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Review

The impact of cystic fibrosis on the working life of patients: A systematic review

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ABSTRACT

Advances in the treatment and management of cystic fibrosis (CF) have led to a substantial increase in patient life expectancy, thus facilitating healthier lives and labour force participation. This review aimed to address the impact of CF on the occupational functioning of patients. A significant proportion of patients were reported to retain a job on a full- or part-time schedule. Less physically demanding occupations were most frequently performed, perhaps due to CF-related inability to sustain a heavy workload. Disease severity parameters (e.g., lung function measurements, or personal, psycho-social, or economic conditions) have been reported as determinant or co-determinant factors for the development of work-related disability. Although further research is necessary, our results may be useful to inform interdisciplinary CF healthcare management, including the assessment of work function, and to define career counselling plans and workplace risk assessment and management strategies to support the personal, social and professional lives of patients.

Introduction

Cystic fibrosis (CF) has been traditionally defined as the most frequent autosomal recessive genetic disorder with severe prognosis among Caucasian populations [1]. The incidence of CF has been estimated to be approximately one sick infant for every 2,500-3,500 live births among white people [2], with a prevalence of approximately 36,000 people in the European Union [3]. However, emerging evidence has demonstrated that CF is a pan-ethnic disease, having been reported in various regions of the world, albeit with a large variability in incidence [1].

The disease is caused by mutations of the cystic fibrosis transmembrane conductance regulator (CFTR) gene, which codes for a ubiquitous glycoprotein located on the apical membrane of epithelial cells [4]. These mutations cause the generation of thick mucus that can negatively affect several tissues, leading to a variety of clinical problems, including chronic pulmonary obstruction, pancreatic insufficiency, malnutrition, or intestinal obstruction [5].

Over the last few decades, advances in CF treatment have transformed this once fatal disease of childhood into a chronic disease of adulthood, as life expectancy in CF patients has significantly improved over time. In Canada, the median age for survival among CF patients increased from 31.9 years in 1990 to 49.7 years in 2012 [6]. A child born in the year 2000 would likely be expected to survive approximately 50 years in the UK [7]. Therefore, the percentage of adults with CF continues to increase, accounting for 56% in 2019, compared to 31.1% in 1989 in the USA [8].

The increased life expectancy and the possibility of achieving healthier and more independent lives of CF patients has enhanced their labour force participation. Indeed, in 2019, approximately two-thirds of US adults with CF reported having been studying or working in full- or part-time jobs, while approximately one-quarter reported being disabled or unemployed [8]. Inevitably, this has raised issues concerning professional vocation, employment prospects, and the ability to perform certain job tasks. However, the expectation for having a job with CF must be balanced against 1) the burden of daily symptoms; 2) the need to maintain a therapeutic regime of daily exercise, physiotherapy, and numerous medications; 3) the prospect of recurring hospitalizations; and 4) the social problems imposed by a systemic, chronic, and progressive illness that may overall impact patients' routines and occupational life [3,9,10].

Therefore, the aim of our review was to provide an updated overview of the impact that CF may have on a patients' ability to function in the workplace in terms of rate of employment, profession type, capacity for work, and potential predic-

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tive factors for employment and work disability. Overall, this review has the potential to advance a more comprehensive process for risk assessment in the workplace. Taking into consideration specific inter- and intra-individual variabilities in a patients' clinical status, the intention is to assess hazardous job tasks or occupational exposures that may characterize a risk for adverse effects on the health of CF workers. Moreover, this review will contribute to more comprehensive, interdisciplinary management of the disease with the aim of improving patients' health outcomes, as well as the quality of their personal, social, and professional lives.

Materials and Methods

A systematic review was undertaken according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses Statement (PRISMA) criteria [11]. The PubMed, Scopus, and ISI Web of Science databases were searched to identify studies addressing the possible relationship between CF and functioning at work, published from 1 January 2000 up to 17 February 2021. The term "cystic fibrosis" was combined through the "AND" Boolean operator with "work" or "occupation" in order to assess the impact of CF on the capacity to function in the work environment. The two lines were additionally combined through the operator "AND" with the keywords "employment" or "work ability" or "disability" in order to assess the impact of the disease on work outcomes. All the titles and abstracts retrieved were independently analysed by two of the authors who made a selection of relevant papers for review. All types of peer-reviewed research articles (i.e., cross-sectional, cohort, case-control, or retrospective studies) published in English exploring the impact of CF on the occupational functioning of patients of working age ($\geq$ 16 years old) were included. Excluded were all non-English language publications as well as all English language reviews, book chapters, conference papers, letters to editors, meeting abstracts, and other types of publications that, despite exploring CF disease, did not provide information on work-related outcomes. The Newcastle Ottawa Scale (NOS) was used to assess the methodological quality of selected papers in order to determine whether a study had addressed the possibility of bias in its design, conduct and analysis [12,13]. The quality assessment was rated as follows: very good (9 or 10 points); good (7 or 8 points); satisfactory (5 or 6 points); or unsatisfactory (0 to 4 points). In case of disagreement between the two reviewers, the remaining authors also evaluated the article, and the judgement put forth by the majority of the reviewers determined the quality rating.

