Ways of coping and survival in Cystic Fibrosis: a 20-year longitudinal study

Janice Abbott[a], Margaret A. Hurley[b], Helen Chadwick[c,d], Daniel Peckham[c,d]

[a] School of Psychology, University of Central Lancashire, Preston, PR1 2HE, UK

[b] Faculty of Health, University of Central Lancashire, Preston, PR1 2HE, UK

[c] Adult Cystic Fibrosis Unit, St James's University Hospital, Leeds Teaching Hospitals NHS Trust, Leeds, LS9 7TF, United Kingdom

[d] Leeds Institute of Medical Research at St James's, University of Leeds, Leeds, LS2 9JT, UK

Corresponding author
Janice Abbott
jabbott@uclan.ac.uk

Keywords: survival; coping; optimism; Cox model.

Running Title: Coping and survival in CF

Abstract

Background: The relationship between ways of coping and health outcomes has been a focus of interest for decades. There is increasing recognition that positive psychological functioning can influence health outcomes beneficially. This work investigated the role of coping in predicting survival in CF.

Methods: A longitudinal observational cohort study with a 20-year follow-up period was undertaken. At entry to the study, demographic and clinical variables were recorded, and ways of coping were assessed using the Cystic Fibrosis Coping Scale which measures four distinct ways of coping: optimism, hopefulness, distraction and avoidance. Survival outcome was measured as time in days from the date of recruitment to exit from the study, where exit was either death, loss to follow-up or the end of the follow-up period.

Results: Survival time was modelled using Cox's proportional hazards model. At baseline, 116 people with CF were recruited. By the census date, 54 people had died (14 men had died during 248,565 person-days of observation and 40 women had died during 358,372 person-days of observation). Optimism was the only way of coping that showed any beneficial effect on survival (RR=0.984, p=0.040) after adjustments for age, gender, $ppFEV_1$ and the three other coping variables measured at baseline.

Conclusion: This work suggests that optimistic coping serves as a prognostic measure of survival in CF beyond key clinical and demographic variables. Ways of coping are modifiable, providing a target for clinical intervention; to improve quality of life and clinical outcomes and potentially increase longevity.

1. Introduction

There are many factors which contribute differentially to survival among people with cystic fibrosis (CF). This includes the Cystic Fibrosis Transmembrane Regulator (CFTR) genotype, severity of lung disease, airway microbiology, number of exacerbations per year, nutritional status, diabetes, gender, birth cohort, age at diagnosis and new-born screening (1-10). Nonclinical variables are also independently predictive of disease progression and survival, including household income/socioeconomic status (SES), and the complex perceptions patients have around how SES affects their health care (11-13). Additionally, the 5-year mortality of patients who screen positive for depression can be twice as high as in those who screen negative (14). Domains of patient-reported health-related quality of life (HRQoL) have also been shown to predict survival beyond key clinical and demographic variables (15).

The interplay between clinical and psychological variables, such as optimism, are important as they influence health outcome. Worldwide, several large cohort studies of people free from disease have demonstrated that dispositional optimism (the extent to which people have positive expectations about their future) predicts longevity (16-18). Data from two US cohort studies; women from the Nurses' Health Study (19) and men from the Veterans Affairs Normative Aging Study (20), followed-up for 10 years and 30 years respectively, noted that individuals with the highest optimism levels, compared to those with the lowest optimism levels, had 1.7 (males) and 1.5 (females) greater odds of surviving to age 85. In both cohorts there was a tendency towards a dose-dependent association of higher baseline optimism levels with increased longevity. Importantly, these relationships remained after adjusting for health behaviours (21). Additionally, a recent meta-analysis of 229,391 participants across 15 studies with a mean follow-up of 13.8 years, indicated that optimistic coping was associated with a lower risk of cardiovascular events and all-cause mortality (22). When examining lung function in healthy men, those with higher levels of optimism had higher predicted forced expiry volume in one second (ppFEV$_1$%) and the decline in ppFEV$_1$% over time was slower (23).

When researchers have evaluated whether optimism predicts mortality in people with existing health conditions, the results are less conclusive (24). This may be due to more complex methodology and the use of generic, rather than condition-specific measures of optimism. Despite the scarcity of studies, there is growing evidence that optimism influences clinical outcomes. Meta-analyses of the association between optimism and chronic conditions report accumulating evidence that optimistic cardiac patients have better disease outcomes including survival, although the evidence in cancer patients is less clear (22,25). The focus has tended to be solely on optimism, rather than on a range of different mindsets/ways of coping, and in part, this is due to the lack of scales available to measure such concepts. A variety of ad hoc and validated generic optimism scales have been employed (25-

26). Nonetheless, dispositional optimism has been consistently found to be positively associated with approach/problem-focused coping strategies, while pessimists engaged in more emotion-focused coping (26).

Adults with CF are continually faced with both short-term and chronic difficulties of varying complexity and controllability (27-28). Recent emphasis has largely focused on negative psychological functioning such as depression and anxiety and how these states negatively impact quality of life and clinical outcomes (29). However, there is increasing recognition that positive psychological functioning, for example, optimism, acceptance, hope and resilience can also influence health (30-31). If a person has good psychological health, their ways of coping with CF (their thoughts, emotions, actions) are considered adaptive and the way they cope affects how they report their adherence to treatments and health-related quality of life (HRQoL) (30-31). Generally, coping with CF in an optimistic way was associated with better HRQoL. High levels of distraction coping (trying to forget CF) were linked to depression and associated with poorer HRQoL (31). The associations between ways of coping and survival have not been evaluated in CF. Such research is important as ineffective and harmful ways of coping are modifiable and provide a target for clinical intervention; to improve HRQoL, clinical outcomes and potentially increase longevity (32). This work evaluates the role of specific ways of coping in predicting survival in CF. An optimistic way of coping was hypothesised to be associated with increased survival in CF.

