Quality of Life Clinical Trials in Patients with Cancer

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• More than 150 years ago, Florence Nightingale used to record that her patients left hospital “dead, relieved, or unrelieved.” But for 60 years the NHS has routinely recorded only whether they left dead or alive.

Timmins BMJ 2008
PRO use Cancer Clinical Trials

• 17,704 interventional trials, 2481 (14.0%) used at least one PRO instrument in 2007
• Only 41% identified the instrument to be used
• PRO use associated with phase (III) randomization (randomized) intervention (behavior) sponsorship (university/research organization)

Scoggins Contemp Clin Trials 2009
PRO use Cancer Clinical Trials

- Of 173 cancer trials 52% specified QoL outcomes in protocol
  - Of those only 1% were QoL outcomes primary
- Only 20% reported QoL outcomes in subsequent publications
- All of trials that did not specify QoL outcomes did not report any

*Schandelmaier et al Ann Oncol 2015 Sept*
Symptoms: Patient vs Provider

• 1,090 patients (2,482 cycles) were included
• Agreement between patients and physicians was low for all toxicities
  – Physician reporting always lower than those reported by patients
• For patients who reported toxicity (any severity), under-reporting by physicians ranged from 40.7% to 74.4%

Figure 1 Conceptualization of PRO constructs.
## Tools used in clinical practice vs. research

**Higginson BMJ 2012**

<table>
<thead>
<tr>
<th>Tools</th>
<th>Use in clinical care/audit</th>
<th>Use in research</th>
<th>Ratio of clinical to research use</th>
</tr>
</thead>
<tbody>
<tr>
<td>Karnofsky Performance Scale (KPS)</td>
<td>214 49.3% 1</td>
<td>77 17.7% 1</td>
<td>2.78</td>
</tr>
<tr>
<td>Edmonton Symptom Assessment Scale (ESAS)</td>
<td>135 31.1% 2</td>
<td>57 13.1% 3</td>
<td>2.37</td>
</tr>
<tr>
<td>Palliative care Outcome Scale (POS)</td>
<td>112 25.8% 3</td>
<td>63 14.5% 2</td>
<td>1.78</td>
</tr>
<tr>
<td>Palliative Performance Scale (PPS)</td>
<td>87 20% 4</td>
<td>34 7.8% 5</td>
<td>2.56</td>
</tr>
<tr>
<td>Palliative Care Assessment tool (PACA)</td>
<td>55 12.7% 5</td>
<td>12 2.8% 12.5</td>
<td>4.58</td>
</tr>
<tr>
<td>Symptom Distress Scale (SDS)</td>
<td>51 11.8% 6</td>
<td>14 3.2% 10.5</td>
<td>3.64</td>
</tr>
<tr>
<td>Support Team Assessment Schedule (STAS)</td>
<td>45 10.4% 7</td>
<td>20 4.6% 8</td>
<td>2.25</td>
</tr>
<tr>
<td>Quality of Life at the End of Life (QUAL-E)</td>
<td>31 7.1% 8</td>
<td>12 2.8% 12.5</td>
<td>2.58</td>
</tr>
<tr>
<td>European Organisation for Research into the Treatment of Cancer – 30 item questionnaire (EORTC QLQ-C30)</td>
<td>29 6.7% 9</td>
<td>52 12% 4</td>
<td>0.56</td>
</tr>
<tr>
<td>McGill Quality Of Life questionnaire (MQOL)</td>
<td>23 5.3% 10</td>
<td>20 4.6% 8</td>
<td>1.15</td>
</tr>
<tr>
<td>European Organisation for Research into the Treatment of Cancer – Quality of Life Questionnaire 15 items for palliative care (EORTC QLQ-C15-Pal)</td>
<td>21 4.8% 11</td>
<td>21 4.8% 5</td>
<td>1.00</td>
</tr>
<tr>
<td>Memorial Symptom Assessment Schedule (MSAS)</td>
<td>17 3.9% 12</td>
<td>14 3.2% 10.5</td>
<td>1.21</td>
</tr>
<tr>
<td>Schedule for the Evaluation of Individual Quality of Life (SEIQoL)</td>
<td>15 3.5% 13.5</td>
<td>11 2.5% 14</td>
<td>1.36</td>
</tr>
<tr>
<td>Hospice Quality of Life Index (HQLI)</td>
<td>15 3.5% 13.5</td>
<td>5 1.2% 17</td>
<td>3.00</td>
</tr>
<tr>
<td>Functional Assessment of Cancer Therapy-General (FACT-G)</td>
<td>14 3.2% 15</td>
<td>20 4.6% 8</td>
<td>0.70</td>
</tr>
<tr>
<td>Rotterdam Symptom Checklist (RSCL)</td>
<td>13 3.0% 16</td>
<td>7 1.6% 15</td>
<td>1.86</td>
</tr>
<tr>
<td>McMaster Quality of Life Scale (MQLS)</td>
<td>4 0.9% 17</td>
<td>1 0.2% 18</td>
<td>4.00</td>
</tr>
<tr>
<td>Missoula-VITAS Quality of Life Index (MVQOLI)</td>
<td>2 0.5% 18</td>
<td>6 1.4% 16</td>
<td>0.33</td>
</tr>
</tbody>
</table>

