20.2) | 22 (17.7) | 6 (4.8) | 3 (2.4) | 56 (45.2) |
| BIA | 7 (5.6) | 3 (2.4) | | 2 (1.6) | 12 (9.7) |
| SF | 3 (2.4) | 2 (1.6) | | | 5 (4) |
| ULT | 1 (0.8) | | 2 (1.6) | | 3 (2.4) |
| TBK | 3 (2.4) | 1 (0.8) | | 1 (0.8) | 5 (4) |
| pQCT | 3 (2.4) | | | | 3 (2.4) |
| ADP | | 1 (0.8) | | | 1 (0.8) |
| MRI | | 1 (0.8) | | | 1 (0.8) |
| Combined BC methods | 22 (17.7) | 11(8.9) | 5 (4) | | 38 (30.6) |

ADP, air displacement plethysmography; BIA, bioelectric impedance analysis; BC, body composition; CF, cystic fibrosis; DXA, dual-energy X-ray absorptiometry; MRI, magnetic resonance imaging; pQCT, peripheral quantitative computed tomography; SF, skinfold; TBK, total body potassium; ULT, ultrasound; %, of all studies.

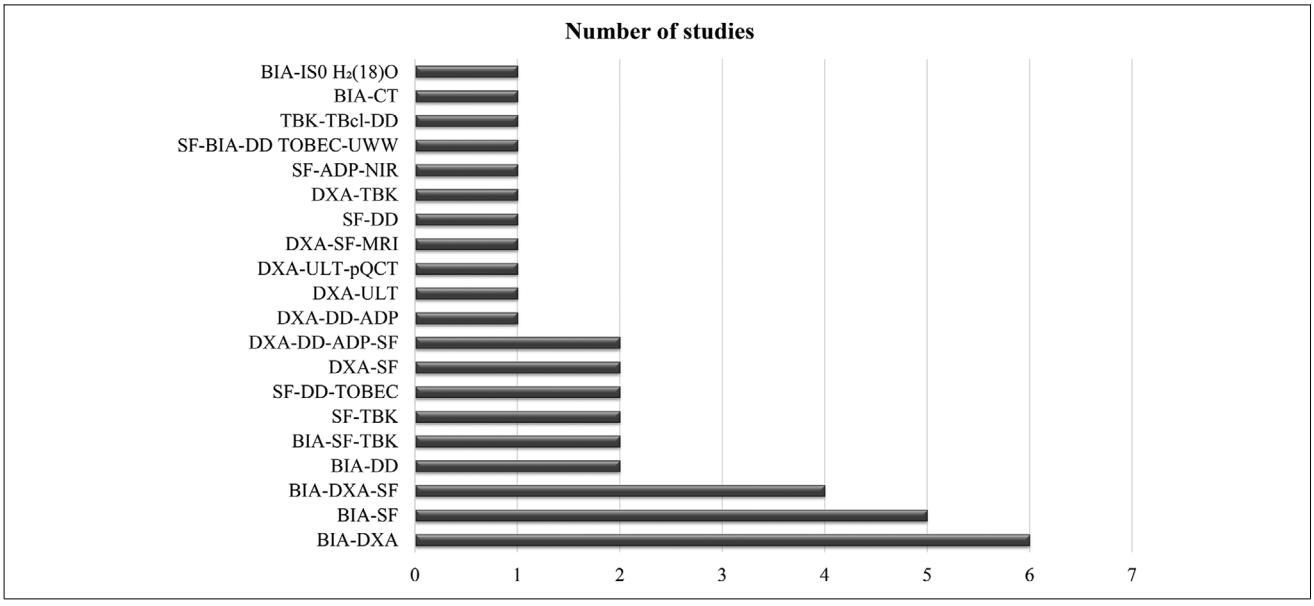


**Figure 2.** Number of studies using >1 method to assess body composition in cystic fibrosis subjects. The y-axis shows combinations of body composition (BC) methods; the x-axis shows the number of studies using each BC combination. ADP, air displacement plethysmography; BIA, bioelectric impedance analysis; CT, computed tomography; DD, deuterium dilution; DXA, dual-energy X-ray absorptiometry; IS0 $H_2(18)O$, isotopic distribution of $H_2(18)O$; MRI, magnetic resonance imaging; NIR, near-infrared interactance; pQCT, peripheral quantitative computed tomography; SF, skinfold; TBK, total body potassium; TOBEC, total body electrical conductivity; ULT, ultrasound.

(ULT),[18,33,70] 3 studies used peripheral quantitative computed tomography (pQCT),[16,71,72] 1 study used air displacement plethysmography (ADP),[73] and 1 study used MRI.[74] Among all studies, 38 (30.6%, see Tables 2 and 3 for details) combined different methods (up to 5 different methods) to assess BC; >50% of the studies applied DXA or BIA. Table 4 and Figure 2 provide an overview on the frequency of application of the various methods, alone or in combination, in different age groups.

*Combined methods to assess BC.* The main aims of these studies in combining different methods were to

(1) validate a BC method against an established reference (12 studies)[10,11,22,25,27,31,75-80] and/or evaluate the agreement between different methods (11 studies)[32,37,38,40,81-86] without specifying a reference BC method and (2) combine different methods (14 studies)[23,26,44,53,55,87-95] to have a more precise BC evaluation. Table S1 in the supplementary material shows the characteristics, main aims, and findings of these studies.

*Validation studies.* Ten studies[10,22,26,32,37,38,75,82,84,96] evaluated the accuracy of BIA in patients with CF using DXA as the reference method (5 of these studies used SF in combination with BIA and DXA).[22,32,38,82,96] Two studies reported a good agreement between BIA and DXA and suggested that BIA could be used for the assessment of BC in child and adult patients with CF[75,82]; however, Ziai et al observed that BIA overestimated FFM in patients with <40 kg of FFM and underestimated for higher FFM values.[37] King et al[32] suggested that both SF and BIA incorrectly estimate FFM in adults with CF compared with DXA, whereas Beaumesnil et al[38] found an excellent correlation between the 3 methods. Two studies proposed the use of population-specific BIA equations to improve the accuracy of the measurements.[25,96] Charatsi et al validated the only CF-specific equation for BIA using DXA as a reference method.[10]