2. Methods

2.1 Design

A longitudinal observational cohort study with a 20-year follow-up period was undertaken.

2.2 Participants and procedure

Consecutive patients who attended an Adult CF Unit in the UK, between June and September 1999, were recruited. Baseline assessments occurred during an out-patient clinic visit whilst patients were clinically stable. Demographic (age, gender), coping and clinical variables were recorded (ppFEV$_1$, BMI, IV access device fitted, B. *Cepacia* Complex [present, absent], Diabetes [present, absent], Nutritional status [no oral calorie supplements prescribed, oral calorie supplements or prescribed enteral tube feeding], and transplant status [not on waiting list, on waiting list or post-transplant]). The Local Research Ethics Committee approved the study and patients gave consent to continue accessing their clinical records for research purposes, and these have been accessed to identify their vital status on 31st December 2019.

2.3 Measures

2.3.1 Survival

Survival outcome was measured as time in days from the date of recruitment to exit from the study where exit was either (a) death, (b) loss to follow-up before 31st December 2019, or (c) the end of the follow-up period on 31st December 2019. Patients exit from the study was flagged as deceased or alive at exit time. Patients whose exit status was unknown on 31st December 2019 were flagged as alive on the date of their last known attendance at the CF Unit.

2.3.2 Coping

Coping was measured at recruitment (baseline) using the Cystic Fibrosis Coping Scale (30-31). This is a disease-specific, patient-derived, validated scale that aligns with Patient Reported Outcome guidance (33). The CF-specific scale enabled patients with CF (pwCF) a role in the development of the scale and ensured that each item was important and meaningful to them. The scale conceptualises coping as a person's cognitive, emotional and behavioural effort to deal with CF disease and its treatment burden. Hence, the scale's theoretical approach is consistent with that of Holohan and Moos (34) and Moos and Schafer (35) in which the method (*cognitive, emotional, behavioural*) and focus (*approach* – focusing attention on CF, *avoidance* – diverting attention away from CF) of coping is considered. The subscale items and their theoretical approach are presented in Table 1. Content validity was achieved from interviews with 143 pwCF, which focused on their CF concerns and the ways of coping used to manage them. Patient's comments informed the generation of the items and the response scale. Construct validity was established following two rounds of questionnaire administration and critical feedback from pwCF (n=174; n=116). Principal component analysis with varimax rotation verified the most meaningful items for pwCF. Four independent factors (scales) were determined, accounting for 76% of the variance. Twenty items measured four distinct ways of coping with CF: optimism (7 items), hopefulness (6 items), distraction (5 items) and avoidance (2 items). Internal reliability measured by Cronbach alpha coefficients was good: optimism (α 0.81), hopefulness (α 0.75), distraction (α 0.74), and avoidance (r=0.72). Test-retest reliability evaluated by Cohen's kappa confirmed the stability of the measure: optimism (k 0.94), hopefulness (k 0.91), distraction (k 0.89), and avoidance (k 0.87). Patients were asked to rate, on a four-point scale, the extent to which they employed each coping strategy (not at all, a little, a moderate amount, a great deal). Scores are calculated for each way of coping and then transformed into values of between 0 and 100 to enable comparison. Higher scores represent greater levels of optimistic, hopefulness, distraction and avoidant coping. These coping data were used as baseline measures to explore the prognostic association between the specific ways of coping and survival. The internal reliability of these measures is excellent in this data set (Cronbach alpha coefficients; optimism (.90), distraction (.84), hopeful (.81) and avoidance (.79).

2.4 Statistical methods

Patient baseline characteristics were described using summary statistics and the t-test and Fisher's exact test were used to compare men and women patients. Pearson's correlations were obtained between the four measures of optimistic, hopefulness, distraction and avoidance coping together with age and $ppFEV_1$ to understand the extent to which these measures were related.

Survival time was modelled using Cox's proportional hazards model (36). The measures of optimistic, hopefulness, distraction and avoidance coping were included together in the analyses of survival time. Analyses used adjustment for age, gender and $ppFEV_1$ at baseline as appropriate. Adjustments for age and gender were needed, a priori, because survival time inevitably depends on the age of the patient (the start of the measured survival time) and, generally, men and women have different average life expectancies. $PpFEV_1$ was included as the main clinical variable likely to influence survival and was deemed to provide a proxy measure for disease severity. Thus, an adjusted analysis which includes all four coping measures allows for the effect of one coping measure to be independently assessed having adjusted for the other coping measures as well as for age, gender and disease severity.

3. **Results**

3.1 Study participants

At baseline, 44 men and 72 women were recruited. By the census date of 31st December 2019, 14 men had died during 248,565 person-days of observation and 40 women has died during 358,372 person-days of observation. Optimistic coping was the most used strategy for pwCF although most respondents employed all four ways of coping to varying degrees (Table 2).

