



Criteria for Determining Disability in Infants and Children: Failure to Thrive

Summary

Overview

The Social Security Administration (SSA) requested that the Agency for Healthcare Research and Quality (AHRQ), through its Evidence-based Practice Center (EPC) program, provide a systematic review of the scientific evidence on whether children, defined by investigators as failing to thrive or grow adequately, have a concurrent disability, or will have one within 6 months. The population of interest includes children age 18 years or younger, both male and female, of all racial, ethnic, and socioeconomic groupings.

The evidence report was prepared to assist SSA in updating its *Listing of Impairments* and revising its disability policy, as may be appropriate.

Causes of Failure to Thrive

The underlying cause of failure to thrive (FTT) is always insufficient usable nutrition. This may occur when sufficient nutrients are not available to the child as a result of social or environmental causes that prevent parents from obtaining, preparing, or offering age-appropriate foods to the child. This growth failure often includes concurrent and potentially persistent disability. This syndrome of under-nutrition, previously termed “non-organic FTT” is recognized as a multifaceted disease. Because of this, the world’s literature on the disabilities of poorly nourished children in developing as well as developed countries becomes relevant to the discussion of disability arising from FTT even in the United States.

In addition, almost any serious pediatric illness can result in FTT. There are three basic mechanisms for this phenomenon:

1) insufficient nutrition is available to the child

because of the child’s inability to feed properly, e.g., severe neurological dysfunction, gastroesophageal reflux, cleft palate; 2) nutrition is adequate but inadequately absorbed and/or utilized (malabsorption syndromes); or 3) the disease process creates added metabolic requirements, e.g., asthma, cardiac failure, thyroiditis. It is not uncommon for FTT to be the first clue to an active disease process which has not yet manifested itself in specific symptomatology.

Whatever its multidimensional causes, FTT affects growing children in many important ways. Severe malnutrition has been shown to cause permanent damage to various parts of the brain and central nervous system, leading to a range of disabilities manifested by aberrant behavioral, cognitive, language, and motor development. In addition, FTT is closely linked with infectious disease. Children who are undernourished (of which FTT is an indicator) consistently have been found to have significant and profound changes in cell-mediated immunity, complement levels, and opsonization that lead to susceptibility to various infections. FTT is also associated with disabilities in cardiac functioning, gastrointestinal conditions, persistently small stature, and other physiological derangements.

Reporting the Evidence

The key question posed by SSA was refined by the EPC Evidence Review Team and technical experts to review the association of five categories of disability with failure to thrive.

Key Question: Among children defined by investigators as failing to thrive or grow adequately, what evidence exists that they have, or will have within 6 months, a concurrent disability?



The following associations between FTT and disability were investigated:

- Persistent disorders of growth following FTT
- Association of FTT with immunologic/infectious outcomes
- Child behavior associated with FTT
- Developmental disorders associated with FTT
- Association of FTT with other psychosocial and family factors

Methodology

Definition of Failure to Thrive

Most clinicians make a diagnosis of FTT when a child's growth in weight and/or in height fails to increase as expected for his or her age. Operationally this is frequently defined as a crossing of two or more standard percentile lines in a standard growth chart. Other clinicians use a definition of FTT that can be assessed without access to growth charts, or that can be assessed at a single point in time. These definitions include children who are persistently at or below the third or fifth percentile for weight, or less than the 80th percentile of median weight-for-height.

Other definitions used commonly in the professional literature include height-for-weight <3rd percentile; weight-for-age less than 3rd or 5th percentile or less than 80 percent of mean for age; weight-for-height <10th percentile; and weight-for-age less than 2 standard deviations below the mean for age. Because of inconsistent definitions it is hard to make comparisons among the various investigative approaches to this syndrome.

Current SSA guidelines consider FTT to be present when there is a fall in weight to below the 3rd percentile or to less than 75 percent of median weight-for-height or age in children under 2-years old. There must be no underlying medical disorder, and growth failure should last, or be expected to last, for at least 12 months.

Earlier research attempted to distinguish FTT that resulted from a known organic disease process from the more common circumstance in which the specific cause for the growth failure is unknown. This distinction is no longer considered useful. Instead, current data suggest that organic and non-organic causes and effects are intertwined in most affected children. This review therefore will not use the terms *organic* or *non-organic* FTT.

Literature Search

Disability is not a specific medical condition that can readily be searched for. Thus, we had to look at many studies with related concepts (i.e., medically definable impairments that are related to disability) to identify potentially relevant studies.