Five studies compared BIA and SF,[31,85,88-90] 1 study compared SF with DD,[86] and another one to near-infrared interactance and ADP; the study found that none of the SF equations agreed with ADP in females with CF.[40] De Waele et al concluded that radial peripheral quantitative computed tomography (pQCT) might help to identify patients with CF with a normal BMC, but it cannot replace DXA as a diagnostic tool.[81] Newby et al compared different methods to evaluate the BC and observed that estimates of BC by total body electrical conductivity (TOBEC), $D_2O$ dilution, and SF produced the same qualitative pattern of body tissue deficit in patients with CF: less FM and less FFM.[97] Three studies compared DXA to the 4-component model,[11] MRI,[80] and TBK,[79] and they all concluded that DXA provided an accurate measurement of BC in patients with CF. Finally, Hatziagorou et al compared ULT with DXA for the assessment of bone health; the study did not support the use of ULT to assess osteopenia and osteoporosis in children with CF.[77]

*Different BC methods in combination.* Thirteen studies combined different methods to have a more precise evaluation of the BC. Two studies used BIA and anthropometry (SF and upper arm circumference)[89,90] to assess BC and suggested that both of these methods may be useful; however, longitudinal studies in children with CF are needed to evaluate their clinical significance in detecting changes in nutrition status. We also found a large heterogeneity across studies in the simultaneous application of BC methods. Two studies[91,92] used DXA to evaluate the BMD and SF to assess the FM, whereas another study[26] used BIA to evaluate the FM and DXA to estimate BMD; Panagopoulou et al used BIA to assess BC and the CT scan to measure the visceral/subcutaneous adipose tissue ratio[93]; Marin et al used DD to measure TBW and FFM, and SF thicknesses were used to measure FM.[95] TBK or total body chlorine were also combined to measure BCM[23,94] and assess body fluid compartments in patients with CF.[87] Only 3 studies applied multicompartment models to have a more precise phenotypic characterization of BC in patients with CF.[53,55,98]

## Discussion

This systematic review examined the current evidence on the assessment of BC in adult and nonadult patients with CF using different BC methods (see Box S1). Considering the low quality of most of the studies and their contrasting results, it is challenging to draw a clear conclusion.

In particular, only a small number of studies (15%) had a longitudinal design, preventing us from proposing clear recommendations on the most reliable methods to monitor changes in BC; however, 9 of these studies found changes in FFM and FM, confirming the importance of long-term monitoring of BC in these patients to improve prognostic outcomes.[23,24,26,34,46,51-53,55] In addition, 30% of the cross-sectional studies aimed to identify the most reliable method to assess BC in these patients, and the results are, on the whole, discordant. Overall, DXA and BIA were the most frequent methods applied for the assessment of BC in patients with CF.

The assessment of BC is important to define the severity and the evolution of CF, and it may allow the early identification of patients with CF at risk of malnutrition and assist with the prescription and/or evaluation of the efficacy of medical and nutrition interventions. Considering the increased energy requirements in patients with CF, the risk of malnutrition is high,[99] and it is related to diverse factors such as intestinal inflammation, impaired liver function,[100] maldigestion, and malabsorption caused by the pancreatic insufficiency.[101] Furthermore, impaired lung function, both in adults and children with CF, is associated with malnutrition and high mortality.[102] On the other hand, there is a clear correlation between an optimal nutrition status and a better lung function, and both of these situations are found to improve survival and clinical outcomes.[103] For these reasons, the evaluation of BC as a sensitive marker of nutrition status is an important step to minimize the nutrition deficit and to ameliorate the clinical outcomes. BMI alone as a measure of optimal health is not sufficient in this population because it does not allow for an evaluation of the different body compartments.[104] In particular, in these patients, it is important to evaluate and monitor FFM since

different studies described a marked reduction of FFM in patients with CF[9,82,105] and a significant association with a more severe lung disease.[106] It is also important to evaluate FM, considering that adiposity and lung function appear to be inversely related.[107] Abdominal fat accumulation in young and adult patients with CF seems to be correlated with chronic inflammation, physical inactivity, and growth hormone decrease.[108] Finally, a number of risk factors for bone loss and low BMD are seen in patients with CF, including nutrition deficiency, chronic inflammation, and chronic use of glucocorticoids.[109]

DXA was the most frequently applied method to evaluate BMD or BMC. This is important because patients with CF are at an increased risk of developing low BMD and fragility fractures[110]; therefore, monitoring the bone status during the growth process is an important step for the prevention of osteoporosis and osteopenia. The European Cystic Fibrosis Bone Mineralisation Guidelines recommend that "DXA is used to assess bone mineral density in all patients from the age of 8–10 years of age"[110] and advise to repeat this measurement every 1–5 years, depending on the presence of risk factors, age of the patient, and results of the previous scan.

The frequent utilization of DXA in this population could be explained by the significant effects of CF on bone health during growth and adulthood.[111,112] In addition, current diagnostic protocols recommend the use of DXA for the assessment of BMD in all patients with CF from 8 years of age.[110]

The main advantage of the DXA method from a nutrition standpoint is the high accuracy and the possibility to obtain detailed information, alongside BMD, on total and segmental lean body mass and FM.[113,114] This is the primary reason why DXA was often chosen (19 studies) as a reference method in the validation of other BC methods. In addition, DXA measurements are essential to build a 4-compartment model of BC.[11,55,98]

BIA was the second most applied method for the evaluation of BC in patients with CF; it directly measures the impedance of the human body (resistance, resistivity, and phase angle), whereas the parameters related to BC (water content, FFM, and FM) are calculated using prediction equations. The basic assumption underlying these equations is that the hydration status is normal and that the water content of FFM is equal to 73%.[115] Since these conditions are not always respected in real life, and particularly in clinical settings, authors considered the raw electric data in their analyses and found a good correlation between these data, clinical status, and prognosis. BIA is often used to measure TBW, as it is highly correlated with the impedance. One study reported an overestimation of TBW with BIA in subjects with CF,[116] whereas 2 other studies reported more accurate measurements of changes in TBW.[76,83] Measurement of hydration status in patients with CF is also critical, as altered fluid transport in epithelial cells, which is related to an imbalance between sodium and chloride transport, may result in changes in water content.[117] This emphasizes again the importance of applying BIA-specific prediction equations to obtain more accurate estimates of BC.

