Nutrition in CF: Looking back, Looking forward….. to a healthy future

Dr Audrey Tierney
Ms Bhey Orwin
Dietitians
Alfred Health
Acknowledgements

– Alfred CF Service team members
– Co-investigators and CF participants of the 1983, 1997 and 2012/2013 Alfred Nutritional status research project
Outline

• Looking back
  – 1980s
  – 1990s
    • Differences Observed and Reasoning

• Looking forward
  – Teachings from 2012/13 Alfred Study
  – Obesity in CF – Is this an issue??
  – Nutritional implications of Ivacaftor
  – Emphasis on Diet Quality
The changing face of nutrition in CF

• Until 1980s
  – High energy/Low fat diet advocated for CF (impossible to achieve)
  – Pancreatic Enzyme Replacement Therapy (PERT) was not available and first preparations were ineffective
  – Mal-digestion and malabsorption
  – Increased requirements with frequent chest infections, poor appetite and inadequate intake
Relationship Between REE and Lung Function

- Challenging and near impossible to meet requirements
- Malnutrition “endemic”

Consequences:
- Poor growth in children
- Stunting
- Decrease body weight
- Decrease body fat
- Delayed pubertal development
- Poor survival
Previous studies at Alfred

- Repeat cross-sectional nutritional status studies
  - 1983: Ibolya Nyulasi
  - 1997: Indi Swan (Richardson et al 2000)

- Stable outpatients (>1 month since admission/ IVAB).
- Anthropometry
- Dietary intake
Females 1983

BMI (kg/m²) %body fat Mid-arm circ (cm)

1983 (n=19)
Females 1983 and 1997

Data show mean(SD).

1983 vs 1997: 
** p<0.005.
Data show mean(SD). 1983 vs 1997: * p<0.05;
Significance between 1983 and 1997

- Changes between 1983 -> 1997
  - 1980s enteric coated enzymes
  - Toronto paper – compared to Boston
  - Liberalisation of high fat diet
  - Significant improvements in nutritional status and survival
  - ↓ % of underweight
  - Normalisation of height - and not significantly different to Australian Average data
  - Dietary intakes shift in macronutrients
  - Higher energy and fat intakes
    - Energy 120-150%; Mean fat intake 35% energy (recommendation: 35-40%)
CF complications: from absence of concern key focus for surveillance and prevention

Examples:
- Osteoporosis (King et al, Alfred)
- Complications of diabetes
  - Cancer
  - Renal disease

Focus in CF Recommendations
- Screening/monitoring
  - Early detection
  - Prevention
  - Management
Rationale for the 2012 nutritional status study

• Timely to repeat the 1997 and 1983 studies
  – Changing patterns of CF as the population ages
  – Major service/management change since 1997

• Route outpatient allied health services in CF in Victoria
  – Newborn screening since 1989.....most of our adult population now Dx by NBS
Data collection

• Demographic and medical data
  – including lung function, co-morbidities

• Nutritional status
  – Height, weight, BMI, circumferences, skinfolds (->% fat)

• Dietary intake
  – 7 day non-weighed food diary
  – Food Frequency questionnaire

• Physical activity questionnaire (Baecke et al 1982): for EER calculation

• Questionnaires on influences on eating habits and food choices
  – Based on Vailas et al 1998; Steptoe et al 1995
## Results

29 males and 30 females participated in 2012-13.

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Mean</strong></td>
<td><strong>SD</strong></td>
</tr>
<tr>
<td><strong>Mean</strong></td>
<td><strong>SD</strong></td>
</tr>
<tr>
<td><strong>Mean</strong></td>
<td><strong>SD</strong></td>
</tr>
<tr>
<td>% Pancreatic insufficient</td>
<td></td>
</tr>
<tr>
<td>% Diabetes Mellitus</td>
<td></td>
</tr>
<tr>
<td>% on enteral nutrition</td>
<td></td>
</tr>
<tr>
<td>% oral nutritional supplements</td>
<td></td>
</tr>
<tr>
<td>% on vitamin and/or mineral supplements</td>
<td></td>
</tr>
<tr>
<td>% Working/studying ≥30h/week</td>
<td></td>
</tr>
<tr>
<td>% Working/studying part-time (&lt;30h/wk)</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>1983 (n=19)</th>
<th>1997 (n=19)</th>
<th>2012-13 (n=30)</th>
</tr>
</thead>
<tbody>
<tr>
<td>BMI (kg/m²)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>%body fat</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mid-arm circ (cm)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Data show mean(SD). 1983 vs 1997: ** p<0.005.

