14. Psychological issues

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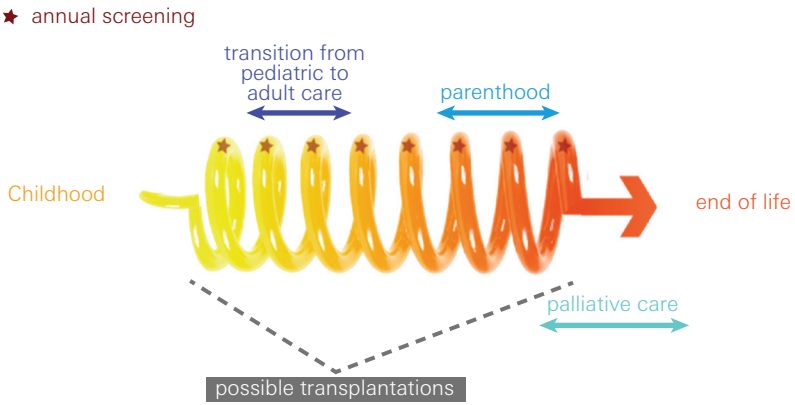
1. INTRODUCTION

- CF is a chronic condition that requires a demanding and time-consuming regimen. CF patients are used to coping with it since childhood, but **survival into adulthood and progressive health decline bring about new challenges.**
- **Depression**, **anxiety**, **disordered eating**, **compliance issues** and **other disturbances reaching a symptomatic level or not**, as well as **unhealthy family dynamics**, **developmental and relational difficulties** and **existential questions** may arise in adult CF patients.
- A large body of research suggests that psychological issues of CF patients
  - are strongly linked to their physical condition and to an increased healthcare utilization and costs
  - have a **major impact on crucial aspects, such as adherence, BMI and lung function**
  - Therefore, psychological prevention, evaluation and possible intervention in patients, their families or significant others should be an integral part of CF care.
  - **CF teams should include a trained psychologist/psychiatrist**, who works in close collaboration with the team members and, if needed, offers advice for the psychological understanding of patients **(Table 1, Figure 1).**

Table 1: Role of the mental health worker in the CF center

Systematic annual screening	Clinical interview, optional questionnaires
	Propose management and coping strategies to improve psychological health and its impact on clinical care
	Organization of appropriate treatment and follow-up
Possible intervention during acute events	Transition from pediatric to adult care
	Parenthood
	Transition to transplantation
	Transition to palliative care
Collaboration with the CF team	Advice for the psychological understanding of patients
	Provide advice that may ease negative issues with patients

Figure 1: Key time-points of interventions of the mental health worker during the life span of adult CF patients



2. IMPACT OF CF ON SENSITIVE ASPECTS OF LIFE

- Like all young adults, at adulthood, CF patients face new challenges that are often heavily affected by CF. Particularly, progressive health decline (mainly loss of lung function) requires more intensive and invasive treatments. **Table 2** presents some examples of the impact of CF on sensitive aspects of life.

Table 2: Examples of the impact of CF on sensitive aspects of life

Life event	Challenges for CF patients
Reaching autonomy	Transition from a pediatric to an adult setting and taking responsibility for treatment
Entering academic studies/education	Adjusting to part-time studies
Planning a professional future	Work interrupted by hospitalizations and medical appointments
Engaging in sentimental relationships/sexuality	Coping with and sharing the limitations in intimacy due to the disease and its treatments
Coping with the desire of a child	Facing fertility problems for males Facing a possible health decline in case of pregnancy Fear of dying before children have grown up
Facing an open future	Dealing with a shortened life expectancy, transplantation and palliative care

- **Normalcy and stigma:** Young CF patients often experience stigma (related for example to repetitive cough or digestive disturbance). The latter is associated with depression, lower QoL (quality of life) and diminished psychological health. Optimism may play a protective role.
- **Quality of life:**
  - Interestingly, QoL is more related to mental health status than to lung function, though QoL of CF patients decreases with health deterioration.
  - Being enrolled in professional life or studying is related to a higher QoL.
  - Coping strategies also influence QoL of CF patients
    - Active coping is positively related to social QoL; greater use of religion, spiritual coping, instrumental coping and acceptance are associated with better emotional QoL.
    - Distraction coping, disengagement and substance abuse are associated with lower emotional QoL.

