Achieving goals by guidelines: myth or reality?

ESPEN guidelines in cystic fibrosis

D. Turck (France)
Guidelines on the nutritional support in cystic fibrosis

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Cystic fibrosis (CF)

• The most frequent hereditary disease among Caucasians (1/4000)

• Exocrine pancreatic insufficiency (85-90%)

• Recurrent respiratory infections (S. aureus, Pseudomonas aeruginosa)

• 95% of patients die of respiratory failure

• Median survival: 35-40 years

• There are as many CFs as there are patients
Evolution of FEV1 (% predicted values) as a function of BMI in adulthood

Cystic Fibrosis Patient Registry, USA, 2004
**Guideline Methodology**

- GRADE System: evidence-based, but also benefit-risk ratio and expert opinion, leading to strong and weak recommendations
- List of relevant questions
- Professional literature search based on PICO, with systematic review/metaanalysis if needed
- Conference calls and live meeting
- Delphi rounds
- External review

Preiser & Schneider, Clin Nutr 2011
Search strategy

• Search phrase
  - cystic fibrosis AND (nutrition* OR diet* OR nourishment OR nutrient OR nutriment OR malnutrition OR malnourishment OR undernourishment OR calorie* OR lipid* OR trace OR vitamin* OR protein* OR taurine OR pancreatic enzyme replacement therapy OR PERT OR fatty OR micronutrient* OR antioxidant* OR probiotic* OR supplement* OR insulin OR enteral OR parenteral OR EN OR TPN OR PN)

• Search results
  - 1593 records were examined. Included: 9 systematic reviews; 15 randomized controlled trials; 5 others
Questions and outcomes defined by the ESPEN WG

- A1 - Malnutrition in CF
- A2 - Nutritional deficiencies in CF
- *A3 - Strategies to prevent malnutrition in CF
- *A4 - Feeding the malnourished CF patient: energy, proteins, lipids, EFA, minerals, trace elements
- *A5 - The role of specific treatments in CF: anti-oxidants, DHA, anti-osteoporotic agents, anti-inflammatory & anabolic agents
# The quality of evidence and definitions

<table>
<thead>
<tr>
<th>Quality</th>
<th>Definition</th>
</tr>
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<tbody>
<tr>
<td>High ($H$)</td>
<td>Further research is very unlikely to change our confidence in the estimate of effect</td>
</tr>
<tr>
<td>Moderate ($M$)</td>
<td>Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate</td>
</tr>
<tr>
<td>Low ($L$)</td>
<td>Further research is likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate</td>
</tr>
<tr>
<td>Very low ($VL$)</td>
<td>Any estimate of effect is very uncertain</td>
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## Developing and grading the clinical guideline recommendation

<table>
<thead>
<tr>
<th>Quality of Evidence</th>
<th>Weighing Risks vs. Benefits</th>
<th>GRADE Recommendation</th>
<th>Clinical Guideline Statement</th>
</tr>
</thead>
<tbody>
<tr>
<td>High to very low</td>
<td>Net benefits outweigh harms</td>
<td>Strong</td>
<td>We recommend</td>
</tr>
<tr>
<td>High to very low</td>
<td>Tradeoffs for patients are important</td>
<td>Weak</td>
<td>We suggest</td>
</tr>
<tr>
<td>High to very low</td>
<td>Uncertain tradeoffs</td>
<td>Further research needed</td>
<td>We cannot make a recommendation at this time</td>
</tr>
</tbody>
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Strategies to prevent malnutrition in CF
• Introduction
  - We recommend centre care including early nutritional management, education and behavioural counselling (VL)
  - We recommend optimal treatment of CF related lung disease (VL)

• Newborns and infants
  - Newborn screening and early management of CF are recommended to prevent malnutrition in CF (VL)
  - We recommend exclusive breastfeeding as the preferred method of feeding for newly diagnosed infants with CF (VL)
  - We recommend a normal infant formula in infants who are not breastfed (VL)
• All age groups

- We recommend pancreatic function assessment and pancreatic enzyme replacement (PERT) in case of pancreatic insufficiency (PI) \((VL)\)

- We recommend energy intake adaptation to achieve normal growth and normal nutritional status, while avoiding obesity \((VL)\)

A much higher energy intake may be necessary, the goal being:

- \(50^{th}\) percentile of weight for length <2 years
- \(50^{th}\) percentile for BMI >2 years
- BMI 22 for female and 23 for male adults

Physical exercise is enforced to decrease the risk for obesity
• All age groups (c’td)

- We recommend that fat-soluble vitamins are supplemented routinely in PI, and in cases of deficiency for pancreatic sufficiency (VL)