Data show mean(SD).
1983 vs 1997: *p<0.05; **p<0.01.
Marked shift in BMI distribution over a 30 year period

- 1983 (n=44)
  - <18: 30
  - 18-20: 32
  - 20-25: 36

- 1997 (n=43)
  - <18: 9
  - 18-20: 82
  - 20-25: 9

- 2012-13 (n=59)
  - <18: 4
  - 18-20: 10
  - 20-25: 69
  - >25: 17

BMI (kg/m²)
Gender divergence in BMI: new in 2012-13

- 1983 and 1997: no gender difference in mean BMI.
- By 2012-13, emergence of gender difference:
  - mean male BMI was 1.8kg/m² higher than females (p<0.001).
Changes in nutritional status over 30 yrs

- Significant ↑s in BMI & indices of fat & muscle stores in both genders between 1983 and 1997.
- Non-significant ↑s in all indices in males b/w 1997 & 2012-13.
- No ↑s in mean female BMI, %fat or MAC b/w 1997 & 2012-13.

Compared with Australian population

- Height normalised
- Weight, BMI lower
- Waist circumference similar
- Hip circumference lower
Dietary intake: 1983 vs 1997 vs 2012-13

Energy intake has remained stable since 1997.
- However, macronutrient composition of the diet has changed
  - ↓ fat intake (total and as % from energy)

<table>
<thead>
<tr>
<th>Nutrient</th>
<th>Males</th>
<th></th>
<th>Females</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>15</td>
<td>22</td>
<td>11</td>
<td>17</td>
</tr>
<tr>
<td>Energy intake</td>
<td>10.9±4.2</td>
<td>12.6±3.1</td>
<td>12.0±3.4</td>
<td>8.2±1.6</td>
</tr>
<tr>
<td>Fat intake (g/day)</td>
<td>91±42</td>
<td>122±37*</td>
<td>99±28</td>
<td>70±18</td>
</tr>
<tr>
<td>Fat as % of energy</td>
<td>31</td>
<td>35*</td>
<td>31¶</td>
<td>27</td>
</tr>
</tbody>
</table>

Statistics for comparisons between cohorts:
(a) 1983 vs 1997: *p<0.05. **p<0.01  
(b) 1997 vs 2012-13: ¶p<0.05  [ p=0.1]
Macronutrient composition: 1997 vs 2012-13

- % E from fat ↓ since 1997: 35% => 31.5% in 2012-13 (p=0.003).
- % E from protein ↑ since 1997: 16.2% => 19.2% in 2012-13 (p<0.0001).
Influences on food choices

It is **very important** or **moderately important** that the food I eat is.......
What about obesity in CF?

• Should we be worried?
Societal Context: The Obesity “Epidemic”

- Prevalence of overweight and obesity is increasing in many westernised and developing countries
  - Childhood obesity
    - ~30% children aged 2-15 years are overweight or obese
  - Overweight and obesity in adulthood
    - Prevalence of obesity in Australia: tripled since 1980

- CF populations in many countries live in the same “obesogenic” environments as the general population
Epidemiology: How common are overweight and obesity in CF?

- Recent Adult data from developed countries:
  - suggest approx. 15-20% adults with CF are overweight or obese

<table>
<thead>
<tr>
<th>Source/report</th>
<th>% Overweight</th>
<th>% Obese</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Canadian CF data registry report 2012</td>
<td>11% M &gt; F (1.5x)</td>
<td>4.7% M=F</td>
<td>Overweight: BMI 26-29</td>
</tr>
<tr>
<td>Australian CF data registry report 2012</td>
<td>BMI&gt;25: M: 27% F: 15%. Adults &gt;30 years: twice the rate of overweight/obesity CF adults 18-29 yrs</td>
<td>4% M&gt;F</td>
<td>Only reports BMI&gt;25</td>
</tr>
<tr>
<td>Stephenson et al, AJCN 2013 (Toronto Canada)</td>
<td>18% M&gt;F</td>
<td>4% M&gt;F</td>
<td>2.5 x increase since 1980s PS: 88% obese; 43% overweight</td>
</tr>
<tr>
<td>King and Tierney et al, n=59</td>
<td>15%</td>
<td>2%</td>
<td>Stable CF outpatient population, 2x ↑ in BMI &gt;25 since 1997</td>
</tr>
</tbody>
</table>
10 participants in 2012-13 had BMI >25kg/m² (17%)
  - All had an abdominal circumference above the population recommendation (F: 80cm; M: 94cm).
  - 50% of these had waist:hip ratio above the recommendation (F: 0.8; M: 0.9).