3. PSYCHOLOGICAL ISSUES IN CF PATIENTS

- **Anxiety and depression**
  - **Prevalence:**
    - Although somewhat debated, recent studies indicate a higher prevalence of anxiety and depression in CF patients compared to the general population.
  - **Consequences of anxiety and depression**
    - In adults, anxiety and depression have been associated with lower lung function, increased chest symptoms, reduced physical functioning, lower BMI and increased frequency of hospitalizations, healthcare utilization and costs.
    - CF patients suffering from anxiety and depression report a lower QoL.
    - Psychological problems such as depression can also lead to conflicts with the CF team and diminished adherence to treatment, often related to doubts about medication efficacy. On the other side, good illness acceptance has been associated with less depressive symptoms and better adjustment to treatment.
- **Other psychological issues**
  - **Disordered eating and eating disorders:**
    - Nutrition is a major issue for CF patients. Pressure to eat and impaired family functioning during meals is often observed.
    - Although a higher prevalence of eating disorders has not been clearly established in CF patients compared to normal adults, CF patients are at risk of disturbed eating attitudes and/or behaviors. When present, they induce poor nutritional status that may lead to retarded or diminished growth, delayed puberty, impaired lung function and reduced survival.
    - Body image: Female CF patients may have a better body image than males, given their preference for a low body weight, but their reduced weight can compromise their survival. In this regard, male CF patients may be more motivated to follow nutritional recommendations. Greater dissatisfaction with body image, poorer self-esteem and lower QoL has been reported in adults with enteral-tube feeding.

- **Psychological distress can be encountered without reaching the intensity of a psychiatric disorder.**
  - The clinical experience with CF patients is richer than what can be grasped by studies which are solely based on psychometric measurements.
  - Longitudinal and qualitative studies may sometimes be better tools to understand developmental processes and to address underlying psychic dynamics and evolution of the patients and their families.
  - Some other psychological issues which may be observed in CF patients are listed in **Table 3.**

Table 3: Psychological issues which may be observed in CF patients

- Disordered eating
- Low self-esteem
- Social dependency
- Social withdrawal
- Feelings of guilt
- Anhedonia
- Disturbed intimacy (e.g. strong desire for intimate relationships, which are at the same time out of reach because of an avoidant behavior due to fears) and/or disturbed sexuality
- Discrepancy between intellectual abilities and a certain emotional immaturity
- Conflicts or ambivalence regarding autonomy issues
- Development of secondary alexithymia*[a] under prolonged, heavy treatment and suffering
- Disturbed family functioning with over – and/or underprotection*[b]
- Traumatic experience of the disease (sometimes related to more specific symptoms such as needle related phobia)

*[a] Difficulty in recognizing or expressing personal emotions

*[b] Within the family, anxiety, repressed aggression and guilt may lead to overprotection and separation/autonomy difficulties

4. ASSESSMENT AND MANAGEMENT

4.1 For CF patients

- **Screening:** An annual screening by a trained psychologist or psychiatrist should be offered to CF patients in order to evaluate their psychological difficulties and possible psychiatric symptomatology. A face-to-face interview is advisable and can be complemented by questionnaires.
  - This annual screening may improve patient understanding and care and is a first step to ease a potential crisis-related subsequent consultation. The main objectives of the annual screening interview with the CF psychologist or psychiatrist are presented in **Table 4**.
  - Although **the use of questionnaires is less preferable than a face-to-face interview** held by a trained psychologist or psychiatrist, in settings where no psychologist works within the team, the use of **questionnaires (Table 5)** can help identify psychological problems for which referral to a mental health worker may be indicated.

- Patients with psychiatric symptoms should be offered **appropriate psychological treatment and follow-up**. If necessary, medication should be introduced by a psychiatrist **(see section 5)**.