3.2 Baseline characteristics by gender

Patient baseline characteristics, separated by gender, are shown in Table 2. Men and women had similar mean ages. There were differences in access device fitted and in use of supplements and enteral tube feeding. Women had a significantly higher score for distraction coping (p=0.011). There was some evidence that women also had a higher mean score for hopefulness coping (p=0.098). Optimistic coping and avoidance coping were on average similar for men and women.

3.3 Correlations between clinical and coping measures at baseline

Correlations between age, $ppFEV_1$ and the four coping measures at baseline are shown in Table 3. There were associations between optimistic and hopefulness coping (0.342 for men and 0.470 for women), between hopefulness and distraction coping (0.345 for men and 0.439 for women) and for women only, between distraction and avoidance coping (0.249 for men and 0.415 for women) and

between optimistic and distraction coping (0.015 for men and 0.345 for women). There was no association between age and coping measures. There was some negative association between $ppFEV_1$ and distraction which occurred because a few men had very high $ppFEV_1$ but low distraction. The presence of correlation between the coping measures justified the need for survival models to include all coping measures together. The correlation between age and $ppFEV_1$ at baseline was negligible indicating that these are unlikely to be confounded cross-sectionally.

3.4 Adjusted Cox models by gender and for pooled data

Adjusted Cox models for men and women separately are shown in Table 4. Results are expressed as relative risk (RR) where RR measures the degree to which the risk of in one group is magnified or reduced relative to another group (such as women compared to men) or the degree to which the risk is magnified or reduced for each increase of one unit in a covariate (such as $ppFEV_1$). A RR greater than one represents increased risk whereas a RR less than one represents a decreased risk. The RR of the coping measures and $ppFEV_1$ were very similar for men and women. The effect of increasing age cross-sectionally at baseline was not significant for men or for women. Separate models for men and women showed no significant effect of the hopefulness, distraction and avoidance coping measures. However, there was an indication of an effect of optimistic coping. These separate models for men and women were likely to be underpowered since only 14 men and 40 women had died. Therefore, the survival data were pooled for men and women and modelled with common coefficients for the coping measures, $ppFEV_1$ and age but separate coefficients for gender (Table 4). In the model for the pooled data, the RR for women was estimated as 1.4 times that for men although the 95% confidence interval was wide. As would be expected $ppFEV_1$ was highly significant ($p<0.001$). Optimistic coping was the only coping measure that showed any beneficial effect on survival (RR=0.984, p=0.040) after having made adjustment for age, gender, $ppFEV_1$ and the three other coping measures.

3.5 Predicted survival curves by gender

The effect of optimistic coping on survival was illustrated by plotting separate predicted survival curves for men and women with above average and below average optimism levels (a score of 68 was the mean value for both groups to two significant figures). The predictions were obtained using mean values of 25.2 years for age, 58.5 for $ppFEV_1$, and scores of 40.9, 38.0 and 46.1 respectively for hopefulness, distraction and avoidance coping (Fig.1). Men with above average optimism had visibly better survival than those with below average optimism and the same was demonstrated for women. However, the difference in survival between those having above and below average optimism was greater for women than for men and women with below average optimism showed the poorest survival of all.

4. Discussion

Psychological processes and behaviour can have powerful impacts on physical health and ultimately survival. In multivariate models, optimistic coping was the only way of coping that emerged as a predictor of survival for people with CF. Those who reported above average levels of optimism when dealing with their progressive disease and high treatment regimen had better survival. These data echo the emerging literature in other conditions (24-25). The male survival advantage seen in the data is well documented in CF (37) and although females employed more distraction coping than males, this way of coping had no bearing on survival. There was insufficient data to model the survival of men and women separately, but the data suggests that there is a gender difference, with women who report below average optimism having a larger differential survival with poorer outcome. This is potentially due to negative thoughts and behaviours characteristic of depressive symptoms which is associated with poorer survival in people with CF (14)

Explanations for the optimistic-survival association may emanate from a combination of behavioural, cognitive, and biological mechanisms. It is noteworthy that optimistic coping was the most used strategy for people with CF. Behavioural mechanisms are likely to be important given that optimists appear to lead healthier lifestyles. In both cross-sectional and longitudinal work, those employing optimistic coping had more appropriate health behaviours (38-39), and they were more likely to set goals and take proactive steps to protect their health (40-41). Indeed, in CF, optimistic coping has been associated with better adherence to treatments (30). Optimists generate more supportive social networks, creating buffers to stressful life events (42) and report greater levels of wellbeing during times of difficulty or adversity (43). Optimistic coping is a cognitive approach strategy, and it is noteworthy that a positive association has been observed between optimism and internal locus of control (ILoC) (44). Indeed, high levels of ILoC predicted greater survival after lung transplantation, in which 63% of the sample were pwCF. (45).

Optimism may directly impact, beneficially, on biological functions and protect individuals during times of heightened stress. Several studies support the notion that optimism can influence diurnal cortisol secretion. In healthy adults, greater optimism was related to a lower cortisol responses (46), suggesting that optimistic coping allows a muted stress response. However, not all studies have found a relationship between optimism and cortisol levels (47). Additionally, optimism has been associated with lower levels of proinflammatory cytokine responses to a stressor, with Interleukin-6, C-reactive protein (CRP), fibrinogen and homocysteine inversely associated with higher optimism scores in healthy adults. (48-50). This could be a chicken and egg scenario; low levels of optimism may be secondary to inflammation rather than low inflammatory markers being caused by an optimistic mindset. Monitoring inflammation and optimism over time would help to understand potential causal pathways.