Other BC methods (ie, CT, MRI, ULT, ADP, pQCT, and TOBEC) were used in 16 studies and applied in different combinations. CT and MRI are currently considered the gold standards for estimating the quality and quantity of muscle mass.[118,119] The main advantage of MRI over CT is a lack of radiation exposure and higher resolution and sensitivity; however, the use of MRI is limited by the technical expertise, costs, and long acquisition time.[120] pQCT could provide a more affordable and practical alternative to the costlier imaging methods; however, the main limitations include a lower accuracy, analysis limited to peripheral anatomical sites, and provision of limited information on muscle and adiposity content.[121] Increasing evidence showed that ULT may be a reliable, accurate, and safe method to measure subcutaneous and visceral fat.[122] However, the lack of standardized methods and the high intraoperator and interoperator variability are the main limitations of this method.[122]

It became evident from this review that a single method is unlikely to provide detailed information on body components; the choice of the BC method should be guided by clinical, research, and logistic factors concerning the stage of the disease, therapeutic plans, research questions, study design, and technical and financial resources. For instance, BIA and SF thickness are easily available and not expensive, but accuracy may be limited in patients with abnormal hydration if appropriate predictive equations are not used. Multicompartment models of BC are the reference BC method as they account for between-individual differences in hydration and density, but their application has so far remained limited to research settings.[123] DXA is certainly the BC method of choice in patients with CF, as it combines the accuracy of a 3-compartment model with the opportunity to obtain information on bone health, lean body mass, and adiposity.

The ESPEN-ESPGHAN-ECFS guidelines on nutrition care for infants, children, and adults with CF clearly recommend the assessment of BC in all patients with CF; however, the degree of evidence on predictive value of BC assessment in patients with CF remains moderate.[5] Longitudinal studies are needed to better define the role of BC in the assessment of nutrition status of patients with CF. The primary aim could be to explore the predictive value of BC for functional and clinical outcomes such as growth trajectories, pulmonary function, recurrent infections, hospitalization, and life expectancy.

Monitoring the nutrition status is an important step in CF care, considering that these are patients at high risk for malnutrition.[124] BC assessment methods vary depending

on their reliability and precision. Each method presents advantages and disadvantages, so 1 unique approach may not be ideal for all circumstances. Furthermore, it is not always possible to have access to a BC method like DD or TBK in the clinical setting. Hence, it is essential to identify the best available options for the assessment of nutrition status of patients with CF in a defined clinical context. DXA provides useful information on FM, FFM, and bone mineral mass, which need to be monitored in subjects with CF and could therefore represent the BC method of choice. DXA is a safe technology, and the dose of ionizing radiation of current instrumentation is below background levels, highlighting the importance of using to evaluate DXA not only the bone health but also total BC. However, monitoring changes in body weight and height (in pediatric populations) or assessment of BC using BIA during routine follow-up visits could also provide information for an early detection of changes in nutrition status.

The mainstay of this review are to include a comprehensive search strategy and no restriction of the search to a specific study design, BC parameters, or method. In addition, the present review includes studies presented as abstracts only, which has further broadened the representativeness of the results. The main limitation of the review is its narrative form, providing only a qualitative assessment of the studies. The large heterogeneity of the studies for BC methods, clinical outcomes, and study design prevented the conduction of a meta-analysis of the results.

## Conclusions

The results showed great variability in the methods used to evaluate BC in patients with CF. As a consequence, clear conclusions cannot be drawn to propose an evidence-based algorithm to assist with the assessment of BC in patients with CF. However, DXA and BIA remain the most frequently applied methods and currently represent, in our opinion, the preferred choice to assess and monitor BC changes in this population.

### Statement of Authorship

M. Siervo, G. Valerio, and P. Calella equally contributed to the conception and design of the research; L. M. Donini and M. Brodlie contributed to the design of the research; P. Calella and J. Taylor contributed to the acquisition and analysis of the data; M. Siervo and L. M. Donini contributed to the analysis of the data; M. Siervo, L. M. Donini, and P. Calella contributed to the interpretation of the data. All authors drafted the manuscript, critically revised the manuscript, agree to be fully accountable for ensuring the integrity and accuracy of the work, and read and approved the final manuscript.

### Supplementary Information

Additional supporting information may be found online in the Supporting Information section at the end of the article.

## References


1. Fanen P, Wohlhuter-Haddad A, Hinzpeter A. Genetics of cystic fibrosis: CFTR mutation classifications toward genotype-based CF therapies. *Int J Biochem Cell Biol*. 2014;52:94-102.
2. Dodge JA, Lewis PA, Stanton M, Wilsher J. Cystic fibrosis mortality and survival in the UK: 1947-2003. *Eur Respir J*. 2007;29(3):522-526.
3. Lai H, Kosorok M, Sondel S. Growth status in children with cystic fibrosis based on the National Cystic Fibrosis Patient Registry data: evaluation of various criteria used to identify malnutrition. *J Pediatr*. 1998;132(3):478-485.
4. Scaparrotta A, Di Pillo S, Attanasi M, et al. Growth failure in children with cystic fibrosis. *J Pediatr Endocrinol Metab*. 2012;25(5-6):393-405.
5. Turck D, Braegger CP, Colombo C, et al. ESPEN-ESPGHAN-ECFS guidelines on nutrition care for infants, children, and adults with cystic fibrosis. *Clin Nutr*. 2016;35(3):1-21.
6. World Health Organization. *Diet, nutrition and the prevention of chronic diseases: report of a Joint WHO/FAO Expert Consultation*. Geneva, Switzerland: World Health Organization, 2003:54-71.
7. Mattsson S, Thomas BJ. Development of methods for body composition studies. *Phys Med Biol*. 2006;51(13):R203-R228.
8. Enright S, Chatham K, Ionescu AA, Unnithan VB, Shale DJ. The influence of body composition on respiratory muscle, lung function and diaphragm thickness in adults with cystic fibrosis. *J Cyst Fibros*. 2007;6(6):384-390.
9. King SJ, Nyulasi IB, Strauss BJG, Kotsimbos T, Bailey M, Wilson JW. Fat-free mass depletion in cystic fibrosis: associated with lung disease severity but poorly detected by body mass index. *Nutrition*. 2010;26(7-8):753-759.
10. Charatsi AM, Dusser P, Freund R, et al. Bioelectrical impedance in young patients with cystic fibrosis: validation of a specific equation and clinical relevance. *J Cyst Fibros*. 2016;15(6):825-833.
11. Williams J, Wells J, Wilson C, Haroun D, Lucas A, Fewtrell M. Evaluation of Lunar Prodigy dual-energy X-ray absorptiometry for assessing body composition in healthy individuals and patients by comparison with the four-component model. *Am J Clin Nutr*. 2005;68:1047-1054.
12. Liberati A, Altman DG, Tetzlaff J, et al. The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate health care interventions: explanation and elaboration. *J Clin Epidemiol*. 2009;62(10):e1-34.
13. Downs S, Black N. The feasibility of creating a checklist for the assessment of the methodological quality of health care interventions. *J Epidemiol Community Heal*. 1998;52:377-384.
14. Bianchi ML, Limonta C, Vai S, Colombo C. Body composition in children and adolescents affected by different chronic diseases. *Bone*. 2009;45(2009):S65-S66.
15. Karthika J, D'Souza G, Devaraj U. European Respiratory Society Annual Congress. *Med Pulm Med*. 2012;34:2012.
16. Brookes DSK, Briody JN, Munns CF, Hill RJ, Davies PSW. Bone structural parameters in pre and pubertal individuals with cystic fibrosis (CF). *Osteoporos Int*. 2011;22(4):S663.
17. Mailhot G. Bone quality in end-stage cystic fibrosis patients. *Pediatr Pulmonol*. 2014;49:E140.
18. Marostica P, Souza R, Baptista R, et al. Ultrasound and adipometer body fat measurement of cystic fibrosis (CF) children and adolescents. *J Cyst Fibros*. 2015;14:S116.
19. Sheikh S, Zemel B, Stallings V, Rubenstein R, Kelly A. The association of lean body mass with pulmonary function in cystic fibrosis. *Am J Respir Crit Care Med*. 2012;185:A5264.
20. Proud D, Rezaie M, Stoakes A, Ketchell I, Duckers J. 254 Body composition; expect the unexpected! *J Cyst Fibros*. 2012;11:S121.
21. Oldroyd B, Rhodes L, Wolfe S, et al. Longitudinal changes in growth, bone parameters and body composition indices in six male paediatric patients with cystic fibrosis. *Bone*. 2009;45:S68.