The main search consisted of a MEDLINE® search from 1966 through December 2000. A broadly sensitive, rather than specific, search strategy was employed to identify relevant studies. The search strategy used the following textwords: failure to thrive, failure to grow, growth retardation, childhood malnutrition, protein-calorie malnutrition, starvation and psychosocial dwarfism. Development of the search strategies was an iterative process that included input from domain experts. Keywords from known relevant studies were used to refine and focus the final search strategies used. Results were limited to studies in age-group under 18 and English language only. Various investigators defined the population of interest differently. We accepted whatever definition the investigator had used to identify children who were not growing as expected. We also inspected references from retrieved primary studies and relevant reviews, and consulted with technical experts and colleagues in order to identify additional studies.

Study Selection

Including studies found from other sources, a total of 10,486 English-language citations were identified in the initial search. An updated MEDLINE® search using the same search strategy was conducted in September 2001 which resulted in additional 480 abstracts.

Titles and abstracts were manually screened by physician members of the EPC and pediatricians to identify potentially relevant articles. Inclusion criteria for article selection were as follows: 1) published articles including at least one disability-related outcome; 2) cross-sectional or longitudinal studies; 3) studies with at least two arms, one of which had a non-FTT or healthy control group; and 4) studies conducted in either developed or developing countries. The third inclusion criteria was added to control for potential confounders for any particular statistically significant outcome or covariate. Studies of sample size of less than 10 subjects per arm, or those concerned primarily with particular diagnoses and conditions were excluded, as were studies published only as abstracts.

The mechanisms of undernutrition have been well-studied in developing countries. In addition, the associations of undernutrition and various outcomes such as cognitive and neurological development and infections are clearly delineated in these conditions. Because undernutrition as applied to developed countries may not be understood or studied as extensively, studies in developing countries were included to help correlate associations made.

Summarizing the Literature

A total of 275 original studies were retrieved for careful evaluation. Detailed examination of these articles identified 52 publications comprising 43 studies that met the inclusion criteria. Detailed data extraction was performed on these 43 studies. Their overall methodologic quality will be described individually below.

Findings

Persistent Disorders of Growth Following Failure to Thrive

Findings From Industrialized Nations. Seven studies compared anthropometric data of FTT patients with healthy comparison groups in developed countries. Most studies were performed in the United States or the United Kingdom, with one study from Israel. The majority of the studies were prospective-longitudinal, and two of the studies were ambidirectional blinded studies. Six out of seven of these studies show a statistically significant association between FTT and sub-optimal weight-for-height and weight-for-age. This growth retardation for the most part persists despite adequate correction of malnutrition. The clinical significance of this degree of growth retardation is not clear.

Findings From the Developing World. Seven studies compared anthropometric data of FTT patients with well-nourished control groups in developing countries. The studies in developing countries mainly compared children with marasmus and kwashiorkor to healthy controls, mostly from outpatient settings, and six of the seven studies found similar associations. One study looked primarily at the effect of home visits on Jamaican children with FTT and found that height for age remained low in the FTT group, even with the intervention. The addition of more adequate nutritional supplementation to such children would be anticipated to aid in these improvements in outcome. Two other studies also showed significant differences in body fat and arm muscle composition in the FTT groups compared to controls; in one of the studies, the decreased body fat and muscle mass had a negative impact on physical performance.

Overall these studies comparing children who were thriving with those who were undernourished in both developed and developing countries show that children with FTT have poorer weight, height, and head growth, and that this poorer growth is often long-standing despite appropriate interventions. Earlier intervention leads to potentially better long-term outcomes. The fact that children who fail to thrive have poorer head growth is not surprising considering that human brain growth is tremendous in the early childhood years and insults during this time may impact permanently on developmental and intellectual outcome. These findings emphasize the importance of early and intensive intervention for children with, or at risk for, FTT so as to prevent permanent growth retardation.

Association of Failure to Thrive With Immunologic/Infectious Outcomes

A total of eight controlled studies were identified for review; four of these focused primarily upon aspects of immune function while four examined clinical infections among FTT children. Studies carried out in developing countries have

variable generalizability for outcomes and policies in the United States.

Of the studies, seven were prospective cross-sectional studies and one study was retrospective. Only two studies were longitudinal; all others were cross-sectional. The principal source of potential bias involved the selection of controls. One study included adults as well as children in the controls; additionally, there were only controls (no FTT patients) entered from the children in an urban study center. The FTT and control groups in one study were from different hospitals serving different social-economic status (SES) populations; in another study controls included children with “nutritional growth retardation,” likely comparable to the United States FTT population.

Studies comparing children who were thriving with those who were undernourished in both developed and developing countries show that children with FTT have such factors as significantly decreased chemotactic response to bacterial endotoxin as well as phagocytosis of zymogen particles; significantly lower percentages of rosette forming cells (a sensitive marker of cellular immune function); and reduced *Candida* killing ability. Studies comparing the same cohort of children also show that children with FTT have significantly greater evidence both clinically and in the laboratory of susceptibility to infection. These findings emphasize the importance of identifying children who are failing to grow normally since their growth failure may be a marker for a variety of chronic and multiple acute infections that would otherwise be hard to identify. In addition, treatment of FTT provides an opportunity to prevent the far more destructive consequences and costs associated with chronic infectious conditions in children.