An optimistic, positive, resilient, problem-focused way of coping has been shown to predict better psychological functioning. It provides positive buffering from life's challenges. Optimism is typically stable over time, but this stability can be interrupted by difficult life events (51). Additionally, meta-analytic results of 29 studies show that it is possible to increase optimism through psychological interventions (52). Systematic reviews and meta-analysis of the efficacy and effectiveness of CBT in randomized clinical trials, concluded that CBT was associated with better outcomes, compared with control conditions, among patients with depression and anxiety, with CBT directly increasing optimistic coping (53-54). The possibility of enhancing optimism to mitigate negative health outcomes using CBT makes these interventions potentially suitable for use with pwCF, although the specific aspects of CBT that increase optimism require investigation. As optimistic coping is a cognitive approach strategy, it is reasonable to hypothesize that the cognitive restructuring element of CBT enhances optimism. Individual psychologists are likely to use such strategies with pwCF but evidenced outcomes from such work is lacking. The 'promoting resilience in stress management' (PRISM) intervention for adolescents and young adults (55) has shown feasibility and acceptability in CF (56) and the results of trials are awaited. Whether an intervention-created optimistic way of coping has the longevity to mimic natural dispositional optimism and produce longer-term health outcomes is unknown.

As with most studies evaluating survival outcomes, ways of coping were only measured at baseline. Although optimism is typically a long-term stable concept (52) modification (for example with CBT), may explain why the literature lacks consistency. In these data, the optimism-survival effect, although significant, may be weaker than envisaged because the influence of optimism may be blurred over time. Measures of optimism are typically generic, and there is a lack of standardization in measures employed in studies evaluating the association between optimism and disease outcomes, from single item scales to the extensively used Life Orientation Test, which undoubtedly adds to difficulties with data interpretation and comparison. This work has employed a disease-specific measure that was generated by people with CF themselves and should therefore be more appropriate (31). This is a single centre study with a small sample, but the focused single centre approach enabled the collection of 20 years of follow-up data that was sufficient to detect an effect. However, the study size is a limitation to the number of predictors that can be included. $ppFEV_1$ was chosen as the most appropriate proxy for all other variables given the limited data resource. CF genotype data and socioeconomic status are important survival predictor variables absent from these analyses. At the start of the study, genotype information was not routinely obtained for all patients. Future work should endeavour to study large patient cohorts, adjusting for all proposed predictors of mortality These models should also include time-dependent variables.

The recent introduction of highly effective CFTR modulators is likely to dramatically change the clinical course of CF and extend survival. These therapies hold great promise for improving clinical outcomes, yet the interplay between anxiety, depression, and ways of coping remain poorly understood and require robust evaluation. Nevertheless, this work provides evidence that coping in an optimistic way serves as a prognostic measure of survival in CF beyond key clinical and demographic variables.

Declaration of Competing Interest

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

CRediT author statement

Janice Abbott: Conceptualization, Study design, Data curation, Formal analysis, Data interpretation, Writing original draft, Writing review & editing. **Margaret A Hurley**: Study design, Formal analysis, Data interpretation, Writing original draft, Writing review & editing**. Helen Chadwick:** Conceptualization, Data curation, Data interpretation, Writing review & editing. **Daniel Peckham:** Conceptualization, Data curation, Data interpretation, Writing review & editing

Acknowledgements

We gratefully acknowledge the valuable input of people with CF who have given their time to engage in this research.

References

1. McKone EF, Goss CH, Aitken ML. CFTR genotype as a predictor of prognosis in cystic fibrosis. Chest 2006;130:1441-7. doi: 10.1378/chest.130.5.1441.
2. Liou TG, Adler FR, FitzSimmons SC, et al. Predictive 5-year survivorship model of cystic fibrosis. Am J Epidemiol 2001;153:345–352.
3. Buzzetti R, Alicandro G, Minicucci L, Notarnicola S, Furnari ML, Giordano G et al. Validation of a predictive survival model in Italian patients with cystic fibrosis. J Cyst Fibros 2012;11:24-29.
4. Desai S, Wong H, Sykes J, Stephenson AL, Singer J, Quon BS. Clinical Characteristics and Predictors of Reduced Survival for Adult-diagnosed Cystic Fibrosis. Analysis of the Canadian CF Registry. Ann Am Thorac Soc. 2018;15:1177-1185. doi: 10.1513/AnnalsATS.201801-037OC.