22. Alicandro G, Battezzati A, Speziali C, Loi S, Colombo C. Accuracy of simple methods to estimate body composition in cystic fibrosis patients. *J Cyst Fibros*. 2012;11:S121.
23. Greer R, Shepherd R, Cleghorn G, Bowling FG, Holt T. Evaluation of growth and changes in body composition following neonatal diagnosis of cystic fibrosis. *J Pediatr Gastroenterol Nutr*. 1991;13(1):52-58.
24. Sheperd RW, Holt TL, Greer R, Cleghorn GJ, Thomas BJ. Total body potassium in cystic fibrosis. *J Pediatr Gastroenterol Nutr*. 1989;9: 200-205.
25. Alicandro G, Bisogno A, Battezzati A, Bianchi ML, Corti F, Colombo C. Recurrent pulmonary exacerbations are associated with low fat free mass and low bone mineral density in young adults with cystic fibrosis. *J Cyst Fibros*. 2014;13(3):328-334.
26. Baker JF, Putman MS, Herlyn K, Tillotson AP, Finkelstein JS, Merkel PA. Body composition, lung function, and prevalent and progressive bone deficits among adults with cystic fibrosis. *Jt Bone Spine*. 2016;83(2):207-211.
27. Borowitz, D., Conboy K. Are bioelectric impedance measurements valid in patients with cystic fibrosis? *J Pediatr Gastroenterol Nutr*. 1994;18(4):453-456.
28. Cemlyn-Jones J, Gamboa F, Loureiro M, Baganha MF. Evaluation of bone mineral density in cystic fibrosis patients. *Rev Port Pneumol*. 2008;14(5):625-634.
29. Driscoll MO, Daniels T. Characterisation of the bone health status by dexa scanning of adult cf patients attending a regional UK centre. *Pediatr Pulmonol*. 2017;50:416.
30. Gronowitz E, Garemo M, Lindblad A, Mellstrom D, Strandvik B. Decreased bone mineral density in normal-growing patients with cystic fibrosis. *Acta Paediatr Int J Paediatr*. 2003;92(6):688-693.
31. Hollander FM, De Roos NM, De Vries JHM, Van Berkhout FT. Assessment of nutritional status in adult patients with cystic fibrosis: Whole-body bioimpedance vs body mass index, skinfolds, and leg-to-leg bioimpedance. *J Am Diet Assoc*. 2005;105(4):549-555.
32. King S, Wilson J, Kotsimbos T, Bailey M, Nyulasi I. Body composition assessment in adults with cystic fibrosis: Comparison of dual-energy X-ray absorptiometry with skinfolds and bioelectrical impedance analysis. *Nutrition*. 2005;21(11):1087-1094.
33. Prais D. The role of quantitative ultrasound in the evaluation of CF related bone status. *Pediatr Pulmonol*. 2010;45:S33.
34. Proud D, Rezaie M, Ketchell RI, Lau D, Duckers J. 196 Change in body composition pre and post lung transplant in adult CF patients. *J Cyst Fibros*. 2016;15:S101.
35. Sheikh S, Gemma S, Patel A. Factors associated with low bone mineral density in patients with cystic fibrosis. *J Bone Miner Metab*. 2015;33(2):180-185.
36. Tejero S, Cejudo P, Quintana-Gallego E, Sañudo B, Oliva-Pascual-Vaca A. The role of daily physical activity and nutritional status on bone turnover in cystic fibrosis: a cross-sectional study. *Brazilian J Phys Ther*. 2016;20(3):206-212.
37. Ziai S, Coriati A, Chabot K, Mailhot M, Richter MV, Rabasa-Lhoret R. Agreement of bioelectric impedance analysis and dual-energy X-ray absorptiometry for body composition evaluation in adults with cystic fibrosis. *J Cyst Fibros*. 2014;13(5):585-588.
38. Beaumesnil M, Chaillou E, Wagner AC, Rouquette A, Audran M, Giniès JL. Composition corporelle des patients mucoviscidosiques – comparaison de 3 techniques de mesure: Anthropometrie, absorptiometrie biphotonique et impedancemetrie. *Arch Pediatr*. 2011;18(4):370-375.
39. Hardin DS, Arumugam R, Seilheimer DK, LeBlanc A. Normal bone mineral density in cystic fibrosis. *Arch Dis Child*. 2001;84(4):363-368.
40. Swisher AK, Yeater R, Moffett K, Baer L, Stanton B. A comparison of methods to determine body fat in individuals with cysticfibrosis: a pilot study. *J Exerc Physiol Online*. 2003;6(2):105-114.