- **Interventions during life events:** In addition to the annual screening, whenever the physician perceives psychological vulnerability in a CF patient, psychological support should be proposed. As previously mentioned, psychological vulnerability may be more evident during life events **(Figure 1, Table 2)**.
- **Transition from pediatric to adult care:** the psychologist should be integrated as soon as possible in the process especially in complex situations. A common meeting with the child's psychiatrist/psychologist in the pediatric ward or at least a first meeting soon after transition is recommended.
- **Parenthood (see also Chapter "*Fertility and pregnancy*"):**
  - The majority of male CF patients (95%) are infertile. Information about infertility has often a strong psychological impact; if assisted reproduction is too expensive, patients may have to renounce biological fatherhood.
  - For females, increased attention for psychological vulnerability is crucial during the antenatal and postnatal periods; complications during pregnancy may lead to psychological suffering and adjustment difficulties with the newborn.
  - Fear of a premature death, before the child has grown up, is common.
- **Transition to transplantation (see also Chapter "*Transplantation*"):**
  - A psychiatric assessment by an expert is part of the pre-transplantation evaluation, in order to assess the patient's psychiatric suitability for transplantation.
  - Psychological support may be necessary and should be systematically offered in this context, since every step in the transplantation process is associated with psychological challenges **(Table 6).**
  - **Transition to palliative care**: psychological support should be offered for the patients, but also family and friends, before and after the patient dies **(see also Chapter, "*Palliative and end-of-life care*")**.

Table 4: Main objectives of the annual screening interview with the CF psychologist or psychiatrist

It helps explore and assess :

- Mental health
- Quality of life
- Potential risk factors for psychological vulnerability
- Resources of the patient
- His/her representations of illness and treatment
- Experiences regarding treatment (including adherence problems, relationship with health care professionals)

Table 5: Questionnaires used in CF

Target	Questionnaire	Available at / Reference
Anxiety/ Depression	PHQ-2 / **PHQ-9***[1,2]	www.phqscreeners.com/
	GAD-2 /**GAD-7***[1,2]	www.phqscreeners.com/
	HADS*[1, 2]	http://opencourses.emu.edu.tr/pluginfile.php/8619/mod_resource/content/1/HADS.pdf
	HDRS*[1,2]	http://dcf.psychiatry.ufl.edu/files/2011/05/HAMILTON-DEPRESSION.pdf
Quality of Life	CFQoL	In: (Gee L. , Abbott, Conway, Etherington, & Webb, 2000)
	CFQ-R*[1,2]	www.psy.miami.edu/cfq_QLab/
Adherence	MMAS*[1,2]	In: (Morisky, Ang, Krousel-Wood & Ward, 2008)
Eating attitudes and Behaviors	CFEAB	In : (Randlesome, Bryon, & Evangeli, 2013)
	Eating Issues & Body Image continuum	www.health.arizona.edu/sites/health/files/continuum2.pdf
Self-esteem	Rosenberg Self-esteem Scale*[1,2]	www.yorku.ca/rokada/psyctest/rosenbrg.pdf

*[1] Available in French
*[2] Available in German

Table 6: Psychological challenges during the transplantation process

Time point	Examples of psychological challenges
Referral for transplantation	Understanding the acuteness of illness and coping with the possibility of death
Waiting period	Fear of dying before an organ is available Guilt of wishing someone to die in order to receive an organ
Post-transplant phase	Integration of someone else's organ Facing a future which was not expected Disillusions regarding a completely symptom-free life

4.2. For parents and siblings

- Research indicates that parents of children and teenagers with CF show elevated rates of anxiety and depression. This probably applies to parents of adult patients and siblings as well. Therefore, special attention should be paid to the parents and siblings. If necessary, the psychologist should be able to refer them for appropriate mental health care.

4.3. For the CF team

- The importance of an integrated disease management approach for CF patients is now well established. In line with this concept, CF teams should **include a trained psychologist/psychiatrist, offering direct consultations for the patients as well as advice to the other team members regarding the psychological understanding of patients (consultation and liaison activity).**
- Considering the psychological impact of working with CF patients, especially in pre-transplant periods or palliative care, **team supervision** by a psychologist/psychiatrist should be offered.
- Issues such as potential negative feelings or conflicts with patients are also part of what can be formally or informally discussed with a psychologist.
- The mental health care worker can provide advice regarding important issues such as adherence. **Table 6** presents examples of coping strategies that may be offered to the CF team in regard to adherence problems.

Table 6: Examples of coping strategies for adherence issues (for physicians and CF nurses)

Prevention and management:

- Address the issue of adherence early, if necessary as soon as the transition begins.
- Talk about it in an open and non-judgmental way, without taboo. Make sure the patient understands the treatment. Avoid using medical jargon.
- Explore reasons for non-adherence with respectful curiosity, and not on the premise that it is due to some defective reasoning of the patient (such as irrational fears or lack of understanding of the severity of the disease)
- Explain that this is a common issue, and that some degree of forgetting or nonadherence is normal.
- Explore patient perception of his/her treatment (is it useful or not?).
- Always be open about the consequences of non-adherence but better make compromises than lose the communication with the patient.
- Set realistic goals. Try to establish an oral contract/agreement the patient feels comfortable with. If necessary, put it on paper in order to make it clear for both patient and health professionals.
- Try to empower the patient and help him/her face his/her responsibilities.
- Address the issue of alternative treatments often used by patients.