5. Stephenson AL, Tom M, Berthiaume Y, Singer LG, Aaron SD, Whitmore GA, Stanojevic S. A contemporary survival analysis of individuals with cystic fibrosis: a cohort study. European Respiratory Journal 2015;45:670-679. DOI: 10.1183/09031936.00119714
6. Courtney JM, Bradley J, McCaughan J, O'Connor TM, Shortt C, Bredin CP, Bradbury I, Elborn JS. Predictors of mortality in adults with cystic fibrosis. Pediatric Pulmonology 2007;42:525-532.
7. Lai HJ, Cheng Y, Cho H, Kosorok MR, Farrell PM. Association between initial disease presentation, lung disease outcomes, and survival in patients with cystic fibrosis. Am J Epidemiol 2004;159:537–46.
8. Kalish LA, Waltz DA, Dovey M, Potter-Bynoe G, McAdam AJ, LiPuma JJ, Gerard C, Goldmann D. Impact of Burkholderia dolosa on lung function and survival in cystic fibrosis. American Journal of Respiratory and Critical Care Medicine 2006;173:421-425.
9. Dodge JA, Lewis PA, Stanton M, Wilsher J. Cystic fibrosis mortality and survival in the UK: 1947–2003. European Respiratory Journal 2007;29:522-526. DOI: 10.1183/09031936.00099506
10. Tridello G, Castellani C, Meneghelli I, Tamanini A, Assael BM. Early diagnosis from new born screening maximises survival in severe cystic fibrosis. ERJ Open Research 2018;4:00109-2017. DOI: 10.1183/23120541.00109-201
11. Oates GR, Schechter MS. Socioeconomic status and health outcomes: cystic fibrosis as a model, Expert Review of Respiratory Medicine 2016;10:967-977. DOI: 10.1080/17476348.2016.1196140.
12. Barr H L, Britton j, Smyth AR, Fogarty AW. Association between socioeconomic status, sex, and age at death from cystic fibrosis in England and Wales (1959 to 2008): cross sectional study. BMJ 2011;343:d4662 doi:10.1136/bmj.d4662.
13. Arpey NC, Gaglioti AH, Rosenbaum ME, How Socioeconomic Status Affects Patient Perceptions of Health Care: A Qualitative Study, Prim Care Community Health 2017;8:169-175. doi: 10.1177/2150131917697439.
14. Schechter MS, Ostrenga JS, Fink AK, Barker DH, Sawicki GS, Quittner AL. Decreased survival in cystic fibrosis patients with a positive screen for depression. J Cyst Fibros 2021;20:120-126 doi: 10.1016/j.jcf.2020.07.020.
15. Abbott J, Hart A, Morton AM, Dey P, Conway SP, Webb AK. Can health-related quality of life predict survival in adults with cystic fibrosis. Am J Resp Crit Care Med 2009;179:54-58. doi:10.1164/rccm.200802-220OC
16. Giltay EJ, Geleijnse JM, Zitman FG, Hoekstra T, Schouten EG. Disposition optimism and all-cause and cardiovascular mortality in a prospective cohort of elderly Dutch men and women. Archives of General Psychiatry 2004;61:1126-1135.
17. Tindle HA, Chang Y, Kuller LH, Manson JE, Robinson JG, Rosal MC. et al. Optimism, cynical hostility, and incident coronary heart disease and mortality in the Wo7men's Health Initiative. Circulation 2009;120:656–662.
18. Brummett BH, Helms MJ, Dahlstrom WG, Siegler IC. Prediction of all-cause mortality by the Minnesota Multiphasic Personality Inventory Optimism-Pessimism Scale scores: Study of a

college sample during a 40-year follow-up period. Mayo Clinic Proceedings 2006;81:1541–1544.
19. Kim ES, Hagan KA, Grodstein F, DeMeo DL, De Vivo I, Kubzansky LD. Optimism and Cause-Specific Mortality: A Prospective Cohort Study. Am J Epidemiol. 2017;185:21-29. doi: 10.1093/aje/kww182.
20. Bell B, Rose CL, Damon A. The Veterans Administration longitudinal study of healthy aging. The Gerontologist 1966;6:179–184.
21. Lee LO, James P, Zevon ES, Kim ES, Trudel-Fitzgerald C, Spiro III A, Grodstein F, Kubzansky LD. Optimism is associated with exceptional longevity in 2 epidemiologic cohorts of men and women. PNAS 2019;116:18357-18362. https://doi.org/10.1073/pnas.1900712116
22. Rozanski A, Bavishi C, Kubzansky LD, Cohen R. Association of Optimism With Cardiovascular Events and All-Cause Mortality: A Systematic Review and Meta-analysis. JAMA Netw Open. 2019 Sep 4;2(9):e1912200. doi: 10.1001/jamanetworkopen.2019.12200.
23. Kubzansky LD, Wright RJ, Cohen S, Weiss S, Rosner B, Sparrow R. Breathing easy: A prospective study of optimism and pulmonary function in the normative aging study, Annals of Behavioral Medicine 2002;24:345–353 https://doi.org/10.1207/S15324796ABM2404_11
24. Ed Diener, Micaela Y. Chan. Happy People Live Longer: Subjective Well-Being Contributes to Health and Longevity. Applied Psychology: Health and Well-Being 2011;3:1–43
25. Schiavon CC, Marchetti E, Gurgel LG, Busnello FM, Reppold CT. Optimism and Hope in Chronic Disease: A Systematic Review. Front. Psychol. 2017;7:2022. doi: 10.3389/fpsyg.2016.02022
26. Nes LS, Segerstrom SC. Dispositional optimism and coping: a meta-analytic review. Pers Soc Psychol Rev. 2006;10(3):235-51. doi: 10.1207/s15327957pspr1003_3.
27. Mitmansgruber H, Smrekar U, Rabanser B, Beck T, Eder J, Ellemunter H. Psychological resilience and intolerance of uncertainty in coping with cystic fibrosis, J Cyst Fibros 2016;15:689-95. doi: 10.1016/j.jcf.2015.11.011.
28. Abbott J. Coping with cystic fibrosis. J R Soc Med 2003;96(Suppl 43):42-50.
29. Quittner AL, Goldbeck L, Abbott J, Duff A, Lambrecht P, Solé A, Tiboshc MM, Brucefors AB, Yüksel H, Catastini P, Blackwell L, Barker D. Prevalence of depression and anxiety in patients with cystic fibrosis and parent caregivers: results of The International Depression Epidemiological Study across nine countries. Thorax. 2014;69:1090–1097. doi:10.1136/thoraxjnl-2014-205983
30. Abbott J, Dodd M, Gee L, Webb AK. Ways of coping with cystic fibrosis: implications for treatment adherence. Disabil Rehabil 2001;23:315-324.
31. Abbott J, Hart A, Gee L, Morton, A, Conway S. Health-related quality of life in adults with cystic fibrosis: the role of coping. Journal of Psychosomatic Research 2008;64:149-157. https://doi.org/10.1016/j.jpsychores.2007.08.017
32. Malouff, J., & Schutte, N. (2017). Can psychological interventions increase optimism? A meta-analysis. The Journal of Positive Psychology, 12, 594 - 604.