41. Hilton NP, Morris AR, Walshaw MJ, Greenwood J, Ledson MJ. WS21.5 The use of serum creatinine to estimate skeletal muscle mass in cystic fibrosis. *J Cyst Fibros*. 2015;14:S40.
42. Solarino G, Vicenti G, Spinarelli A, Abate A, Carrozzo M, Cagnetta VMB. Assessing bone mineral density in Italian adult cystic fibrosis patients: a cross sectional study. *J Biol Regul Homeost Agents*. 2015;29:79-85.
43. Tierney AC, Edgeworth D, Williams E, et al. Ivacaftor and its effects on body composition in adults with G551D related cystic fibrosis. *J Cyst Fibros*. 2015;14:S50.
44. Williams J, Crabtree N, Benden C, Suri R, Jaffe A, Fewtrell M. Longitudinal changes in bone mass in children with cystic fibrosis: effect of size adjustment using bone mineral apparent density. *Arch Dis Child*. 2010;95(1):95-97.
45. Alexia J. Murphy, Alford, RJ, Hill DP. Body cell mass in children with clinical conditions. *Eur J Clin Nutr*. 2015;69:S10-S19.
46. Bisogno A, Alicandro G, Bianchi ML, Colombo C. 273 Low fat free mass index is a risk factor for hospitalization in adult patients with cystic fibrosis. *J Cyst Fibros*. 2013;12:S118.
47. Roddy M, Elnazir B, McDonnell C, Nadeem M, Greally P. The bone mineral density of children with CF. *Bone Abstr*. 2013;2:177.
48. Nadeem M. Longitudinal changes in bone mineral density (BMD) in young people with cystic fibrosis (CF). *Ir J Med Sci*. 2010; 179:S12.
49. Jaksic M, Sharma S, Fenwick S, Cundy T, Byrnes C. Bone mineral density, bone mass acquisition and nutritional status in children and adolescents with cystic fibrosis. *J Cyst Fibros*. 2016;15:S100.
50. Bianchi ML, Romano G, Saraifoger S, Costantini D, Limonta C, Colombo C. BMD and body composition in children and young patients affected by cystic fibrosis. *J Bone Miner Res*. 2006;21(3): 388-396.
51. De Meer K, Gulmans VA, Westerterp KR, Houwen RH, Berger R. Skinfold measurements in children with cystic fibrosis: monitoring fat-free mass and exercise effects. *Eur J Pediatr*. 1999;158(10): 800-806.
52. King SJ, Nyulasi IB, Bailey M, Kotsimbos T, Wilson JW. Loss of fat-free mass over four years in adult cystic fibrosis is associated with high serum interleukin-6 levels but not tumour necrosis factor-alpha. *Clin Nutr*. 2014;33(1):150-155.
53. Stettler N, Kawachak DA, Boyle LL, et al. A prospective study of body composition changes in children with cystic fibrosis. *Ann NY Acad Sci*. 2000;904:406-409.
54. Ujhelyi R, Treszl A, Vasarhelyi B, et al. Bone mineral density and bone acquisition in children and young adults with cystic fibrosis: a follow-up study. *J Pediatr Gastroenterol Nutr*. 2004;38(4):401-406.
55. Williams JE. Body composition in young children with cystic fibrosis. *World Rev Nutr Diet*. 2013;106:168-173.
56. Puiman PJ, Francis P, Buntain H, Wainwright C, Masters B, Davies PSW. Total body water in children with cystic fibrosis using bioelectrical impedance. *J Cyst Fibros*. 2004;3(4):243-247.
57. Djeddi D. Influence of body composition on FEV(1), FEV(6), FEV(1)/FEV(6) and peak expiratory flow rate. *J Pediatr Gastroenterol Nutr*. 2010;50:E1-E217.
58. Scott DG, Atlas A, Goyette A, Bustami R. Validation of hand-to-foot bioelectrical impedance analysis with air-displacement plethysmography in the assessment of body composition in pediatric cystic fibrosis patients. *Pediatr Pulmonol*. 2012;47:314.
59. Junge S, Stein L, Schluter K, Hoyng C. Phase angle (PA) from bioelectrical impedance analysis (BIA) in children with cystic fibrosis (CF). *J Cyst Fibros*. 2012;11:S121.
60. Almajan-Guta B, Avram C, Rusu A, et al. Improvement of body composition parameters after an individualized training program in young patients with CF. *J Cyst Fibros*. 2012;11:S107.