The % shown is the valid % of individuals responding yes or no to the question. Rankings are shown for highest % use in clinical care/audit and then for research. Tied rankings are assigned the mid ranking of all those with the same tied scores.
Life derives its quality from the ability and capacity of the individual to satisfy certain human needs.

**QoL** is good when most needs are fulfilled and poor when few needs are satisfied.
PRO’s for Oncologists

QOPI=Quality Oncology Practice Practice

• ASCO initiative for integrating continuous quality improvement into patient-centered clinical practice

• PRO’s include pain, and “emotional well-being”

• N/v but only in relation to ensuring prophylaxis with emetogenic regimens

*Siegel et al, J Oncol Pract, Mar 2015;11(2):247-253*
PRO’s for Oncologists

Barbera cancer 2010

- Edmonton Symptom Assessment Scale
- >45 000 oncology outpatients in Ontario
- Included patients treated with curative intent

Table 2. Percentage of Patients Reporting Each ESAS Symptom

<table>
<thead>
<tr>
<th>Score</th>
<th>Tired</th>
<th>Well Being</th>
<th>Appetite</th>
<th>Anxious</th>
<th>Pain</th>
<th>Drowsy</th>
<th>Shortness of Breath</th>
<th>Depression</th>
<th>Nausea</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>24.5</td>
<td>27.3</td>
<td>40.8</td>
<td>43.0</td>
<td>47.4</td>
<td>50.2</td>
<td>51.2</td>
<td>55.9</td>
<td>75.1</td>
</tr>
<tr>
<td>1</td>
<td>7.8</td>
<td>10.4</td>
<td>9.3</td>
<td>9.8</td>
<td>9.0</td>
<td>8.4</td>
<td>8.7</td>
<td>8.2</td>
<td>6.8</td>
</tr>
<tr>
<td>2</td>
<td>9.9</td>
<td>11.3</td>
<td>8.2</td>
<td>10.5</td>
<td>8.6</td>
<td>8.5</td>
<td>8.1</td>
<td>8.6</td>
<td>5.1</td>
</tr>
<tr>
<td>3</td>
<td>10.5</td>
<td>10.0</td>
<td>7.4</td>
<td>8.9</td>
<td>7.8</td>
<td>7.4</td>
<td>7.1</td>
<td>7.0</td>
<td>3.6</td>
</tr>
<tr>
<td>4</td>
<td>8.7</td>
<td>7.8</td>
<td>6.0</td>
<td>5.9</td>
<td>5.7</td>
<td>5.2</td>
<td>5.2</td>
<td>4.9</td>
<td>2.2</td>
</tr>
<tr>
<td>5</td>
<td>11.5</td>
<td>14.4</td>
<td>10.8</td>
<td>8.0</td>
<td>6.7</td>
<td>6.5</td>
<td>6.4</td>
<td>6.2</td>
<td>2.6</td>
</tr>
<tr>
<td>6</td>
<td>6.7</td>
<td>5.3</td>
<td>4.0</td>
<td>3.5</td>
<td>4.1</td>
<td>3.7</td>
<td>3.4</td>
<td>2.7</td>
<td>1.4</td>
</tr>
<tr>
<td>7</td>
<td>7.2</td>
<td>5.0</td>
<td>4.0</td>
<td>3.6</td>
<td>3.9</td>
<td>3.7</td>
<td>3.6</td>
<td>2.4</td>
<td>1.2</td>
</tr>
<tr>
<td>8</td>
<td>7.0</td>
<td>4.5</td>
<td>4.2</td>
<td>3.4</td>
<td>3.6</td>
<td>3.5</td>
<td>3.3</td>
<td>2.2</td>
<td>1.0</td>
</tr>
<tr>
<td>9</td>
<td>3.3</td>
<td>2.1</td>
<td>2.4</td>
<td>1.6</td>
<td>1.5</td>
<td>1.6</td>
<td>1.7</td>
<td>1.0</td>
<td>0.6</td>
</tr>
<tr>
<td>10</td>
<td>3.0</td>
<td>2.1</td>
<td>3.1</td>
<td>1.8</td>
<td>1.8</td>
<td>1.4</td>
<td>1.6</td>
<td>1.2</td>
<td>0.6</td>
</tr>
</tbody>