33. Federal Drugs Agency. Guidance for industry. Patient-reported outcome measures: Use in medical product development to support labeling claims. Draft guidance, February 2006.
34. Holohan CJ, Moos RH. Personal and contextual determinants of coping strategies. J Pers Soc Psychol 1987;52:946-955.
35. Moos RH, and Schaefer JA. Coping resources and processes: current concepts and measures. In Goldberger L, Breznitz S editors. Handbook of stress: theoretical and clinical aspects. 2nd ed. New York: Free Press; 1993. p. 234-257.
36. Cox DR. Regression models and life tables (with discussion). J R Statist Soc B 1972;34:187–220
37. McIntyre K. Gender and survival in cystic fibrosis. Curr Opin Pulm Med. 2013 Nov;19(6):692-7. doi: 10.1097/MCP.0b013e328365af49.
38. Boehm JK, Chen Y, Koga H, Mathur MB, Vie LL, Kubzansky LD. Is optimism associated with healthier cardiovascular-related behavior? meta-analyses of 3 health behaviors. Circ Res. 2018;122(8):1119-1134. doi:10.1161/ CIRCRESAHA.117.310828
39. Hingle MD, Wertheim BC, Tindle HA, et al. Optimism and diet quality in the Women's Health Ini tiative.J Acad Nutr Diet. 2014;114(7):1036-1045. doi:10.1016/j.jand.2013.12.018
40. Progovac AM, Donohue JM, Matthews KA, et al. Optimism predicts sustained vigorous physical activity in postmenopausal women. Prev Med Rep. 2017;8:286-293. doi:10.1016/j.pmedr.2017.10.008
41. Schou I, Ekeberg O, Ruland CM. The Mediating Role of Appraisal and Coping in the Relationship between Optimism-Pessimism and Quality of Life. Psychooncology 2005;14:718-727. https://doi.org/10.1002/pon.896
42. Brissette I, Scheier M F, Carver C S. The role of optimism in social network development, coping, and psychological adjustment during a life transition. Journal of Personality and Social Psychology 2002;82:102–111. https://doi.org/10.1037/0022-3514.82.1.102
43. Scheier MF, Carver CS, Bridges MW. Optimism, Pessimism, and Psychological Well-Being. Optimism and Pessimism: Implications for Theory, Research, and Practice 2001;1:189-216. https://doi.org/10.1037/10385-009
44. Abdullah MQ. Optimism/Pessimism and Its Relationship with Locus of Control Among Children and Adolescents. Mathews J Psychiatry Ment Health 2018;3:017.
45. Burker EJ, Evon DM, Galanko J, Egan T. Health locus of control predicts survival after lung transplant. J Health Psychol. 2005;10:695-704. doi: 10.1177/1359105305055326. PMID: 16033791.
46. Lai JCL, Evans PD, Ng SH, Chong AM, Siu OT, Chan CL. et al. Optimism, positive affectivity, and salivary cortisol. British Journal of Health Psychology 2005;10:467– 484. http:// dx.doi.org/10.1348/135
47. Endrighi R, Hamer M, Steptoe A. Associations of trait optimism with diurnal neuroendocrine activity, cortisol responses to mental stress, and subjective stress measures in healthy men and women. Psychosom Med 2011;73:672-678 10.1097/PSY.0b013e31822f9cd7

48. Steptoe A, O'Donnell K, Badrick E, Kumari M, Marmot M. Neuroendocrine and inflammatory factors associated with positive affect in healthy men and women: The Whitehall II study. American Journal of Epidemiology 2008;167:96– 102.
49. Stellar JE, John-Henderson N, Anderson CL, Gordon AM, McNeil GD, Keltner D. Positive affect and markers of inflammation: discrete positive emotions predict lower levels of inflammatory cytokines. Emotion 2015;15:129-33. doi: 10.1037/emo0000033.
50. Ikeda A, Schwartz J, Peters JL, Fang S, Spiro A, Sparrow D, Vokonas P, Kubzansky LD. Optimism in relation to inflammation and endothelial dysfunction in older men: the VA Normative Aging Study. Psychosom Med. 2011;73:664-71. doi: 10.1097/PSY.0b013e3182312497.
51. Scheier MF, Carver CS. Dispositional optimism and physical health: a long look back, a quick look forward. Am. Psychol. 2018;73:1082-1094, 10.1037/amp0000384
52. Malouff JM, Schutte NS. Can psychological interventions increase optimism? A meta-analysis. J. Posit. Psychol. 2017;12:594-604, 10.1080/17439760.2016.1221122
53. van Dis EAM, van Veen SC, Hagenaars MA, Batelaan NM, Bockting CLH, van den Heuvel RM, Cuijpers P, Engelhard IM. Long-term Outcomes of Cognitive Behavioral Therapy for Anxiety-Related Disorders: A Systematic Review and Meta-analysis. JAMA Psychiatry 2020;77:265-273. doi: 10.1001/jamapsychiatry.2019.3986.
54. O'Neal PD, Jackson A, McDermot F. A review of the efficacy and effectiveness of cognitive-behaviour therapy and short-term psychodynamic therapy in the treatment of major depression: implications for mental health social work practice. Australian Social Work 2014:67:197-213.
55. Rosenberg AR, Yi-Frazier JP, Eaton L, Wharton C, Cochrane K, Pihoker C, Baker KS, McCauley E. Promoting Resilience in Stress Management: A Pilot Study of a Novel Resilience-Promoting Intervention for Adolescents and Young Adults With Serious Illness. J Pediatr Psychol. 2015;40:992-9. doi: 10.1093/jpepsy/jsv004.
56. Toprak D, Nay L , McNamara S , Rosenberg AR , Rosenfeld M, Yi-Frazier JP. Resilience in adolescents and young adults with cystic fibrosis: A pilot feasibility study of the promoting resilience in stress management intervention. Pediatr Pulmonol 2020;55:638-645.doi: 10.1002/ppul.24574.