61. Hatziagorou E, Katseni V, Karagiozoglou-Lampoudi T, Lampoudis D, Tsanakas J. Conventional and novel assessment tools for the evaluation of nutrition status of children with cystic fibrosis. *J Cyst Fibros*. 2013;12:S119.
62. Svekusova M, Feketeova A, Podracka L. 284 Bioimpedance spectroscopy-derived body composition indices reveal lean tissue mass depletion in pediatrie cystic fibrosis patients. *J Cyst Fibros*. 2011;10(1):S72.
63. Proud D, Rezaie M, Ketchell RI, Lau D, Duckers J. 191 Test–retest reliability of bioelectrical impedance and hand grip strength over 1 year in adult patients with cystic fibrosis. *J Cyst Fibros*. 2016;15: S99-S100.
64. King SJ, Sekuloska Z, Gallo R, et al. 210 Changes in the nutritional status and dietary intake of adults with cystic fibrosis since 1997. *J Cyst Fibros*. 2014;13:S100.
65. Forte GC, Pereira JS, Drehmer M, Simon MI. Anthropometric and dietary intake indicators as predictors of pulmonary function in cystic fibrosis patients. *J Bras Pneumol*. 2012;38(4):470-476.
66. Ionescu AA, Chatham K, Davies CA, Nixon LS, Enright S, Shale DJ. Inspiratory muscle function and body composition in cystic fibrosis. *Am J Respir Crit Care Med*. 1998;158(4):1271-1276.
67. Miller M, Ward L, Thomas BJ, Cooksley WG, Shepherd RW. Altered body composition and muscle protein degradation in nutritionally growth-retarded children with cystic fibrosis. *Am J Clin Nutr*. 1982;36(3):492-499.
68. McNaughton SA, Shepherd RW, Greer RG, Cleghorn GJ, Thomas BJ. Nutritional status of children with cystic fibrosis measured by total body potassium as a marker of body cell mass: lack of sensitivity of anthropometric measures. *J Pediatr*. 2000;136(2):188-194.
69. Thomson M, Bucolo S, Thomas B, Holt T, Shepherd R. The body cell mass and altered protein energy metabolism in cystic fibrosis. *Asia Pac J Clin Nutr*. 1995;4(1):141-142.
70. De Waele D, Biervliet V, Louis, O, et al. Quantitative ultrasound results at the fore-arm are independent of anthropometry in children and adolescents with cystic fibrosis. *Osteoporos Int*. 2013;24(7):2015-2024.
71. Bai W, Binkley TL, Wallace JW, Carver TW, Specker BL. Peripheral quantitative computed tomography (pQCT) bone measurements in children with cystic fibrosis. *Pediatr Pulmonol*. 2016;51(1):28-33.
72. Brookes DSK, Briody JN, Munns CF, Davies PSW, Hill RJ. Cystic fibrosis-related bone disease in children: examination of peripheral quantitative computed tomography (pQCT) data. *J Cyst Fibros*. 2015;14(5):668-677.
73. Alvarez JA, Ziegler TR, Millson EC, Stecenko AA. Body composition and lung function in cystic fibrosis and their association with adiposity and normal-weight obesity. *Nutrition*. 2016;32(4):447-452.
74. Gruet M, Decorte N, Mely L, et al. Skeletal muscle contractility and fatigability in adults with cystic fibrosis. *J Cyst Fibros*. 2016;15(1): e1-e8.
75. Dusser P, Elie C, Nguyen HA, Sermet-Gaudelus I. WS16.8 Validation of bioelectrical impedance for routine monitoring of nutritional status in cystic fibrosis patients. *J Cyst Fibros*. 2013;12:S33.
76. Azcue M, Fried M, Pencharz PB. Use of bioelectrical impedance analysis to measure total body water in patients with cystic fibrosis. *J Pediatr Gastroenterol Nutr*. 1993;16(4):440-445.
77. Hatziagorou E, Christoforidis A, Avramidou V. Bone mineral density and quantitative ultrasound in children and adolescents with cystic fibrosis. *J Cyst Fibros*. 2010;9:S84.
78. Quirk P, Ward LC, Thomas BJ, Holt TL, Shepherd RW, Cornish BH. Multiple frequency bioelectrical impedance for the prediction of total body potassium in cystic fibrosis. *Clin Nutr*. 1995;14(6): 348-353.
79. Slosman DO. Assessment of whole body composition with dual energy x-ray absorptiometry. *Radiology*. 1992;185:593-598.
80. Wells GD, Heale L, Schneiderman JE, et al. Assessment of body composition in pediatric patients with cystic fibrosis. *Pediatr Pulmonol*. 2008;43(10):1025-1032.
81. De Waele, K, Louis O, Goemaere S, et al. "Can quantitative ultrasound replace bone mineral assessment by DXA or pQCT in patients with cystic fibrosis?" *Bone*. 2009;45:S73-S74.
82. Ionescu AA, Evans WD, Pettit RJ, Nixon LS, Stone MD, Shale DJ. Hidden depletion of fat-free mass and bone mineral density in adults with cystic fibrosis. *Chest*. 2003;124(6):2220-2228.
83. Quirk PC, Ward LC, Thomas BJ, Holt TL, Shepherd RW, Cornish BH. Evaluation of bioelectrical impedance for prospective nutritional assessment in cystic fibrosis. *Nutrition*. 1997;13(5):412-416.
84. Salamoni F, Roulet M, Gudinchet F, Pilet M, Thiebaud D, Burckhardt P. Bone mineral content in cystic fibrosis patients: correlation with fat-free mass. *Arch Dis Child*. 1996;74(4):314-318.
85. Spicher V, Roulet M, Schaffner C, Schutz Y. Bio-electrical impedance analysis for estimation of fat-free mass and muscle mass in cystic fibrosis patients. *Eur J Pediatr*. 1993;152:222-225.
86. Tomezsko JL, Scanlin TF, Stallings VA. Body composition of children with cystic fibrosis with mild clinical manifestations compared with normal children. *Am J Clin Nutr*. 1994;59(1):123-128.
87. Borovnicar DJ, Stroud DB, Bines JE, Haslam RHM, Strauss BJG. Comparison of total body chlorine, potassium, and water measurements in children with cystic fibrosis. *Am J Clin Nutr*. 2000;71(1): 36-43.
88. Gordon CM, Anderson EJ, Herlyn K, et al. Nutrient status of adults with cystic fibrosis. *J Am Diet Assoc*. 2007;107(12):2114-2119.
89. Groeneweg M, Tan S, Boot AM, de Jongste JC, Bouquet J, Sinaasappel M. Assessment of nutritional status in children with cystic fibrosis: conventional anthropometry and bioelectrical impedance analysis. A cross-sectional study in Dutch patients. *J Cyst Fibros*. 2002;1(4): 276-280.
90. Hauschild DB, Barbosa E, Moreira EAM, et al. Nutrition status parameters and hydration status by bioelectrical impedance vector analysis were associated with lung function impairment in children and adolescents with cystic fibrosis. *Nutr Clin Pract*. 2016;31(3): 378-386.
91. Henderson RC, Madsen CD. Bone mineral content and body composition in children and young adults with cystic fibrosis. *Pediatr Pulmonol*. 1999;27(2):80-84.
92. Henderson RC, Madsen CD. Bone density in children and adolescents with cystic fibrosis. *J Pediatr*. 1996;128(1):28-34.
93. Panagopoulou P, Fotoulaki M, Manolitsas A, Pavlitou-Tsiontsi E, Tsitouridis I, Nousia-Arvanitakis S. Adiponectin and body composition in cystic fibrosis. *J Cyst Fibros*. 2008;7(3):244-251.
94. Shepherd RW, Greer RM, McNaughton SA, Wotton M, Cleghorn GJ. Energy expenditure and the body cell mass in cystic fibrosis. *Nutrition*. 2001;17(1):22-25.
95. Marín VB, Velandia S, Hunter B, et al. Energy expenditure, nutrition status, and body composition in children with cystic fibrosis. *Nutrition*. 2004;20(2):181-186.
96. Alicandro G, Battezzati A, Bianchi ML, et al. Estimating body composition from skinfold thicknesses and bioelectrical impedance analysis in cystic fibrosis patients. *J Cyst Fibros*. 2015;14(6): 784-791.
97. Newby MJ, Keim NL, Brown DL. Body composition of adult cystic fibrosis patients and control subjects as determined by densitometry, bioelectrical impedance, total-body electrical conductivity, skinfold measurements, and deuterium oxide dilution. *Am J Clin Nutr*. 1990;52(2):209-213.
98. Williams JE, Wells JCK, Benden C, et al. Body composition assessed by the 4-component model and association with lung function in 6-12-y-old children with cystic fibrosis. *Am J Clin Nutr*. 2010;92(6): 1332-1343.