</table>

ESAS indicates Edmonton Symptom Assessment System.
Symptom screening rate in Ontario since 2009.

José Pereira et al. JOP doi:10.1200/JOP.2014.001390

©2014 by American Society of Clinical Oncology
ESAS

Edmonton Symptom Assessment System:
(revised version) (ESAS-R)

Please circle the number that best describes how you feel NOW:

<table>
<thead>
<tr>
<th>Symptom</th>
<th>0</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
<th>8</th>
<th>9</th>
<th>10</th>
<th>Worst Possible</th>
</tr>
</thead>
<tbody>
<tr>
<td>No Pain</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Pain</td>
</tr>
<tr>
<td>No Tiredness</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Tiredness</td>
</tr>
<tr>
<td>(Tiredness = lack of energy)</td>
<td></td>
<td></td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No Drowsiness</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Drowsiness</td>
</tr>
<tr>
<td>(Drowsiness = feeling sleepy)</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>No Nausea</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Nausea</td>
</tr>
<tr>
<td>No Lack of Appetite</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Appetite</td>
</tr>
<tr>
<td>No Shortness of Breath</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Breath</td>
</tr>
<tr>
<td>No Depression</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Depression</td>
</tr>
<tr>
<td>(Depression = feeling sad)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No Anxiety</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Anxiety</td>
</tr>
<tr>
<td>(Anxiety = feeling nervous)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Best Wellbeing</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Wellbeing</td>
</tr>
<tr>
<td>(Wellbeing = how you feel overall)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No Other Problem (for example constipation)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Other Problem</td>
</tr>
</tbody>
</table>

Completed by (check one):
- Patient
- Family caregiver
- Health care professional caregiver
- Caregiver-assisted

Patient’s Name ________________________________

Date ____________________ Time ________________
EORTC

• Multiple QOL questionnaires available for use—general through specialized to disease process
• Available for use for research and clinical settings
• Most commonly used EORTC QLQ-C30
• Groups.eortc.be/qol/sites/default/files/img/slider/specimen_qlq-c30_english.pdf

Zikos et al, J Natl Cancer Inst, 2016;108(5)
EORTC QLQ-C30 (version 3)

We are interested in some things about you and your health. Please answer all of the questions yourself by circling the number that best applies to you. There are no "right" or "wrong" answers. The information that you provide will remain strictly confidential.