No data on these circumferences reported in previous studies.
BMI and lung function in CF

• High BMIs do not appear to confer FEV$_1$% benefits in CF:
  – plateau or minimal gain above BMI 25 (or 85th %ile in children) in most epidemiological analyses

Source:
UK CF Registry 2012
Obesity in CF: Clinical disadvantage

• Ineligibility for lung transplant listing
  – Upper limit at Alfred Hospital: BMI 29 (all indications)

• ?? Risk of type 2 diabetes  
• ?? Risk of cardiovascular disease  ) unknown in CF
• ?? Risk of obesity-related cancers  )
Possible contributors to +ve energy balance leading to excess fat accumulation in CF

- **Energy intake too high**
  - Promotion of high energy high fat diet
  - Unregulated/unmonitored use of oral supplements
  - Lifelong practices – “more is better”

- **Energy losses lower than expected accounted for**
  - Pancreatic Sufficient patients: little/no maldigestion
  - Improved PERT preparations and usage in PI patients
  - Better management of other contributors to maldigestion/malabsorption (e.g. acid suppression, management of liver disease)
  - “Beneficial” side effects of newer CF medications: Ivacaftor
Possible contributors to +ve energy balance leading to excess fat accumulation in CF

• Less requirement for “catch-up” growth
  – Newborn screening => lifetime care
  – Better nutrition surveillance and improved dietetic resourcing: earlier detection and intervention

• Physical activity:
  – CF-specific and the broader obesogenic environment
  – ↓ Habitual activity “Energy conservation”
  – ↓ exercise and physical activity:
    • Routine
    • During acute illnesses
  – Impact of treatment burden/time, fatigue, depression
Possible contributors to +ve energy balance leading to excess fat accumulation in CF

• ↓ Degree of hypermetabolism associated with acute/chronic CF lung disease?
  – Better management of lung disease
  – Optimisation of lung function
  – Prevention of acute exacerbations
    • medications, airway clearance therapies
Nutritional Challenges in Adults post Ivacaftor

Ivacaftor: The first mutation-specific drug for CF
Ivacaftor Leads to Weight Gain

Why?

Ramsey et al, NEJM 2011;365:1663
How Might Ivacaftor Lead to Weight Gain?

• Enzymes working better - Improvements in fat and nutrient absorption
• More efficient energy use
• Improved appetite (less inflammation)
• Decreased work of breathing, decrease in resting metabolic rate
Initial Weight Gain in Adolescents and Adults taking Ivacaftor Levels Off Over Time

STRIVE

Absolute Change in Weight (kg, mean ± SE)

Week

-2  0  4  8  12  16  20  24  28  32  36  40  44  48  52  56  60  64  68  72  76  80  84  88  92  96  100  104  108  112  116  120  124  128  132  136  140  144

Ivacaftor initiated in PERSIST study

Ivacaftor → Ivacaftor
Placibo → Ivacaftor

N=77
N=67

McKone et al ECFC 2013
Evolution of overweight/obesity in CF

• Therefore, it is easy to see how the current environment + current therapies for CF may be negating the need for a *high energy diet* in many people with CF

• Continuing with this traditional approach to diet may be contributing to excessive weight gain in some people with CF
• Surveillance & Monitoring to identify those at risk

• Nutritional status:
  – Weight and BMI / BMI %iles – current practice
  – Identification of excess adipose tissue deposition
Monitoring: Dietary intake and food habits

• Dietetic monitoring and intervention to identify and manage individuals who don’t need high energy/high fat diets
  – Our data from 2012-13: A high fat diet is not a priority for the stable outpatient adult population
    – Stronger preference for protein, fibre and micronutrient food sources