99. Culhane S, George C, Pearo B, Spoede E. Malnutrition in cystic fibrosis: a review. *Nutr Clin Pract*. 2013;28(6):676-683.
100. Debray D, Kelly D, Houwen R, Strandvik B, Colombo C. Best practice guidance for the diagnosis and management of cystic fibrosis-associated liver disease. *J Cyst Fibros*. 2011;10(2):S29-S36.
101. Li L, Somerset S. Digestive system dysfunction in cystic fibrosis: challenges for nutrition therapy. *Dig Liver Dis*. 2014;46(10):865-874.
102. Stallings VA, Stark LJ, Robinson KA, Feranchak AP, Quinton H. Evidence-based practice recommendations for nutrition-related management of children and adults with cystic fibrosis and pancreatic insufficiency: results of a systematic review. *J Am Diet Assoc*. 2008;108(5):832-839.
103. Kalnins D, Wilschanski M. Maintenance of nutritional status in patients with cystic fibrosis: new and emerging therapies. *Drug Des Devel Ther*. 2012;6:151-161.
104. Thibault R, Pichard C. The evaluation of body composition: a useful tool for clinical practice. *Ann Nutr Metab*. 2012;60(1):6-16.
105. Engelen MPKJ, Schroder R, Van der Hoorn K, Deutz NEP, Com G. Use of body mass index percentile to identify fat-free mass depletion in children with cystic fibrosis. *Clin Nutr*. 2012;31(6):927-933.
106. Ionescu AA, Nixon LS, Evans WD, et al. Bone density, body composition, and inflammatory status in cystic fibrosis. *Am J Respir Crit Care Med*. 2000;162(3):789-794.
107. Fenger R V, Gonzalez-Quintela A, Vidal C, et al. The longitudinal relationship of changes of adiposity to changes in pulmonary function and risk of asthma in a general adult population. *BMC Pulm Med*. 2014;14:208.
108. Chaves CRM, Cunha ALP. Estado nutricional e distribuição de gordura corporal em crianças e adolescentes com Fibrose Cística. *Cien Saude Colet*. 2015;20(11):3319-3328.
109. Javier R-M, Jacquot J. Bone disease in cystic fibrosis: what's new? *Joint Bone Spine*. 2011;78(5):445-450.
110. Sermet-Gaudelus I, Bianchi ML, Garabédian M, et al. European cystic fibrosis bone mineralisation guidelines. *J Cyst Fibros*. 2011;10(2):S16-S23. https://doi.org/10.1016/S1569-1993(11)60004-0.
111. Haslam RH, Borovnicar DJ, Stroud DB, Strauss BJ, Bines JE. Correlates of prepubertal bone mineral density in cystic fibrosis. *Arch Dis Child*. 2001;85(2):166-171.
112. Hardin DS, Arumugam R, Seilheimer DK, LeBlanc A, Ellis KJ. Normal bone mineral density in cystic fibrosis. *Arch Dis Child*. 2001;84(4):363-368.
113. St-Onge M-P, Wang J, Shen W, et al. Dual-energy x-ray absorptiometry-measured lean soft tissue mass: differing relation to body cell mass across the adult life span. *J Gerontol A Biol Sci Med Sci*. 2004;59(8):796-800.
114. Johnson Stoklossa CA, Forhan M, Padwal RS, Gonzalez MC, Prado CM. Practical considerations for body composition assessment of adults with class ii/iii obesity using bioelectrical impedance analysis or dual-energy x-ray absorptiometry. *Curr Obes Rep*. 2016;5(4):389-396.
115. Khalil SF, Mohktar MS, Ibrahim F. The theory and fundamentals of bioimpedance analysis in clinical status monitoring and diagnosis of diseases. *Sensors (Basel)*. 2014;14(6):10895-10928.
116. Richards ML, Bell SC, Edmiston KA, Davies PSW. Assessment of bioelectrical impedance analysis for the prediction of total body water in cystic fibrosis. *Asia Pac J Clin Nutr*. 2003;12(2):161-165.
117. Quinton PM, Bijman J. Higher bioelectric potentials due to decreased chloride absorption in the sweat glands of patients with cystic fibrosis. *N Engl J Med*. 1983;308(20):1185-1189.
118. Cruz-Jentoft AJ, Baeyens JP, Bauer JM, et al. Sarcopenia: European consensus on definition and diagnosis: report of the european working group on sarcopenia in older people. *Age Ageing*. 2010;39(4):412-423.
119. Mourtzakis M, Prado CMM, Lieffers JR, Reiman T, McCargar LJ, Baracos VE. A practical and precise approach to quantification of body composition in cancer patients using computed tomography images acquired during routine care. *Appl Physiol Nutr Metab*. 2008;33(5):997-1006.
120. Andreoli A, Garaci F, Cafarelli FP, Guglielmi G. Body composition in clinical practice. *Eur J Radiol*. 2016;85(8):1461-1468.
121. Erlandson MC, Lorbergs AL, Mathur S, Cheung AM. Muscle analysis using pQCT, DXA and MRI. *Eur J Radiol*. 2016;85(8):1505-1511.
122. Wagner DR. Ultrasound as a tool to assess body fat. *J Obes*. 2013;2:280713.
123. Müller MJ, Braun W, Pourhassan M, Geisler C, Bosy-Westphal A. Application of standards and models in body composition analysis. *Proc Nutr Soc*. 2015;75(2):181-187.
124. Ionescu AA, Nixon LS, Luzio S, et al. Pulmonary function, body composition, and protein catabolism in adults with cystic fibrosis. *Am J Respir Crit Care Med*. 2002;165(4):495-500.
125. Chirita-Emandi A. Longitudinal changes of bone mineral content in children with cystic fibrosis. *Horm Res Paediatr*. 2014;82:S1.
126. Cordioli S, Perlini S, Volpi S, D'Orazio C, Amenta G, Assael BM. Dietary intake and DXA total body measurements in children and adolescents with cystic fibrosis. *J Cyst Fibros*. 2010;9:S88.
127. Gornicka G, Kowalska M, Chojna E, et al. Bone mass in children with cystic fibrosis. *J Cyst Fibros*. 2010;9:S84.
128. Mead L, Watson H, Haworth CS, Floto RA. 205 Hand grip strength and DXA in adults with cystic fibrosis. *J Cyst Fibros*. 2015;14:S110.
129. Mielus M, Sands D, Oralewska B, Ołtarzewski M. Comparison of cystic fibrosis adolescents with normal and low bone mineral density. *J Cyst Fibros*. 2012;12:S33.
130. Rousseau-Nepton I, St-Laurent LC, Fillion M, Milot M. Cross sectional study of bone health in children with cystic fibrosis in Quebec, Canada. *J Bone Miner Res*. 2012;27:S1.
131. Simovik V. Bone health in children with cystic fibrosis. *Respirology*. 2011;16:S2.
132. Boguszewski MCS, Kamoi TO, Bento Radominski R, et al. Insulin-like growth factor-1, leptin, body composition, and clinical status interactions in children with cystic fibrosis. *Horm Res*. 2007;67(5):250-256.
133. Buntain HM, Greer RM, Schluter PJ, et al. Bone mineral density in Australian children, adolescents and adults with cystic fibrosis: a controlled cross sectional study. *Thorax*. 2004;59(2):149-155.
134. Conway SP, Oldroyd B, Brownlee KG, Wolfe SP, Truscott JG. A cross-sectional study of bone mineral density in children and adolescents attending a Cystic Fibrosis Centre. *J Cyst Fibros*. 2008;7(6):469-476.
135. Donovan DS, Jr., Papadopoulos A, Staron RB, et al. Bone mass and vitamin D deficiency in adults with advanced cystic fibrosis lung disease. *Am J Respir Crit Care Med*. 1998;157(1):1892-1899.
136. Duveau E, Beringue FI, Pellier I, Audran M, Ginies JL. Étude de la minéralisation osseuse de patients mucoviscidosiques par absorptiométrie biphotonique à rayons X. *Archives de Pédiatrie*. 1999;6(7):720-724.
137. Elkin SL, Williams L, Moore M, Hodson ME, Rutherford OM. Relationship of skeletal muscle mass, muscle strength and bone mineral density in adults with cystic fibrosis. *Clin Sci*. 2000;99(4):309-314.
138. Elkin SL, Fairney A, Burnett S, et al. Vertebral deformities and low bone mineral density in adults with cystic fibrosis: a cross-sectional study. *Osteoporos Int*. 2001;12(5):366-372.
139. Enright S, Chatham K, Ionescu AA, Unnithan VB, Shale DJ. The influence of body composition on respiratory muscle, lung function and diaphragm thickness in adults with cystic fibrosis. *J Cyst Fibros*. 2007;6(6):384-390.