Please fill in your initials:  
Your birthdate (Day, Month, Year):  
Today's date (Day, Month, Year): 31

<table>
<thead>
<tr>
<th>Number</th>
<th>Question</th>
<th>Not at All</th>
<th>A Little</th>
<th>Quite a Bit</th>
<th>Very Much</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Do you have any trouble doing strenuous activities, like carrying a heavy shopping bag or a suitcase?</td>
<td>1 2 3 4</td>
<td>1 2 3 4</td>
<td>1 2 3 4</td>
<td>1 2 3 4</td>
</tr>
<tr>
<td>2.</td>
<td>Do you have any trouble taking a long walk?</td>
<td>1 2 3 4</td>
<td>1 2 3 4</td>
<td>1 2 3 4</td>
<td>1 2 3 4</td>
</tr>
<tr>
<td>3.</td>
<td>Do you have any trouble taking a short walk outside of the house?</td>
<td>1 2 3 4</td>
<td>1 2 3 4</td>
<td>1 2 3 4</td>
<td>1 2 3 4</td>
</tr>
<tr>
<td>4.</td>
<td>Do you need to stay in bed or a chair during the day?</td>
<td>1 2 3 4</td>
<td>1 2 3 4</td>
<td>1 2 3 4</td>
<td>1 2 3 4</td>
</tr>
<tr>
<td>5.</td>
<td>Do you need help with eating, dressing, washing yourself or using the toilet?</td>
<td>1 2 3 4</td>
<td>1 2 3 4</td>
<td>1 2 3 4</td>
<td>1 2 3 4</td>
</tr>
</tbody>
</table>

**During the past week:**

<table>
<thead>
<tr>
<th>Number</th>
<th>Question</th>
<th>Not at All</th>
<th>A Little</th>
<th>Quite a Bit</th>
<th>Very Much</th>
</tr>
</thead>
<tbody>
<tr>
<td>6.</td>
<td>Were you limited in doing either your work or other daily activities?</td>
<td>1 2 3 4</td>
<td>1 2 3 4</td>
<td>1 2 3 4</td>
<td>1 2 3 4</td>
</tr>
<tr>
<td>7.</td>
<td>Were you limited in pursuing your hobbies or other leisure time activities?</td>
<td>1 2 3 4</td>
<td>1 2 3 4</td>
<td>1 2 3 4</td>
<td>1 2 3 4</td>
</tr>
<tr>
<td>8.</td>
<td>Were you short of breath?</td>
<td>1 2 3 4</td>
<td>1 2 3 4</td>
<td>1 2 3 4</td>
<td>1 2 3 4</td>
</tr>
<tr>
<td>9.</td>
<td>Have you had pain?</td>
<td>1 2 3 4</td>
<td>1 2 3 4</td>
<td>1 2 3 4</td>
<td>1 2 3 4</td>
</tr>
<tr>
<td>10.</td>
<td>Did you need to rest?</td>
<td>1 2 3 4</td>
<td>1 2 3 4</td>
<td>1 2 3 4</td>
<td>1 2 3 4</td>
</tr>
<tr>
<td>11.</td>
<td>Have you had trouble sleeping?</td>
<td>1 2 3 4</td>
<td>1 2 3 4</td>
<td>1 2 3 4</td>
<td>1 2 3 4</td>
</tr>
<tr>
<td>12.</td>
<td>Have you felt weak?</td>
<td>1 2 3 4</td>
<td>1 2 3 4</td>
<td>1 2 3 4</td>
<td>1 2 3 4</td>
</tr>
<tr>
<td>13.</td>
<td>Have you lacked appetite?</td>
<td>1 2 3 4</td>
<td>1 2 3 4</td>
<td>1 2 3 4</td>
<td>1 2 3 4</td>
</tr>
<tr>
<td>14.</td>
<td>Have you felt nauseated?</td>
<td>1 2 3 4</td>
<td>1 2 3 4</td>
<td>1 2 3 4</td>
<td>1 2 3 4</td>
</tr>
<tr>
<td>15.</td>
<td>Have you vomited?</td>
<td>1 2 3 4</td>
<td>1 2 3 4</td>
<td>1 2 3 4</td>
<td>1 2 3 4</td>
</tr>
</tbody>
</table>