In the "Results" section, the findings of the studies are summarized with the aim of defining the impact of CF on multiple aspects of patients' occupational lives. First, the rate of employment and possible predictive factors for retaining a job are addressed. Attention is also paid to defining the type of work tasks performed by CF patients. We primarily focus on assessing those CF workers who are engaged in skilled jobs, defined as work requiring a certain set of skills and formal education, as compared to unskilled jobs, which do not require specific training. The type of worker ranges from those employed in white-collar activities, which are typically performed in an office environment and involve clerical, administrative, or managerial duties, to those employed in blue-collar jobs that include some form of manual or trade-related work. Dedicated paragraphs explore the rate of and risk factors for work disability, which is defined as long-term limitations due to severe physical or mental impairments resulting from CF that prevent patients from having gainful employment and that qualify them for social security system benefits.

Results

The preliminary search retrieved 37, 55, and 41 references from the PubMed, Scopus and ISI Web of Science databases, respectively, for a total of 133 articles. Fifty-two duplicates were removed from the total number of papers. Out of the remaining 81 articles, 66 were excluded because they did not meet the inclusion criteria based on examination of the title and abstract. A careful analysis of the reference list accompanying the selected articles was performed, although no additional relevant publications could be added to the previously detailed literature search. Overall, a total of 15 publications were retrieved for review (Figure 1). Full texts of all articles considered suitable were obtained and subjected to critical evaluation.

Regarding study design, 12 investigations were cross-sectional studies [14-25] and three were retrospective cohort studies [26-28]. Using NOS criteria, all of the searches were able to be classified, at a minimum, as being of "good quality", with three of the searches being classified with a rating of "very good quality" [18,19,26]. Upon stratification of the articles according to timing of publication, we found six papers that were published within the first decade of the time period under investigation (2000-2010) [14,15,17,18,22,23]; nine were published within the second investigated decade (2011-2021) [16,19,20,21,24-28]. Concerning the geographical setting of the studies, six were conducted in North America (four in the USA and two in Canada) [14-17,23,24], three in Australia [18,19,25], and six in Europe [20-22,26-28].

A large variability emerged in the investigation sample size, ranging from 50 to 3,458 CF patients and from 15 to 745 CF lung-transplanted (LT) survivors having been enrolled in the revised occupational studies. Concerning the representativeness of the samples, the participation rate was generally $\geq$ 50% (45-67%) of the total population presenting to the clinical centres at which the studies had been performed [16,17,18,21,22]. In some cases, CF registries representative of nearly all the affected people in a country [26] or nearly all the CF- LT patients in a specific period of time [24] were employed. More limited numbers of CF patients were able to be enrolled in studies examining LT survivors, although in all cases, authors referred to the total number of people undergoing transplant in the various hospitals during well-defined time periods [23,25-28].

With regard to demographic characteristics, the vast majority of the studies [17-22,24,28] revealed a slightly greater percentage of CF patients to have been male. The age of the investigated populations ranged from 16 to 70 years, with median and average values primarily concentrated in the age group between 19 and 35 years. Disease severity was generally assessed through pulmonary function test results, particularly the forced expiratory volume in 1 second (FEV1), expressed as the percentage of the predicted value. However, great variability was seen in this parameter, with mean percentages$\pm$standard deviations (SD) ranging from lower values of 25.4$\pm$12.2% [24] and 27.7$\pm$8.8% [14,15] in patients who had undergone or were preparing for lung transplantation, respectively, suggesting severe pulmonary function impairment, to up to 82.9$\pm$24%, representing the best values for patients under routine care [16]. The following paragraphs describe specific results of these studies in order to detail the impact of CF on the work functioning of patients and to extrapolate potential predictive factors for work disability.