Table 1. Subscales and theoretical approach[1] of the Cystic Fibrosis Coping Questionnaire

Optimistic coping items	**Distraction coping items**
I put it into perspective - it could be worse I feel optimistic I try to look at it differently - to see the positive or funny side I try to do something positive I do what I can under the circumstances I accept it I have confidence in the doctors and treatment Optimistic coping reflects a *cognitive approach strategy*. The person accepts their CF and is optimistic about the future. They are resilient, problem focused and determined not to let CF get them down. They reappraise the situation to find something positive in it and have confidence in the health professionals.	I treat myself to something special I do something to take my mind off it I make sacrifices in the short-term because I know it will do me good I cry, eat, drink, or take drugs I feel helpless, there is nothing I can do Distraction coping reflects a *behavioural and emotional avoidance strategy*. People do things to forget CF and to make themselves feel better, such as treating themselves to something special, drinking alcohol, venting emotions without really facing the problem; it is an escape from the world of CF.
Hopefulness coping items	**Avoidance coping items**
I'm just hoping it will be alright I talk to my friends and family I talk to a professional who knows about CF I'm looking forward to a time in the future when it will be better I pray I talk to other with CF Hopefulness coping reflects a *behavioural approach strategy*, with the hope that things will turn out for the better.	I avoid it whenever possible I try to put it out of my mind Avoidance coping is a *cognitive avoidance strategy*, reflecting a denial and minimization of their CF disease.

[1]The scale's theoretical approach is consistent with that of Holohan and Moos (34) and Moos and Schafer (35) in which the method (*cognitive, emotional, behavioural*) and focus (*approach* – focusing attention on CF, *avoidance* – diverting attention away from CF) of coping is considered.

Table 2 Baseline demographic, coping and clinical measures at coping assessment by gender.

	Men N=44			Women N=72			Test[1]
	Mean	SD	Range	Mean	SD	Range	p-value
Demographic:							
Age (years)	25.9	6.7	17 to 45	24.7	6.7	16 to 50	0.339
Coping:							
Optimistic	68.4	18.8	28 to 100	67.7	20.7	10 to 100	0.850
Hopefulness	32.1	17.0	5 to 72	43.1	19.2	10 to 100	0.098
Distraction	32.6	16.1	0 to 60	41.3	18.2	0 to 80	0.011
Avoidance	44.7	28.7	0 to 100	47.0	29.0	0 to 100	0.671
Clinical:							
$ppFEV_1$	66.9	26.0	23 to 133	53.4	22.0	14 to 123	0.003
BMI	21.7	2.8	17.2 to 30.2	21.2	3.2	15.7 to 30.0	0.337
	%	n		%	n		p-value
IV access device	27.3	12		48.6	35		0.032
B cepacia complex	4.5	2		6.9	5		0.708
CF-related diabetes	15.9	7		26.4	19		0.252
Oral nutritional supp	52.3	23		29.2	21		0.041[2]
Enteral tube feeds	13.6	6		25.0	18		0.041[2]
Post-transplant	6.8	3		1.1	8		0.459

[1] Testing for gender difference, [2]Same test.

Table 3 Pearson's correlation between age and ppFEV$_1$at coping assessment and coping measures by gender.

	Men N=44		Women N=72	
	Correlation coefficient	p-value	Correlation coefficient	p-value
Age and ppFEV$_1$	-0.040	0.798	0.034	0.776
Age and Optimistic	-0.001	0.993	0.076	0.528
Age and Hopefulness	-0.262	0.086	0.204	0.086
Age and Distraction	-0.259	0.090	-0.045	0.708
AGE and Avoidance	0.185	0.228	0.086	0.472
ppFEV$_1$and Optimistic	0.137	0.375	0.071	0.552
ppFEV$_1$and Hopefulness	-0.005	0.973	-0.060	0.619
ppFEV$_1$and Distraction	-0.322	0.033	-0.152	0.203
ppFEV$_1$and Avoidance	-0.248	0.104	0.118	0.325
Optimistic and Hopefulness	0.342	0.024	0.470	<0.001
Optimistic and Distraction	0.015	0.922	0.354	0.002
Optimistic and Avoidance	-0.066	0.670	0.159	0.181
Hopefulness and Distraction	0.345	0.022	0.439	<0.001
Hopefulness and Avoidance	0.099	0.524	0.083	0.488
Distraction and Avoidance	0.249	0.104	0.415	<0.001

Table 4 Models for survival time (days) from coping assessment to exit, adjusted for age in years and $ppFEV_1$ at coping assessment and gender where applicable. Relative risks (RR) estimated by Cox regression.