For the following questions please circle the number between 1 and 7 that best applies to you:

<table>
<thead>
<tr>
<th>Number</th>
<th>Question</th>
<th>Not at All</th>
<th>A Little</th>
<th>Quite a Bit</th>
<th>Very Much</th>
</tr>
</thead>
<tbody>
<tr>
<td>29.</td>
<td>How would you rate your overall health during the past week?</td>
<td>1 2 3 4 5 6 7</td>
<td>Very poor</td>
<td>Excellent</td>
<td></td>
</tr>
<tr>
<td>30.</td>
<td>How would you rate your overall quality of life during the past week?</td>
<td>1 2 3 4 5 6 7</td>
<td>Very poor</td>
<td>Excellent</td>
<td></td>
</tr>
</tbody>
</table>

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PROMIS®

- NIH repository of PRO measures
- Separate scales for children and adults
- Not restricted to cancer
- nihpromis.org
PRO and Clinical Outcomes

• Random assignment 766 patients at MSK report 12 symptoms vs usual care
• HRQL improved intervention group
  – Instrument EuroQol EQ-5D
• Less ED, hospitalization (secondary outcomes)
• Survival trend towards intervention
• Intervention group on chemo longer (8.2 vs 6.3)

*Basch et al, JCO, Feb 2016;34(6):557-565*
Proportion of patients with health-related quality-of-life changes at 6 months compared with baseline.

Ethan Basch et al. JCO doi:10.1200/JCO.2015.63.0830
PRO and Clinical Outcomes

• Measured rates of ESAS screening at outpatient visits for non metastatic breast cancer over 2 year period
• Rate of ED presentations 43% lower in patients with ESAS screening at some point vs none
• Multiple ESAS screenings diminished ED presentation risk even more

Barbera et al, Support Care Cancer 2015 Oct;23(10):3025-32
HRQoL and Prognostication

• Several studies indicate lower scores HRQoL portend poorer survival
• Zikos et al J Natl Cancer Inst. 2015 Dec
  – Over 17,000 patients in PROBE database
  – HRQoL increased prognostic accuracy 6-8%
• Steel et al Cancer 2014 Dec
  – HRQoL in HCC/cholangio sig assoc with survival
• Lee et al Palliat Support Care 2015 Aug
  – Global QoL, anorexia, ECOG sig assoc with survival
The Patient-Reported Outcomes and Behavioural Evidence dataset subgrouped by cancer sites.


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HRQoL and Prognostication

• 104 studies show global quality of life, function domains and symptom scores such as appetite, fatigue and pain were the most important indicators, individually or in combination, for survival

• Which specific HRQOL parameter is the best predictor?

Montezari Health Qual Life out 2009
Figure 3  Overall survival curves stratified by QLQ-C30 appetite loss score  QLQ-C30=the European Organisation for Research and Treatment of Cancer quality-of-life core questionnaire.

Chantal Quinten, Corneel Coens, Murielle Mauer, et al.