3.1. Employment status

The reviewed studies demonstrated that a significant portion of CF patients retained a paid job, both on full- or part-time schedules, with a global worldwide employment rate ranging from 44% to 86% in the investigated period with comparable rates be-

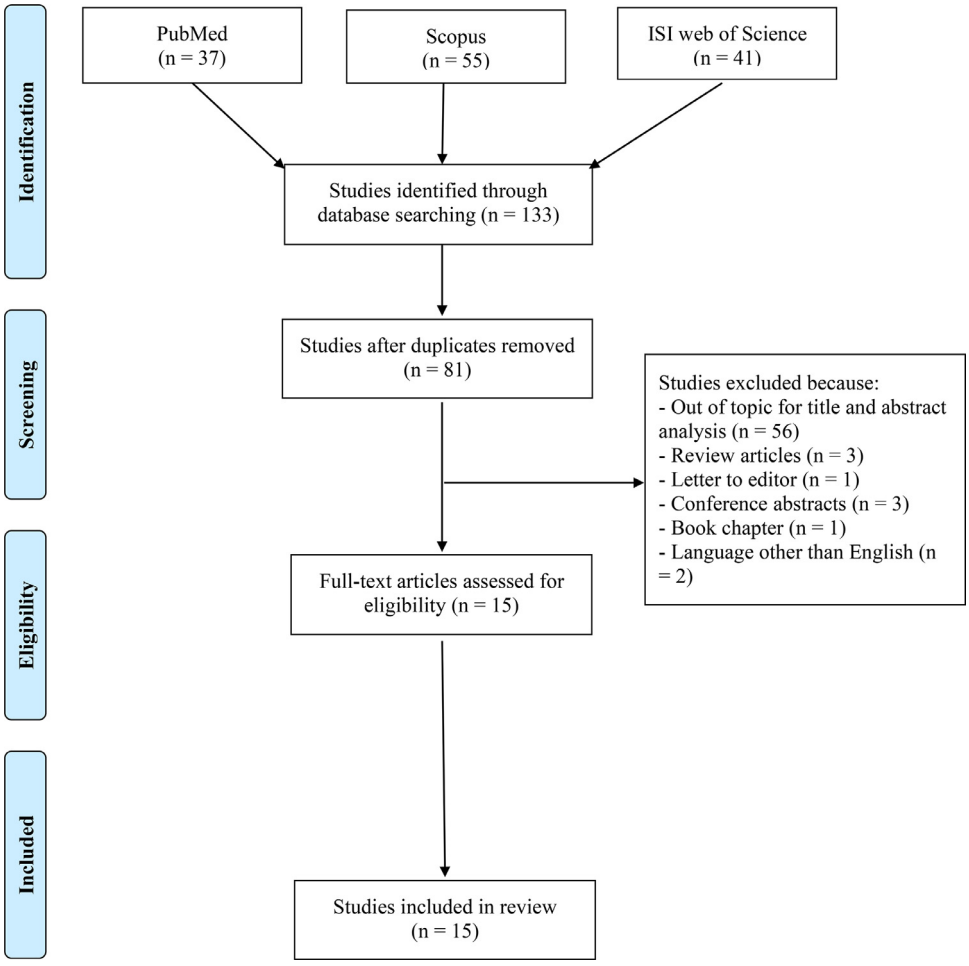

Fig. 1. Flow diagram of literature search

tween countries; there was no clear time-related trend in the two decades explored (Table 1) [14-22].

In North America, employment rates of 48% and 79% were reported in the period of 2003-2005 among US [14,15] and Canadian CF patients [17], respectively. In keeping with these latter percentages, European results demonstrated that, in 2013, 46.6% of UK CF patients held full- or part-time jobs [26], while in a subsequent study, published in 2014, 65% were reported to be either employed or pursuing education [20]. Similarly, employment percentages of 60% and 57% were determined in 2009 and 2011 in Belgian [22] and French [21] patients, respectively. Hogg et al. [18] in 2007 and Lian et al. [19] in 2019, respectively, reported slightly higher employment rates of 72% and 86% in groups of Australian patients.

In general, respondents did not feel that CF affected their employment status. In fact, only a minority of North American CF patients reported having stopped or changed any particular work or job duties due to the disease (22% and 18%, respectively) [16] or having been unemployed at the time of survey due to CF-induced poor health (12%) [17]. Among the European patients not employed and not seeking a job (18-30%), more than half revealed CF as the reason for discontinuing work or for inactivity [20,21].

Concerning the employment schedule, greater percentages (37%-68%) of working patients [14,15,17-20,22] reported having full-time jobs, while lower proportions (18%-46%) reported having part-time jobs [16,17,19]. Among CF employees with full-time jobs, 40% to 68% were engaged in activities lasting >30 hours/week [14,15,18-20]. When employment experiences were investigated according to the age of the CF patients (16-25 years old), those >22 years of age were more likely to report working >30 hours/week (65%) compared to those 21 years of age or younger (24%) [16]. In Canada, 23% of the enrolled population were employed part-time or were volunteering due to inability to maintain employment due to CF [17]. The mean number of hours worked per week by part-time Australian CF workers (18%) was 16±7 [19]. Concerning work adjustments, the vast majority of UK employed patients (92%) required some schedule rearrangement, including getting time off for appointments, adjustment of hours (30%), or working in a flexible mode (54%) or from home (17%) [20].