Child Behavior Associated With Failure to Thrive

Fifteen studies examined the relationship between FTT and behavioral disorders. Evidence will be presented in three areas.

Evidence of Concurrent Feeding-Related Behavior Problems Associated With Failure to Thrive. Four studies noted concurrent feeding disorders in children diagnosed with FTT. Behavior problems were more common in children with FTT, even beyond those children who were known to be failing to grow on the basis of neurological or other organic damage or disease. Children had such factors as increased negative affect and decreased positive affect during feeding compared to controls, with no difference in non-feeding situations. Severity of malnutrition, but not presence of organic disease, was associated with affective outcomes. Also, parents reported more feeding problems during infancy for the FTT cases, and described their children as uninterested or poor eaters.

Evidence Suggesting Other Concurrent Behavioral Problems. Four studies examined behavior problems that were either diagnosed concurrently with diagnosis or within the ensuing weeks or months. These behavior problems were

related to evidence of insecure attachment, and problems with communication and with mood/affect. The FTT groups scored significantly lower than controls on reports describing affect and communication skills, matched for such factors as age, sex, and race.

Evidence Regarding Behavior Problems Detected in Followup After a Diagnosis of Failure to Thrive. Seven studies evaluated children with FTT for behavioral disorders. When compared to the controls, the index groups had significantly more family problems, poor psychological development, or behavioral deficits as measured by a variety of behavioral screening questionnaires or checklists used in the studies.

Developmental Disorders Associated With Failure to Thrive

FTT is consistently associated with evidence of neurologic disabilities. Insufficient intake of both macro- and micronutrients exerts diverse functional and structural effects on the nervous system, with effects particularly likely to persist if they occur during the vulnerable periods of most rapid development. Since FTT most often occurs in early life, during the period of most rapid postnatal brain development, developmental concomitants and lasting sequelae are to be expected. In addition, FTT appears to heighten developmental vulnerability to other adverse environmental factors. In addition, subtle neurologic deficits may interfere with the normal progression of feeding skills, even in the absence of clinically evident palsies. They contribute to FTT by interfering with the child's ability to take in adequate nutrients. We present data from three domains.

Oral Motor and Other Neurologic Findings

Five prospective, epidemiologic, and observational studies consistently noted increased rates of feeding difficulties in children with FTT with some investigators also noting clinically poorly specified "neurologic" findings other than in feeding skills. Since these studies are often based on parental report, it is difficult to disaggregate true subtle neurologic (either oral motor or sensory) deficits in feeding from parental perceptions and from learned behaviors. However, delays in acquisition of mature feeding skills are a consistent finding in every study where they have been assessed.

Developmental/Cognitive Impairments Concurrent With the Identification of Failure to Thrive

Historically, developmental delay was considered by some authors as one of the criteria necessary for a diagnosis of FTT in addition to growth failure. It is only in recent decades that children have been labeled as FTT on the basis of weight gain alone. Thus many older studies do not include children who are failing to thrive but developing normally. In addition it is difficult to mask testers to the differences in size between

acutely underweight FTT children and normally growing comparison children of the same age. Therefore some experimenter effect cannot be ruled out in the studies summarized below.

There are three United States studies, two based on hospitalized children and the other on a sample not hospitalized but drawn from an outpatient inner city clinic (Mackner, Starr, Jr., and Black, 1997). In all three studies, the average Bayley Mental Development Index (MDI) scores were strikingly and significantly lower in children who had been identified with FTT compared to the control groups.

Two studies from the United Kingdom reported similar findings. Infants with FTT had scores that were significantly lower than controls on both the Bayley MDI (98.2 vs. 108.5) and Psychomotor Development Index (PDI) (96.7 vs. 103.6). At 36 months, the Stanford Binet IQ scores were lower for children with FTT, 84.7 vs. 89.9 for non-FTT, $p < 0.007$.

Developmental/Cognitive Function in Later Childhood Among Survivors of Early Failure to Thrive

Four studies evaluated developmental/cognitive function in later childhood among survivors of early FTT. Three of the four were United Kingdom studies and one was a United States study. Two were ambidirectional longitudinal studies, one prospective longitudinal, and the fourth, an ambidirectional cross-sectional study. Two were of high quality, and two of low quality. In one study, children with a history of FTT were found to have clinically and statistically significant cognitive deficits. The remaining three studies found that FTT was associated with decreased cognitive, motor, or neurological measures compared to controls.

