Mental health and cystic fibrosis: Time to move from secondary prevention to predictive medicine

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LETTER TO THE EDITOR

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To the Editor,

Thanks to advances in care over the last six decades, in countries with well-developed healthcare systems the onus of cystic fibrosis (CF) care has progressively shifted to adult populations. Median survival age for CF is now in the late forties and the recent introduction of CF transmembrane conductance regulator modulators is expected to further improve the survival rates.1

In spite of these improvements and the positive outlook, CF is still a life-limiting condition with chronic symptoms and a heavy daily treatment burden. Not surprisingly, depression and anxiety are reported to be among the most frequent CF comorbidities.2 Depression is a common psychiatric condition characterized by depressed mood and loss of interest in most activities, and it may affect thoughts, feelings, behaviors, physical health and impair social and occupational functioning. Anxiety can be described as a "state of intense apprehension, uncertainty, and fear resulting from the anticipation of a threatening event or situation to the degree that normal physical and psychological functioning is disrupted".3

The largest study conducted on depression and anxiety detection in CF population is the International Depression/Anxiety Epidemiological Study that screened more than 6000 patients with CF aged 12 years and older across nine countries, reporting depressive and anxiety prevalence rates 2 to 3 times higher in the study population, as compared with the general population; the gap increased to three to four times in CF patients with at least one parent with depression or anxiety symptoms.3

The association between CF, depression and anxiety is complex: depressive and anxiety symptoms can be associated with decreased lung function, lower body mass index, lower adherence to treatment and health-related quality of life (HRQoL), higher sleep disorders rates, more frequent hospitalizations and greater healthcare costs.3

Besides, the risk of depression in patients with CF is associated with age and household members’ mental health.

In a European multi-center study the prevalence of depression in patients with CF increased with age from 6% in the 12 to 20 year old group to 11% in the 21 to 30 year old group, and 14% in the 31 to 50 year old group. The trend was interpreted as an age-dependent association with increasingly severe lung disease and higher expectations (eg, financial and family independency).4

Parental depression and anxiety can affect CF patients’ adherence and health outcomes. Depression is more common among mothers that have often been found to be overly involved and protective of CF sons.5

Overall, data from the literature strongly argue for a significant association between CF and mental health issues and the need to screen both patients and parents to identify and manage mental health comorbidities and to provide adequate treatment.2

This evidence led to the establishment of the International Committee on Mental Health in patients with CF that identified and recommended the best screening tools and the best intervention practices.6 The patient health questionnaire (PHQ-9) and the generalized anxiety disorder (GAD-7) were recommended for depression and anxiety annual screening both in CF patients and parent caregivers because of their brevity, high positive predictive value and good reliability. PHQ-9 and GAD-7 are used both as secondary prevention tools to screen symptoms on an annual basis, as well as to monitor treatment response. In addition, the Columbia suicide severity screen use was suggested to measure suicide ideation in individuals who screened positive for suicide risk.

However, because of the complexity of CF disease and the potential mental health implications, more attention should be paid to potential risk factors in childhood and adolescence to be used as potential prime target for interventions in later psychiatric disorders.

Kraeelin’s hypothesis that temperament can predispose to or be a risk factor for later psychiatric disorders has been confirmed by several studies. Temperament can be defined as a "genetically determined emotional reactivity to the environment, which—in combination with life experiences—leads to the development of personality traits."7 In the eighties, based on Kaeppelin’s work, the Armenian psychiatrist Hagop Akiskal proposed criteria to define five different temperaments: depressive (low levels of energy and introversion), cyclothymic (chronic cycling of mood polarities with unstable self-esteem and energy), hyperthymic (increased levels of energy and optimism), irritable (irritable and angry behaviors), and anxious (worrying attitudes).7

Akiskal et al developed the Temperament Evaluation of Memphis, Pisa, Paris and San Diego-autoquestionnaire version (TEMPS-A), a self-report, yes-or-no type questionnaire, designed to quantify temperament in psychiatric patients and healthy subjects since the adolescence.7 The subscales (depressive, cyclothymic, hyperthymic, irritable and anxious) of the TEMPS-A attempt to capture not only emotional, cognitive, psychomotor and circadian traits which might
predispose one to major mood disorders, but could also serve an
adaptive role in an evolutionary context.

According to Akiskal, affective temperaments would play a key
role in the clinical presentation and evolution of mood episodes and
would influence course of illness, symptoms’ severity, and treat-
ment’s response. Moreover, evidence from the literature confirmed
that cyclothymic, depressive, and irritable temperaments are more
frequently associated with a higher risk of suicidal behaviors,
whereas hyperthymic temperament seems to be a protective factor.3

In particular, adolescence temperament traits have been shown
to be associated with mood and anxiety disorders in later life.7
Furthermore, the stability of temperament across development
would suggest that it can be act as a potential risk factor for later
mood and anxiety disorders.

Identifying adolescents at higher risk of developing mood and
anxiety disorders allow to plan, implement and monitor targeted
preventive interventions in the context of CF care and management.
These should include multi-disciplinary supportive interventions de-
ivered by teams of ad hoc trained pneumologists, psychologists, and
psychiatrists with regular follow-up visits. Accurate information
around the risk to develop depressive and anxiety symptoms, their
treatment and prognosis, should be given to patients with CF and
families to help them in the long-term management of their condition.

To the best of our knowledge, no prospective studies have in-
vestigated temperament traits in patients with CF and parents and
the possible association between temperament and later onset of
mood and anxiety disorders. Temperament could also modulate the
impact of life-limiting chronic condition, such as CF on different do-
 mains, including coping strategies, HRQoL, and adherence to treat-
ments. In addition to temperament, it would be interesting to assess
the predictive value of other biological traits, like sensitivity in be-
 havioral inhibition and behavioral activation systems, related to
mood disorders in patients with CF.

CF mental healthcare is at a turning point. New pharmacological
CF treatments will improve survival, with a growing number of adult
patients requiring good quality of life and social functioning.

According to the predictive medicine model that aims to identify
patients at risk of developing a disease, the evaluation of tempera-
ment, behavioral inhibition and activation, and other potential bio-
 logical traits in childhood and adolescence could allow to move from
the current secondary prevention screening strategy to a better
comprehension of risk factors for depressive and anxiety disorders
in patients with CF, so as to support a patient-centered approach to CF
mental health care.

CONFLICT OF INTERESTS
The authors declare that there are no conflict of interests.

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