Regarding LT patients, employment rates ranging from 40% to 72% have been reported over the 5-year post-surgical period [21,23-25,27], a percentage comparable to that found in the general CF population [24]. The 2019 retrospective study by Ochman et al. [27] demonstrated that among 20 LT recipients in Poland, CF patients had the highest chance of employment after transplantation (40%). In a more recent study [28], the percentage of employment increased according to the post-surgical time, with values of 25% to 75% at <1 year and >10 years after lung transplantation, respectively.

3.2. Job classification

To assess the professional careers undertaken by CF patients, it is critical to understand which kind of occupational activities can be sustained by CF-affected workers and how the disease could influence employment choices and aspirations. Generally, skilled professions were represented in the vast majority of the investi-

Table 1
Demographic, clinical characteristics, and occupational outcomes in CF patients

Study Location	Study Design	CF patients	Clinical features of the disease	Occupational outcomes	Quality Rating according to NOS	Reference
North Carolina, USA	Cross-sectional	Total number: 183 (91M; 92F)	FEV1 (% of predicted) (mean±SD): 54.6±22.6% in routine CF care; 27.7±8.8% in pursuing lung transplantation	Employment rate: currently employed (~48%); patients unemployed at the time of the evaluation but employed in the past (16%). Mean hours worked/week: 32.7. Job classification: work outside the home (n= 73; 84%) or inside the home (n= 14; 16%); skilled or semi-skilled jobs (21%); unskilled jobs (6%); professional, technical or managerial occupations (53.4%); sales or clerical (29.5%); other occupations (17.1%)	Good	Burker et al. [14,15]
Boston, USA	Cross-sectional	Total number: 68 (57%F); Age (mean±SD): 19.7±2.8 years	FEV1 (% of predicted) (mean±SD): 82.9±24%. Missed workdays per month due to CF (average): 0: 53%; 1-2: 29%; 3-7: 15%; >7: 3%.	Employment rate: currently employed < 20 h/week (46%); 20-30 h/week (17%); 30-40 h/week (23%); ≥ 40 h/week (14%). Average missed work day/months due to CF: 0 (53%); 1-2 (29%); 3-7 (15%); >7 (3%). Job classification: job requiring walking or hand and arm use (41%); mostly standing (18%); mostly sitting (24%); heavy lifting or carrying (13%). Perception of the impact of CF on employment: chances for getting job [strongly agree (11%); strongly disagree (33%)]; stressful balance between employment and CF [strongly agree (11%); strongly disagree (30%)]. Career counselling: formal career counselling (2%); discussed career choice with anyone at the CF centre (16%)	Good	Demars et al. [16]
Vancouver, Canada	Cross-sectional	Total number: 73 (46M, 27F); Age (mean±SD): 29.6±1.0 years	FEV1 (% of predicted) (mean±SD): 53.4±2.7%. Shwachman-Kulczycki (S-K) scoring system (mean±SD): 67.2±2.0. Mean IV antibiotic courses in last 2 years: 1.1 ± 0.3 in employed; 2.8 ± 0.5 in employed-limited; 3.0 ± 1.1 in unemployed-limited patients	Employment rate: currently employed (n=37; 50%); employed-limited due to CF (n= 25; 34%); unemployed- limited due to CF (n= 11; 15%)	Good	Frangolias et al. [17]
Melbourne, Australia	Cross-sectional	Total number: 50 (29M, 21F); Age (mean±SD): 27.7±5.9 years	FEV1 (% of predicted) (mean±SD): 51.8±20.3%. Admission rate: 1.0±1.34	Employment rate: any employment (n= 47; 94%); currently unemployed (n=14; 28%); currently employed > 30 hours/week (n= 20; 40%); stopped work due to CF (n= 17; 34%); past job change due to CF (n= 18; 36%).	Very good	Hogg et al. [18]
Perth, Australia	Cross-sectional	Total number: 50 (29M, 21F); Median age: 30 years (range 25- 36)	FEV1 (% of predicted) (mean±SD): 60±18%	Employment rate: currently employed (n= 43; 86%); full time employed (n=34; 68%); part-time employed (n= 9; 18%); unemployed (n= 7; 14%). Mean±SD hours worked/week: 34±14 and 16±7 in full-time and part-time workers. Job classification: manager (n= 4; 9%); professional (n= 13; 30%); technician or trader (n= 7; 16%); community and personal service worker (n= 8; 19%); clerical and administrative workers (n= 7; 16%); sales workers (n= 1; 2%); machinery operators or drivers (n= 2; 5%); labourers (n= 1; 2%)	Very good	Lian et al. [19]