140. Hatziagorou E, Christoforidis A, Avramidou V. Bone mineral density and quantitative ultrasound in adults with cystic fibrosis. *EurJEndocrinol*. 2002;146:531-536.
141. Kendler DL, Wong L, Frangolias DD, Pare PD, Raboud J, Wilcox PG. Role of exercise and nutrition status on bone mineral density in cystic fibrosis. *J Cyst Fibros*. 2003;2:163-170.
142. María R, Sánchez P, Almonacid C, et al. Estudio de la densidad mineral ósea en pacientes adultos con fibrosis quística. *Medicina Clinica*. 2004;123(3):81-84.
143. Grey AB, Ames RW, Matthews RD, Reid IR. Bone mineral density and body composition in adult patients with cystic fibrosis. *Thorax*. 1993;48(6):589-593.
144. Ionescu AA, Nixon LS, Evans WD, et al. Bone density, body composition, and inflammatory status in cystic fibrosis. *Am J Respir Crit Care Med*. 2000;162(3 Pt 1):789-794.
145. Ionescu AA, Nixon LS, Luzio S, et al. Pulmonary function, body composition, and protein catabolism in adults with cystic fibrosis. *Am J Respir Crit Care Med*. 2002;165(4):495-500.
146. Kelly A, Schall JI, Stallings VA, Zemel BS. Deficits in bone mineral content in children and adolescents with cystic fibrosis are related to height deficits. *J Clin Densitom*. 2008;11(4):581-589.
147. Lucidi V, Bizzarri C, Alghisi F, et al. Bone and body composition analyzed by Dual-energy X-ray Absorptiometry (DXA) in clinical and nutritional evaluation of young patients with cystic fibrosis: a cross-sectional study. *BMC Pediatr*. 2009;9:61.
148. Moriconi N, Kraenzlin M, Müller B, et al. Body composition and adiponectin serum concentrations in adult patients with cystic fibrosis. *J Clin Endocrinol Metab*. 2006;91(4):1586-1590.
149. Pedreira CC, Robert RGD, Dalton V, et al. Association of body composition and lung function in children with cystic fibrosis. *Pediatr Pulmonol*. 2005;39(3):276-280.
150. Putman MS, Baker JF, Uluer A, et al. Trends in bone mineral density in young adults with cystic fibrosis over a 15year period. *J Cyst Fibros*. 2015;14(4):526-532.
151. Reix P, Bellon G, Braillon P. Bone mineral and body composition alterations in paediatric cystic fibrosis patients. *Pediatr Radiol*. 2010;40(3):301-308.
152. Rochat T, Slosman DO, Pichard C, Belli DC. Body composition analysis by dual-energy x-ray absorptiometry in adults with cystic fibrosis. *Chest*. 1994;106(3):800-805.
153. Rossini M, Viapiana O, Del Marco A, de Terlizzi F, Gatti D, Adami S. Quantitative ultrasound in adults with cystic fibrosis: correlation with bone mineral density and risk of vertebral fractures. *Calcif Tissue Int*. 2007;80(1):44-49.
154. De Schepper J, Roggen I, Van Biervliet S, et al. Comparative bone status assessment by dual energy X-ray absorptiometry, peripheral quantitative computed tomography and quantitative ultrasound in adolescents and young adults with cystic fibrosis. *J Cyst Fibros*. 2012;11(2):119-124.
155. Sheikh S, Zemel BS, Stallings VA, Rubenstein RC, Kelly A. Body composition and pulmonary function in cystic fibrosis. *Front Pediatr*. 2014;2:1-7.
156. Stalvey MS, Anbar RD, Konstan MW, et al. A multi-center controlled trial of growth hormone treatment in children with cystic fibrosis1470. *Pediatr Pulmonol*. 2012;47(3):252-263.
157. Street ME, Spaggiari C, Ziveri MA, et al. Analysis of bone mineral density and turnover in patients with cystic fibrosis: associations between the IGF system and inflammatory cytokines. *Horm Res*. 2006;66(4):162-168.