Work in collaboration with:

- **The caregivers,** to explore whether the patient can benefit from a supportive group such as family or friends.
- **The mental health worker,** in order to detect psychological suffering or mental health issues related to non-compliance. The psychologist can also provide the patient with specific tools or therapy (e.g. motivational interviewing).
- **The social worker,** in order to explore the social or financial issues possibly related to non-adherence.
- **The physiotherapist,** to set treatment goals.

Table 7: Psychiatric drugs and specific considerations in CF – not an exhaustive list

Classes		Pharmacological considerations	CF-related considerations
***Antidepressants**[a]*			
1st choice	**Selective serotonin reuptake inhibitors (SSRI)**	– Drug interactions through inhibition of liver P450 enzymes*[b] – Relative contraindication to use with linezolid – QT prolongation*[c]	– Reported associations with bleeding risk, bone fractures (observational studies) – Weight gain
		Citalopram: lower probability of drug interactions compared to other SSRI, dose-dependent QT interval prolongation Escitalopram: lower probability of drug interactions compared to other SSRI Fluoxetine: long half-life, strong inhibitor of CYP 2D6 Paroxetine: mild anticholinergic side effects Sertraline: diarrhea more frequent compared to other SSRI	
2nd choice	**Serotonin-norepinephrine reuptake inhibitors (SNRI)**	– Administering with food may reduce nausea without influencing absorption	– Anticholinergic side effects (indirect decrease of the parasympathetic tone) – Reported associations with bleeding risk, bone fractures (observational studies)
		Duloxetine: inhibitor of CYP2D6*[a] Venlafaxine: QT prolongation*[b], possible increase in diastolic blood pressure and/or heart rate	
3rd choice	**Tricyclic and tetracyclic antidepressants**	– Sedative properties (blockage of histamine receptors). – Lethal potential of overdosing (SSRI, SNRI are considered safer in this regard) – Drug interactions as substrates of P450 enzymes*[b]	– Anticholinergic symptoms (higher rates compared to SSRI, SNRI) – Cardiovascular screening before treatment initiation

	Monamine oxidase inhibitors	Not considered first-line antidepressants (need of dietary restrictions, many drug interactions and side-effects)	– Not considered first-line antidepressants (need of dietary restrictions, many drug interactions and side-effects) – Anticholinergic symptoms
	Other antidepressants	Mirtazapine, trazodone: to be considered in case of sleep disorders	– Anticholinergic symptoms (usually mild)
Anxiolytics	**Benzodiazepines**	– Inhibitors of the CYP3A4 system increase the risk of benzodiazepine toxicity whereas inducers of the CYP3A4 system may decrease their effectiveness*[a]	Avoid use in patients with respiratory insufficiency
		Lorazepam: fewer P450 interactions compared to other benzodiazepines Oxazepam: fewer P450 interactions compared to other benzodiazepines	
Antipsychotics		Extrapyramidal side effects, QT prolongation*[b] Potential weight gain and development of a metabolic syndrome	Anticholinergic symptoms
CNS stimulants			Dry mouth, decreased appetite and weight loss Cardiovascular side effects

*[a] SSRI, SNRI and tricyclics have also demonstrated their efficacy for anxiety disorders. SSRIs (especially sertraline and escitalopram) are the first-line agents for the long term treatment of anxiety disorders whereas benzodiazepines are used mostly to manage acute symptoms. There is a delay of 1-6 weeks for the effect of SSRIs on depression and 4-8 weeks for the effect on anxiety disorders.

*[b] Details on inhibitors, inducers and substrates of P450 enzymes can be found in http://medicine.iupui.edu/clinpharm/ddis/main-table and http://bioinformatics.charite.de/supercyp/index.php?site=home.