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Table 1 (*continued*)

Study Location	Study Design	CF patients	Clinical features of the disease	Occupational outcomes	Quality Rating according to NOS	Reference
Aberdeen, Birmingham, Newcastle, United Kingdom	Cross-sectional	Total number: 254 (137M, 117F); Median age: 26 years (range 16-70)	FEV1 (% of predicted) (mean): 60%. Median IV antibiotic courses in 12 months: 2 (range 0- 12)	Employment rate: employed (n= 112; 44%); self-employed (n= 15; 6%); in education (n= 38; 15%); not in paid employment (n= 76; 30%); full-time homemakers (n= 9; 4%); retired (n= 3; 1%); ever worked (n= 202; 80%). Median hours worked/week: 37.3 (22.0- 40.0). Not in paid employment: ever worked (71%), currently seeking a job (24%); stopped job due to CF (69%). FEV1% predicted: 63% (58.6- 67.3%) and 48% (42.7- 52.8%) in employed and not employed patients, respectively	Good	Targett et al. [20]
United Kingdom	Retrospective cohort	Total number: 3548 (2020M, 1528F); Median age: 21.5 years (IQR 20.5- 27)	FEV1 (% of predicted) (median): 65.3% (IQR 45.8- 83.7)	Employment rate: employed (n= 1613; 46.6%): unemployed (n= 1845; 53.4%)	Very good	Taylor-Robinson et al. [26]
Paris, France	Cross-sectional	Total number: 207 (107M, 100F); Age (mean±SD): 30.7±8.7 years	FEV1 (% of predicted) (mean±SD): 54.0 ± 21.8; ≥70% in n= 43 (22%); <40% in n= 57 (29%). Mean IV antibiotic courses (number/year): 1.87± 2.2. Lung transplantation: n= 11 (5.3%)	Employment rate: students (n= 39; 18.8%); employed (n= 117; 56.5%): unemployed (n= 13; 6.3%); inactive (n= 30; 15%). Not in paid employment: inactive due to CF (73%). Job classification: professionals (n= 29; 25%); intermediate positions (45; 39%); clerical professions (n= 37; 32%); blue collar workers (n= 5; 4%). CF related disability: workers considered to have limitations in their job due to CF (55%); CF prevented them from achieving a career (67%); CF was a cause of lower income (37%)	Good	Labourde-Casterot et al. [21]
Leuven, Belgium	Cross-sectional	Total number: 57 (29M, 28F); Age (mean±SD): 26.79±8.15 years	FEV1 (% of predicted) (mean±SD): 65.09±22.18. Pseudomonas aeruginosa colonization status: negative n= 13); positive non-multi-resistant (n= 20); positive multi-resistant (n= 24). Central venous implantable device: yes (n= 20); no (n= 37)	Employment rate: employed (n= 34, 60%); unemployed (n= 23, 40%). Work and medical status: working patients had a significantly higher FEV1% predicted (mean 70 vs. 57) than non-working patients. All non-working patients had Pseudomonas aeruginosa in their sputum, while among workers 13 were negative and 21 were positive. Non-working patients had a central venous implantable device and took caloric supplements significantly more often than working patients.	Good	Havermans et al. [22]
Toronto, Canada	Cross-sectional	Total lung transplanted survivors: n= 117 (57M, 60F); CF pre-transplanted diagnosis: n= 25 (22%); CF patients mean age: 34 years	NA	Employment rate in CF patients: employed (n= 18; 42% of the total lung transplanted employed subjects): unemployed (n= 7; 9% of the total lung transplanted unemployed subjects)	Good	Cicutto et al. [23]

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Table 1 (*continued*)