Baseline quality of life as a prognostic indicator of survival: a meta-analysis of individual patient data from EORTC clinical trials
The Lancet Oncology Volume 10, Issue 9 2009 865 - 871
Finances and QoL

• Lung and colorectal cancer patients
• Compared less than 2 month financial reserve vs > 12 months
• Diminished financial reserve led to:
  – Increased pain reporting (BPI)
  – Increased overall symptom burden (EORTC QLQ-C30)
  – Decreased QoL (Euro-QoL-5)

Lathan et al JCO 2016 May 20
Unadjusted means of baseline patient-reported quality-of-life measures by financial strain and cancer type.
PRO Opportunities

• Discussed “lost opportunities and lessons learned”
  – No clear PRO hypotheses
  – No PRO endpoints or insensitive endpoints
  – Collection of poor quality PRO data
  – PRO differences in treatment arms ignored
  – Poor reporting quality

Friedlander et al Ann Oncol 2016 Apr
PRO’s in Cachexia Research

- Appetite
- Other symptoms including fatigue
- Quality of Life questionnaires
- Weight
- Caloric intake
- Lean body mass
- Fat
- Strength and endurance
- Systemic inflammation
- Spontaneous Physical activity
- Resting Energy expenditure
- Survival
Assessment of Cachexia in clinical Practice using PRO’s

• Edmonton Symptom Assessment Scale
• Palliative care Outcome Scale
• abridged PG-SGA
Scored Patient-Generated Subjective Global Assessment (PG-SGA)

History (Boxes 1-4 are designed to be completed by the patient.)

1. **Weight** *(See Worksheet 1)*

   In summary of my current and recent weight:

   I currently weigh about ______ pounds
   I am about ______ feet _______ tall

   One month ago I weighed about _______ pounds
   Six months ago I weighed about _______ pounds

   During the past two weeks my weight has:
   □ decreased (1) □ not changed (0) □ increased (9)  

2. **Food Intake:** As compared to my normal intake, I would rate my food intake during the past month as:
   □ unchanged (0)
   □ more than usual (9)
   □ less than usual (1)
   
   I am now taking:
   □ normal food but less than normal amount (1)
   □ little solid food (2)
   □ only liquids (3)
   □ only nutritional supplements (3)
   □ very little of anything (4)
   □ only tube feedings or only nutrition by vein (9)

3. **Symptoms:** I have had the following problems that have kept me from eating enough during the past two weeks (check all that apply):
   □ no problems eating (0)
   □ no appetite, just did not feel like eating (9)
   □ nausea (1)
   □ constipation (1)
   □ mouth sores (2)
   □ things taste funny or have no taste (1)
   □ problems swallowing (2)
   □ pain; where? (1) _______
   □ other** (1) ______________________

   **Examples: depression, money, or dental problems

4. **Activities and Function:** Over the past month, I would generally rate my activity as:
   □ normal with no limitations (9)
   □ not my normal self, but able to be up and about with fairly normal activities (1)
   □ not feeling up to most things, but in bed or chair less than half the day (2)
   □ able to do little activity and spend most of the day in bed or chair (3)
   □ pretty much bedridden, rarely out of bed (3)

Additive Score of the Boxes 1-4

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Important Needs of Patients (and Families)

• Significance of weight loss and decreased intake
  clear indicators of disease progression
• Conflict between family members and healthcare providers
  “selective neglect”
• Conflict in the patient-family unit
  family members try to pressure relative to eat
• Cascade of Losses
  sensory pleasure, healthy body, usual activity, enjoyment of family mealtime
• Alterations in body image
  affects feminity/masculinity, self confidence, and sense of identity and purpose.