Summary

At the time of identification, FTT is associated with lower than expected developmental test scores, especially in clinically identified hospitalized children. However, even in samples identified epidemiologically rather than by clinicians, FTT is associated on average with roughly two-thirds of a standard deviation decrease in developmental test scores, so that many more FTT children will score in the Supplemental Security Income qualifying range of developmental delay than children in a reference population.

Association of Failure to Thrive With Other Psychosocial and Family Factors

Thirteen studies assessed diverse risks associated with FTT. These studies were from developed countries (eight from the United States, four from the United Kingdom, and one from Israel) and populations were highly comparable. Five studies were prospective longitudinal, three were prospective cross-sectional, two each were retrospective longitudinal or ambidirectional cross-sectional, and one, ambidirectional longitudinal.

There is persuasive evidence that FTT is associated with a variety of other difficulties that may themselves secondarily predict or cause significant disability. Categories of associations include socioeconomic factors (lower income, lower maternal education, less enriched family environment/interactions); neonatal morbidity; acute illnesses and hospitalizations; neurological/anatomical abnormalities; family dysfunction; and abuse/neglect. Clearly these factors may precede the infant's FTT and/or occur subsequent to it. These variables are almost certainly multiply interrelated and the directions of causation impossible to describe in a linear fashion (for example, poverty may be one factor that leads to malnutrition, which increases the risk of illness/disability, which leads to increased poverty).

Future Research

The studies comprising this report, though insufficient in number and variable in their methodologic quality and their potential biases, were of sufficient validity to provide significant information regarding the association of FTT with disability. The variety and long-term nature of the disabilities associated with FTT have major impact on the child, the family, and society.

Notwithstanding this, it may well be that the most significant finding of this review was the paucity of information available on the subject. Much remains to be learned regarding the extent and specifics of these associations and disabilities. Even more remains to be determined as to the optimal management of these patients.

The following recommendations for future research address specific problematic issues and limitations identified from review of existing research:

- One of the central problems in interpreting these studies was the heterogeneity of definitions of FTT. This variability in case definition makes it unclear how well the population at risk is being identified at present. Future research should apply a uniform definition of FTT. This would serve to facilitate comparison and perhaps even allow a meta-analysis of studies. It would also define more clearly the true prevalence of FTT.
- Within the definition of FTT, provisions should be made for categorization based upon 1) severity and 2) longevity or duration of growth failure. The data currently available indicate that both of these factors are strong predictors not only for the risk of associated disabilities but for potential response to therapy as well. Refining the classification of the FTT population in this way would facilitate identification of the relative risk of disability for an individual FTT child. It would also help in the evaluation of intervention studies.
- Although it is clear that the degree of disability increases with increasing severity of growth failure, this is an imprecise correlation especially in children with mild to moderate FTT. Since the majority of FTT that is seen in

the United States tends not to be the most severe forms of marasmus and kwashiorkor, future research should specifically target those children with mild to moderate growth failure.

- Similarly, more research needs to be conducted in the United States or in developed countries with comparable social-economic structures and health care systems.
- Special emphasis should be given to outcomes focusing on neurodevelopmental and cognitive disorders. The data presented in this report indicate that this is likely one of the areas of strongest impact of FTT and certainly one with the greatest relevance for long-term disability. Specifically, very few studies have focused on the issue of FTT and brain growth during the immediate post-neonatal period and early infancy. This is one of the most critical periods for dendritic arborization, axonal myelination, and the development of cognitive functions. More studies are needed in this area.
- Further study is also needed on the association of FTT with general health outcomes because of their potential impact on the health care system. Beyond the risk to the individual child, the data linking FTT to increased risk of infections and poorer general health may have important implications at a broader level. Such data may help us understand the true "cost" of FTT and prove useful in evaluating intervention strategies.
- In order to better define the true nature and extent of the disabilities associated with FTT, more studies are needed that prospectively follow children for a sufficient duration to capture the more complex disabilities that may result from FTT.

A consistent finding among the studies reviewed was the ineffectiveness of existing intervention programs. Although strictly beyond the focus of this report, much work still needs to be done on developing effective treatment programs for children with FTT. Unfortunately, the optimal intervention will yet require better definition of the complex physical, medical, cognitive, and psychosocial problems associated with FTT.

Availability of the Full Report

The full evidence report from which this summary was taken was prepared for AHRQ by Tufts-New England Medical Center Evidence-based Practice Center under Contract No. 290-97-0019. It is expected to be available in spring 2003. At that time, printed copies may be obtained free of charge from the AHRQ Publications Clearinghouse by calling 800-358-9295. Requesters should ask for Evidence Report/Technology Assessment No. 72, *Criteria for Determining Disability in Infants and Children: Failure to Thrive*. Internet users will be able to access the report online through AHRQ's Web site at www.ahrq.gov.



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