Study Location	Study Design	CF patients	Clinical features of the disease	Occupational outcomes	Quality Rating according to NOS	Reference
USA	Cross-sectional	CF lung transplanted survivors: n= 745 (400M, 345F); Age (mean±SD): 31.2±8.0 and 32.6±9.5 years in employed and unemployed subjects, respectively	FEV1 (% of predicted) (mean): 25.4±12.2% in employed; 27.6±15.3% in unemployed	Employment rate: employed (n= 358; 48%): unemployed (n= 387; 52%); employed females (n= 140; 39%); unemployed females (n= 205; 53%);	Good	Krivchenia et al. [24]
Melbourne, Australia	Cross-sectional	Total number of lung transplanted survivors: n= 100 (45M, 55F); CF pre-transplanted diagnosis: n= 31 (31%); Age of the total group (mean±SD): 50±13 years	NA	Employment rate in CF patients: employed (n= 17; 55% of CF subgroup)	Good	Cumming et al. [25]
Zabrze, Poland	Retrospective cohort	Total number of lung transplanted survivors: n= 67 (41M, 26F); CF pre-transplanted diagnosis: n= 15 (22.4%); Age of the total group (mean): 43 years	NA	Employment rate in CF patients: employed (n= 8; 40% of the employed survivors); unemployed (n= 7; 16.3% of the unemployed survivors)	Good	Ochman et al. [27]
Zurich, Switzerland	Retrospective cohort	CF lung transplanted survivors: n= 84 (45M, 39F); Age (mean±SD): 28.9±8.4 years	Six-minute walking test distance (mean±SD): 390.5±105.6 metres	Employment rate: <1 year, employed (n= 23; 28%), unemployed (n= 60; 72%); 1-3 years, employed (n= 51; 64%), unemployed (n= 29; 39%); 3-5 years, employed (n= 44; 75%), unemployed (n= 15; 25%); 5- 10 years, employed (n= 31; 69%), unemployed (n= 14; 31%); > 10 years, employed (n= 21; 75%), unemployed (n= 7; 25%)	Good	Radtke et al. [28]

CF, cystic fibrosis; FEV1, forced expiratory volume in one second; IQR, interquartile range; NA, not applicable; IV, intravenous; SD, standard deviation.

gated CF populations [14,15,19,21]. In Laborde-Castérot et al. [21], in fact, only 4% of the patients were involved in blue-collar activities, while professionals, intermediate positions, and clerks represented 25%, 39%, and 32%, respectively. Similar observations were previously made by Burker et al. [14,15], demonstrating that the majority of participants were engaged in professional, technical, or managerial occupations, such as teaching, law, or social work. It is also likely that skilled jobs are more easily able to accommodate different health conditions. In a more recent investigation of Australian CF patients [19], 30% were professional workers, followed by community and personal service workers (19%).

Jobs performed by CF patients were mostly sedentary or involved light physical activity (70%) [21]. When younger, 16-25-year-old CF patients were investigated regarding the characteristics of their occupation [16], a greater percentage were involved in jobs requiring physical effort, including walking or using hands and arms in moderate exertion (41%), standing (18%), or heavy lifting or carrying objects (13%), while only 24% reported that their job involved mostly sitting. Moreover, 76% of the investigated population reported that they never thought about changing jobs due to physical demands. However, the differing demographic features of the enrolled population, particularly the younger age and the prevalent part-time work experienced by these subjects, may have affected these findings.

3.3. Work disability

Work disability results from the complex interplay between biological, personal, environmental, and social factors. None of the studies specifically focused on work disability among CF patients. Conversely, all the investigations assessed either changes in job or career choices, as well as limitations in duties, or complete cessation of employment as possible indirect indicators of reduced work ability (Table 1). Hogg et al. [18] found that in half of their Australian sample (50), CF affected choice of occupation, career, or decision to seek employment. Over a third had to change specific job duties or cease work because of CF. In Laborde-Castérot et al. [21], more than half of the workers indicated that they had job limitations due to CF. More specifically, 67% and 37% thought that CF prevented them from having a career or was a cause of lower income, respectively. When a younger population was investigated by Demars et al. [16], most of the respondents (63%) disagreed on the role of CF in impacting their chance of getting a job. However, 41% agreed with the idea that balancing employment and CF care was stressful. When work disability was evaluated through assessment of absenteeism and presenteeism [19], the results showed that the CF patients attended work when expected to and rated their work performance similar to that of their co-workers.

3.4. Predictive factors for employment and work disability

Evidence related to CF factors predictive of employment and work disability is currently limited. Concerning disease severity issues, conflicting evidence was reported for lung function parameters [17,19,22,24]. In fact, while some investigations found that subjects with a higher predicted FEV1% were more likely to be employed [19,20,22], including after lung transplantation [24], Burker et al. [14] demonstrated that half of the CF population investigated was employed, although a low mean level of FEV1% was retrieved (31.9%).