	Men N=44			Women N=72			Men and women n=116		
	RR	95% CI	p-value	RR	95% CI	p-value	RR	95% CI	p-value
Demographic characteristic:									
Men							1.000	Reference	
Women							1.407	0.735 to 2.693	0.302
Age (years)	0.925	0.829 to 1.031	0.158	1.014	0.964 to 1.066	0.594	0.991	0.949 to 1.034	0.670
Clinical condition:									
$ppFEV_1$	0.961	0.931 to 0.992	0.015	0.964	0.947 to 0.981	<0.001	0.965	0.951 to 0.979	<0.001
Coping measure:									
Optimistic	0.985	0.952 to 1.019	0.374	0.984	0.966 to 1.002	0.080	0.984	0.969 to 0.999	0.040
Hopefulness	1.003	0.962 to 1.046	0.870	1.005	0.986 to 1.024	0.618	1.008	0.992 to 1.025	0.337
Distraction	0.990	0.950 to 1.032	0.638	0.999	0.974 to 1.024	0.923	0.998	0.977 to 1.018	0.828
Avoidance	1.005	0.986 to 1.023	0.636	1.005	0.992 to 1.018	0.444	1.004	0.994 to 1.014	0.458

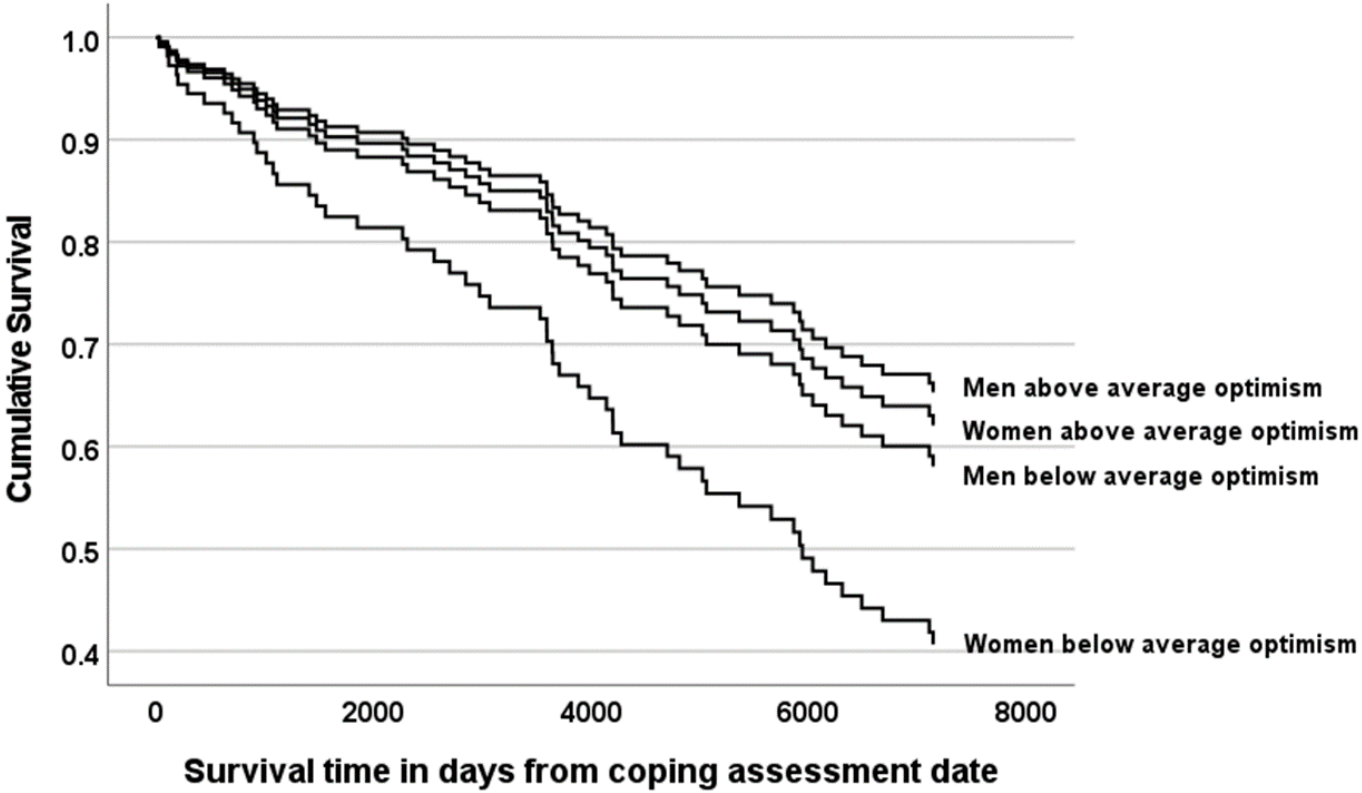

Figure 1 Caption

Predicted survival curves for men and women with above and below average optimism levels (average score = 68). Simplified version of model given in Table 4.