- We suggest that fatty acid status is monitored and linoleic acid supplementation given if needed (VL)

- We suggest that sodium status is monitored and sodium chloride supplementation given if needed (VL)

- We recommend that all patients are closely monitored for treatment adherence, especially in adolescents (VL)
• Nutritional monitoring

- We recommend nutritional monitoring and follow-up, which include centre visits every 4 weeks in the first year of life, later at least every 3 months *(VL)*

- We recommend measuring weight and length/height at each visit, calculating weight for length percentile up to 2 years, BMI percentile for children and BMI for adults *(VL)*

- We suggest bone health assessment after the age of 8 years *(VL)*
CONSENSUS STATEMENT: Guide to Bone Health and Disease in Cystic Fibrosis


*J Clin Endocrinol Metab 90: 1888–1896, 2005

European cystic fibrosis bone mineralisation guidelines

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**FEV₁ as a function of age and presence of diabetes related to CF**

Mean FEV₁ in case of diabetes: 52%; in the absence of diabetes: 72%

• **Glucose tolerance**
  - We recommend annual screening of CF patients from 10 years of age for CF-related diabetes (RD) by OGTT (VL).
  
  - We recommend early initiation of therapy in patients with impaired glucose tolerance who have CF-RD. This should include a normal diet, insulin, self-management education and moderate aerobic exercise (VL).
  
  - We recommend early initiation of therapy in patients with impaired glucose tolerance who do not have CF-RD. This should include a normal diet, self-management education and moderate aerobic exercise. This may include insulin in patients with impaired clinical condition (VL).
Clinical Care Guidelines for Cystic Fibrosis-Related Diabetes

A position statement of the American Diabetes Association and a clinical practice guideline of the Cystic Fibrosis Foundation, endorsed by the Pediatric Endocrine Society

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The CFRD Guidelines Committee

Diabetes Care, volume 33, number 12, December 2010
Feeding the malnourished CF patient
• **Dietary counselling**
  - We recommend that all undernourished patients receive nutritional counselling, accurate assessment of dietary intake and PERT, and close follow-up from a CF dietitian (VL)

  - We recommend that undernourished infants, children and adults with CF are encouraged to eat a high fat diet (VL)

• **Behavioural intervention**
  - We recommend behavioural aspects of feeding be taken into consideration and addressed with all carers (VL)
• Oral supplementation

- We recommend that the use of oral nutritional supplements should be considered in children and adults with CF who fail to achieve optimal growth rates and nutritional status, despite maximising oral dietary intake and PERT (L)

- We do not recommend the routine supplementation of any single protein or amino acid (VL)
• Enteral tube feeding (ETF) - No RCTs

- We recommend that ETF is considered when oral interventions have failed to achieve acceptable rates of growth and nutritional status *(VL)*

- We recommend that the choice of route and timing of administration should be assessed on an individual basis *(VL)*

- We recommend the routine use of polymeric feeds *(VL)*
Enteral tube feeding for cystic fibrosis (Review)

Conway S, Morton A, Wolfe S
We recommend that parenteral nutrition is only used when there is a contra-indication to enteral nutrition or when enteral nutrition is not tolerated (VL)
The role of specific treatments in CF
- **Antioxidants**
  - We do not recommend the routine supplementation of antioxidants (vitamin C, vitamin E, β-carotene, selenium) *(L)*

- **Omega 3**
  - We do not recommend the routine supplementation with omega 3 *(L)*

- **Omega 6**
  - We suggest that fatty acid status is monitored and linoleic acid supplementation given if needed *(L)*
• **Appetite stimulants**
  - We do not recommend the routine use of appetite stimulants (megestrol acetate, cyproheptadine) \((L - M)\). They may be of help in patients when measures aimed at increasing energy intake have failed.

• **Growth hormone**
  - We do not recommend the routine use of growth hormone \((H)\)
Effectiveness of Recombinant Human Growth Hormone (rhGH) in the Treatment of Patients With Cystic Fibrosis

Agency for Healthcare Research and Quality
Advancing Excellence in Health Care • www.ahrq.gov

October 2010
Conclusion

• The level of evidence we have found is low to very low. RCTs included few patients; many of them were cross-over; analysis of sample size was lacking in almost all of them; many were of short duration; most of them are methodologically weak.

• The scarcity of data shows the need to issue a plan for well planned, multi-center RCTs, to answer the questions that are the most relevant for patients.
On behalf of the ESPEN WG
Thank you for your kind attention


ESPEN Guidelines Committee Co-Chair S Schneider