Intravenous antibiotic courses, oxygen treatment, and an FEV1 less than 70% predicted were associated with a higher risk of disability according to Laborde-Castérot et al. [21], although other studies have failed to confirm these results [17,19]. In fact, Frangolias et al. [17] reported that neither changes in FEV1, resting peripheral oxygen saturation (SpO_2), nor IV antibiotic courses were useful in predicting disability. Moreover, no differences between full-time and part-time groups with respect to FEV1 and FVC values could be determined, further supporting the idea that FEV1 is a poor predictor of work disability status [19].

Additional health parameters were assessed as possible predictive factors for driving work disability, although definitive conclusions could not be extrapolated. Regarding Pseudomonas aeruginosa (PA) colonization status, Havermans et al. [22] found that a greater number of non-working patients (n=23) had PA in their sputum compared to working patients. Non-working patients more often had a central venous implantable device (PAC) and took more caloric supplements than did employed patients. In examining the energy cost of work, Frangolias et al. [17] argued that worse health conditions could be responsible for working at a higher percentage of maximal oxygen consumption. This may cause workers to perceive their jobs as more labour intensive. Indeed, a higher energy cost for work was reported by part-time, limited workers compared with the full-time, non-limited group.

However, other patient characteristics appear to be independent additional risk factors for disability, even taking into account disease severity. Laborde-Castérot et al. [21] showed that patients who were single had an increased risk for work disability. In Hogg et al. [18], the disability index was dependent on age and hospital admission rate. Interestingly, work capacity, in terms of hours worked per week, was positively correlated with age and inversely correlated with fewer hospital admissions, but not with gender. Demars et al. [16] further confirmed the positive role of age in affecting work ability. More specifically, they reported that older respondents (ages 22–25 years) more likely agreed with the statement that balancing employment and CF care was stressful compared to younger patient respondents 19–21 or 16–18 years of age (55% vs. 26% vs. 14%, respectively). However, Frangolias et al. [17] failed to confirm age, adult age at CF diagnosis, or gender as significant predictors of disability. Higher body mass index (BMI) and more days in the hospital were associated with improved and reduced employment chances, respectively [26]. Educational level has been demonstrated to be positively associated with the chance of obtaining a job [14,15,17,20,21]. Specifically, the attainment of “higher than high school education” was associated with greater odds of being employed (OR 2.96) [20], and higher levels of education were related to a greater number of hours worked per week [14,15]. Additionally, educational level was found to be inversely correlated with an increased risk for work disability [21].

Concerning the possible role of socio-economic inequality in employment outcomes, Taylor-Robinson et al. [26] demonstrated that in a cohort of CF affected patients those from the most deprived quintile were less likely to be employed compared to their counterparts in the least-deprived quintile. Deprivation appeared to modify the effects of lung function on employment chances. Indeed, having poor lung function was more damaging to the employment chances of the most disadvantaged quintile than for that of those least disadvantaged.

Discussion and conclusions

This review represents an attempt to provide an updated overview of the possible implications of CF on patients’ work function. Although the limited and fragmented data available do not allow us to extrapolate definitive conclusions, interesting issues emerged from our analyses.

The employment record of adults with CF worldwide was generally good. Almost half of the investigated patients were employed at the time of the surveys [14,17-21,26]. Although some variability could be due to the intrinsic differences among national employment markets, or healthcare or welfare provision, these data represent an overall encouraging finding. However, it cannot be ex-

cluded that such results might be related to selection bias due to a "healthy worker effect". Workers in better health might gain and maintain employment, while those with poorer health might experience unemployment to a greater degree. Currently available studies also highlight the good workforce participation of CF patients after lung transplantation [21,23-25,27,28].

Concerning the type of job performed, a greater proportion of adults with CF were employed in non-manual occupations, primarily managerial, professional, clerical, or service jobs. This may reflect the choice by patients for less physically demanding tasks due to their inability to sustain a high workload, or for professional jobs more easily modifiable given a possible decline in health [14,15,21,29]. These results may suggest that CF workers in a tertiary position are likely to be only slightly limited or not limited at all and are in line with the full-time employment reported in a significant proportion of the participants [16,17,18,20]. However, in some cases, staying employed may require flexibility at the workplace or in work schedule [18,20,21]. The physical fatigue experienced by CF patients and/or the need for a longer time to complete their care may be responsible for requiring changes at work [18,21].