*[c] Examples of QT prolonging agents: azole antifungals, macrolides, quinolones

5. PHARMACOTHERAPY

- Introduction of an antidepressant drug should be discussed with the CF team and the psychologist/psychiatrist.
- Most adverse effects are dose dependent, some are transient [e.g. nausea and headaches for Specific Serotonin Reuptake Inhibitors (SSRI)] and others persistent (e.g. anticholinergic effects).
- Therapeutic drug monitoring (TDM) is recommended in case of potential interactions, suspected genetic metabolism anomaly or to document adherence.
- Secondary effects relevant to CF:
  - Many molecules are associated with anticholinergic symptoms (e.g. constipation, dry secretions) at various degrees, and these may be particularly problematic in CF patients.
  - The associations of SSRI (and Serotonin-Norepinephrin Reuptake Inhibitors – SNRI) with bleeding risk (notably gastrointestinal bleeding) and bone fractures are based on observational studies and are not unequivocally established.
- CF patients often receive multiple medications:
  - Drug interactions with psychiatric drugs usually concern inhibition or induction of liver P450 metabolism or potentiation of common secondary effects (e.g. QT prolongation).
  - Of note, the relative contraindication to administer linezolid in patients receiving SSRI due to the risk of serotonin syndrome.

6. REFERENCES

1. Abbott J, Morton AM, Musson H, et al. Nutritional status, perceived body image and eating behaviours in adults with cystic fibrosis. Clin Nutr 2007;26:91-9.
2. Canoui P, Simon G. [Psychological and social aspects of mucoviscidosis with recommendations for centers of care]. Arch Pediatr 2001;8 Suppl 5:906s-19s.
3. Conway S, Balfour-Lynn IM, De Rijcke K, et al. European Cystic Fibrosis Society Standards of Care: Framework for the Cystic Fibrosis Centre. Journal of cystic fibrosis : official journal of the European Cystic Fibrosis Society 2014;13 Suppl 1:S3-22.
4. Duff AJ. Depression in cystic fibrosis; Implications of The International Depression/Anxiety Epidemiological Study (TIDES) in cystic fibrosis. Paediatric respiratory reviews 2015;16 Suppl 1:2-5.
5. Fidika A, Herle M, Goldbeck L. Symptoms of depression impact the course of lung function in adolescents and adults with cystic fibrosis. BMC Pulm Med 2014;14:205.
6. Gee L, Abbott J, Conway SP, Etherington C, Webb AK. Development of a disease specific health related quality of life measure for adults and adolescents with cystic fibrosis. Thorax 2000;55:946-54.
7. Mc Hugh R, Mc Feeters D, Boyda D, O'Neill S. Coping styles in adults with cystic fibrosis: implications for emotional and social quality of life. Psychol Health Med 2016;21:102-12.
8. Morisky DE, Ang A, Krousel-Wood M, Ward HJ. Predictive validity of a medication adherence measure in an outpatient setting. J Clin Hypertens (Greenwich) 2008;10:348-54.
9. Nobili RM, Duff AJ, Ullrich G, et al. Guiding principles on how to manage relevant psychological aspects within a CF team: interdisciplinary approaches. Journal of cystic fibrosis : official journal of the European Cystic Fibrosis Society 2011;10 Suppl 2:S45-52.

10. Quittner AL, Abbott J, Georgiopoulos AM, et al. International Committee on Mental Health in Cystic Fibrosis: Cystic Fibrosis Foundation and European Cystic Fibrosis Society consensus statements for screening and treating depression and anxiety. Thorax 2016;71:26-34.
11. Randlesome K, Bryon M, Evangeli M. Developing a measure of eating attitudes and behaviours in cystic fibrosis. Journal of cystic fibrosis : official journal of the European Cystic Fibrosis Society 2013;12:15-21.
12. Snell C, Fernandes S, Bujoreanu IS, Garcia G. Depression, illness severity, and healthcare utilization in cystic fibrosis. Pediatr Pulmonol 2014;49:1177-81.
13. Standards for the clinical care of children and adults with cystic fibrosis in the UK (2nd Edition), 2011. Available in www.cysticfibrosis.org.uk/the-work-we-do/clinical-care/consensus-documents.
14. Webb AK, Bryon M. The International Depression Epidemiological Study (TIDES): unfinished business? Thorax 2014;69:1067-8.
15. Yohannes AM, Willgoss TG, Fatoye FA, Dip MD, Webb K. Relationship between anxiety, depression, and quality of life in adult patients with cystic fibrosis. Respir Care 2012;57:550-6.