• Ensure appropriate use of nutrition support (esp oral nutritional supplements)
  – Includes criteria for commencing and ceasing ONS
  – Consider intermittent vs routine use
  – Hanna and Weiner (2014): found that 19% of overweight/obese children received ONS
Prevention of overweight / obesity: CF Guidelines and goals

• We now have strong epidemiological evidence for emergence of overweight and obesity in CF population
• This exists alongside malnutrition

• CF nutrition guidelines – ideally should focus on:
  – Goals of nutrition at both ends of the spectrum:
    □ normal growth
    □ prevention of malnutrition AND
    □ prevention of overnutrition
  – In the era of newborn screening/lifetime care:
    • ↑ energy intake for catch-up growth is required in fewer pts
    – Individualisation of energy and macronutrient targets to meet nutrition goals and priorities – including pancreatic status
Potential dietary options: Focus on Diet Quality

Nutritional quality of the diet for long-term metabolic health:

• Shift from saturated to unsaturated fats
• Shift from energy-dense diet to nutrient-dense diet
• Consider Mediterranean Diet
  – Epidemiological and intervention studies
  – ↓ All-cause mortality
  – ↓ Cardiovascular mortality
  – ↓ Cancer mortality
  – ↓ Degenerative diseases eg, Alzheimer’s disease
  – ↓ diabetic retinopathy
Potential dietary options: Mediterranean diet

• Features of a Mediterranean diet
  – High fat – mostly unsaturated fat (olive oil is the major fat used)
  – Moderate protein – fish, legumes, lower intakes of red meat
  – High fruit and vegetable intake
  – Wholegrain breads, grains and cereals – moderate amounts
  – Moderate dairy – yoghurt, white cheese
  – Small amounts alcohol
Summary

- Since the landmark finding in the late 1980s that an unrestricted fat diet was associated with improved nutritional status and survival, a high energy high fat diet has been one of the cornerstone recommendations for CF management.

- Previous research at The Alfred CF Service showed marked improvements in nutritional status and nutrient intakes of the adult outpatient CF population were achieved between 1983 and 1997 which were attributable to higher energy and fat intakes resulting from liberalisation of the diet.

- Since then, a gender divergence has emerged. Nutritional status of adult males has tended to increase, while females appeared to have plateaued.

- With ageing of the CF population, there is concern about emergence of overweight/obesity, and related complications (metabolic disease, cancer).
Discussion

- Energy intakes stable in 2012-13 compared with 1997

- However, macronutrient composition of the diet has changed: fat intake slower compared with 1997.
  - Dietary intake data + questionnaires suggests high fat diet less important to this adult CF cohort
  - Protein, fibre and the nutrient density of foods are motivators of food choice for a greater % of adults.

- Limitation: Results not generalisable to sicker/frequently admitted CF population.
Looking Forward

• Haven’t eradicated underweight - emergence of underweight in 2012/13 data
• Query chance finding
• Query more young women striving to be thin - societal desire
• Pregnancy in CF – worldwide experience
• Gene Therapies
• Gut function – myriad of symptoms not explained by enzymes, not just about enzymes and reflux
• Probiotics; Fish oils
• Complementary medicine
Conclusions

- With improvements in CF management and survival, “endemic” malnutrition is largely of a bygone era
  - Normal nutritional status is achievable for majority of CF
  - Overweight / obesity are emerging in children and adults with CF
- Obesity in CF is not solely confined to older adults, PS or mild lung disease
- The potential impact of obesity on the health, functional status and longevity of the CF population is not yet clear
- Now is the time to act: nutrition recommendations for CF need to address the diverse range of nutrition priorities amongst the CF population
- CF-specific evidence for most weight loss dietary and medical options for obesity is lacking.
# Advocacy - CF Dietitians

## Collaboration Highlights

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>CF Interest Group</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Formed n=5</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>First CF Dietitian Practice Survey⁴</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pancreatic Enzyme</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Replacement Therapy</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>in CF: Guidelines</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Review of Pancreatic</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Enzyme Replacement</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Therapy Practice</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Second CF Dietitian Practice Survey 2006 Australian Clinical Practice Guidelines for Nutrition in CF²</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Third CF Dietitian Practice Survey⁷</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Work commences on CF PEN pathways and guidelines</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CF Interest Group</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>n=219</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Successful Business Case: Dietitian on Australian CF Data Registry Advisory Committee</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>