With more adult patients with CF in the workplace and in light of the progressive nature of the disease, the issue of work disability inevitably arises. However, none of the studies specifically assessed the work ability in CF patients reporting some limitations in job activities, while others used job changes or cessation [16,18,20] as a proxy for the reduced ability to continue work duties. However, work disability is a multifactorial process and involves interactions among specific job characteristics (physical demands, job pace, flexibility in work schedule), the particular physical/clinical impairments of individual patients, and the ability to cope with changing physical and financial status (psychological factors and the culture of the workplace setting) [16]. This complex interplay may explain the conflicting data reported on the predictive role of illness severity measured by FEV1 [14,17,19,21,22,26], intravenous antibiotic courses [17,21], oxygen treatment [21], or the Shwachman-Kulczycki score of CF health status [18,21] on work disability. This relies on the fact that these parameters characterise only the biological impairments caused by the disease. Additionally, in this regard, further studies should investigate in depth the impact of different genetic mutations and related treatment strategies on occupational limitations. In fact, preliminary data has shown that loss in school productivity and activity impairments are significantly lower in CF students with the G551D mutation who were treated with a novel genetic CFTR modulator therapy compared to those patients with the F508del mutation managed using standard of care [30]. Some additional demographic features, including age [18] and personal characteristics, such as education [14,15,17,20] and socio-economic status [22,26], seem to play a key role in determining (or co-determining) work disability and employment status. Overall, this further supports the idea that behavioural and psychological factors, including mood and depression [14], are central to the development and course of the disease, in turn also affecting the ability to work. Indeed, from a public and occupational health policy perspective, it highlights the importance of addressing the psychosocial needs of patients and organising multidisciplinary healthcare teams to offer psychosocial support and coping skills to CF workers.

Concerning the possible impact of occupational features on the work functioning of individuals with CF, none of the reviewed studies explored in depth the role of work environments, job features, or work tasks with respect to employment or disability outcomes. Apart from type of occupation held, risk factors experienced, physical workload and work organizational issues were not addressed in the analyses. This may limit an adequate risk assessment in the workplace, suitable job counselling, and the possibility of adopting preventive and protective measures to ensure safer work conditions specifically tailored for CF patients. More deeply understanding critical issues related to the job activities impacting the work-life-disease balance may be helpful to provide guidance to formal job counselling or discussion on career choice in the routine healthcare practice of CF [5]. In this regard, it seems important to promote the relevance of a multidisciplinary approach, including occupational physicians, in order to help patients make appropriate professional choices.

Although the quality of the papers was generally good, the cross-sectional nature of the vast majority of the studies currently prevents causal inferences in the relationship between the disease and occupational impairments. In this regard, prospective investigations should be aimed at assessing the possible link between CF, taking into consideration the global ageing of patients, the variable stages of severity and treatment approaches, and differing work-related outcomes over time. This may be important to achieve a better categorisation of prognostic information and, thus, define suitable vocational and employment professional counselling. Additionally, the impact of the disease on several work-related outcomes, such as career choice, employment status, absence due to sickness, work ability, and factors predictive of disability should be addressed in a comprehensive analysis. Moreover, the limited knowledge on task requirements and occupational risk factors potentially affecting work ability and performance should be investigated together with other features of the work that may potentially influence an individual's behaviour. These may include the culture of the employment setting, the characteristics of co-workers, employer/coworkers support, disease disclosure, and workplace concerns, all of which may contribute to the ability to cope with the various stages of health status. It is important to understand how increased socialization and the resulting social support that may come from the work environment might produce health benefits.

In conclusion, although preliminary, our results stress the importance for clinicians to carefully assess the work function of their CF patients as part of routine clinical management. Now that more individuals with CF are living into adulthood, it seems even more important to understand the impact that the physical and emotional implications of CF may have on educational and vocational attainment, workforce participation, employment experiences, and career development. This may support the achievement of a multidisciplinary, comprehensive management of the disease that may include not only clinical approaches adequate to specific patient categories and aimed to obtain suitable control of pulmonary infections, PA colonization and aggressive nutritional supplementation but also adequate support of patients' occupational health. This latter approach should be finalized to adequately balance daily care demands with employment duties. The adoption of daily and monthly work timetables suitable for therapies and follow-ups, formal career counselling or job guidance related to CF, and the adaptation of workplace environments and job organization to CF patient needs, allowing work flexibility and adequate collaboration with colleagues and employers, may be useful to this aim. Overall, this may prevent negative consequences on patients' occupational lives, thus improving the social inclusion, self-esteem, financial situation, and quality of life of CF workers [17]. Understanding which job tasks could be more dangerous for CF workers may support a tailored risk assessment process and suitable management strategies that can ultimately help patients lead more productive lives, supporting their self-esteem and quality of life. All these efforts will guarantee CF patients comprehensive, interdisciplinary healthcare management. Such an approach, taking into account their need for career counselling, vocational rehabilitation guidance and job accommodation, may impact the success of how individuals balance the competing needs of seeking employment

with maintenance of health status, overall improving disease outcomes, as well as their personal, social and professional lives.

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Supplementary materials

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