S. McClement, 2004
### Table 2

**Patient-reported outcomes in cancer cachexia clinical trials.**

Wheelwright, Sally; Johnson, Colin

DOI: 10.1097/SPC.0000000000000168

<table>
<thead>
<tr>
<th>Trial ID</th>
<th>Target n</th>
<th>Intervention</th>
<th>Primary outcome</th>
<th>Secondary outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACTRN12615000167561</td>
<td>286</td>
<td>Physical activity programme</td>
<td>Katz Index, physical performance test questionnaire</td>
<td>CES-D, QLQ-C30, GSI, TEQ, 6-min walk test and sit to stand test, Physical performance, depression, HRQOL and leisure time exercise</td>
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<tr>
<td>IRCT2013081410297N2</td>
<td>70</td>
<td>Pentoxifyline</td>
<td>Arm circumference and SF-36</td>
<td>Side-effects, BMI, HRQOL</td>
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<tr>
<td>IRCT2014050511375N3</td>
<td>40</td>
<td>Captopril</td>
<td>QLQ-C30</td>
<td>Self-reported eating-related distress and weight-related distress VAS, Self-reported family and friends are pressuring me to eat VAS (FAACT), Psychological wellbeing, distress, feeling pressured and coping mechanism</td>
</tr>
<tr>
<td>ISRCTN22427358</td>
<td>200</td>
<td>Psychoeducational DVD</td>
<td>Psychological well being as measured by GHG-12</td>
<td>None listed</td>
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<tr>
<td>JPRN-JapicCTI-111415</td>
<td>162</td>
<td>ONO-7643 (Anamorelin hydrochloride)</td>
<td>Efficacy and safety</td>
<td>None listed</td>
</tr>
<tr>
<td>JPRN-JapicCTI-142451</td>
<td>170</td>
<td>ONO-7643 (Anamorelin hydrochloride)</td>
<td>Efficacy and safety</td>
<td>None listed</td>
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<tr>
<td>JPRN-UMINO00014335</td>
<td>30</td>
<td>Theracurmin</td>
<td>Expression of cytokines</td>
<td>Nutrition status, HRQOL score</td>
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<tr>
<td>NCT02666363</td>
<td>100</td>
<td>Parenteral nutrition</td>
<td>Changes in body composition</td>
<td>QLQ-C30, HRQOL</td>
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<tr>
<td>NCT02072057</td>
<td>25</td>
<td>Rocaltolib</td>
<td>Body weight at 3 months</td>
<td>Body weight, lean body mass, resting energy expenditure, activity energy expenditure, BMI, Tumour assessment, grip strength, QLQ-C30, nutritional history, number of adverse events and stair climbing test</td>
</tr>
<tr>
<td>NCT02148159</td>
<td>60</td>
<td>Acupuncture</td>
<td>Percentage weight change</td>
<td>Appetite VAS, simplified NAQ score, COPE</td>
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<tr>
<td>NCT02350855</td>
<td>62</td>
<td>Nutrient rich bread mix</td>
<td>Body weight</td>
<td>Appetite, food intake, symptoms and function</td>
</tr>
<tr>
<td>NCT02359123</td>
<td>40</td>
<td>Cannabics capsules</td>
<td>Weight gain of ≥10% from baseline weight</td>
<td>Appetite, nutritional intake, TNF-α level, correlation between THC levels and primary outcome, QLQ-C30, FAACT, CAPE, grip strength</td>
</tr>
<tr>
<td>NCT02400398</td>
<td>37</td>
<td>Peptamen enteral nutrition</td>
<td>Weight change from baseline</td>
<td>ECOG performance status, QLQ-C30, tumour biomarkers, food intake, smell and taste alteration, muscle strength and survival</td>
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<tr>
<td>NCT02416570</td>
<td>24</td>
<td>Clostridiums</td>
<td>Feasibility of a phase 3 study</td>
<td>Tolerability, safety and effect</td>
</tr>
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</table>

CAPE, Community Assessment of Psychic Experiences; CES-D, Centre for Epidemiological Studies Depression Inventory; DVD, digital video disc; ECOG, Eastern Cooperative Oncology Group; FAACT, Functional Assessment of Anorexia/Cachexia Therapy; GHQ-12, General Health Questionnaire; GSI, TEQ, Godin Shephard leisure time exercise questionnaire; HRQOL, health-related quality of life; PRO, patient-reported outcomes; NAQ, Nutritional appetite questionnaire; PG-SGA, patient-generated subjective global assessment; QLQ-C30, European Organisation for the Research and Treatment of Cancer QLQ-C30; SF-36, Short form health survey; THC, tetrahydrocannabinol; TNFα, tumour necrosis factor alpha; VAS, visual analogue scale.
Clinical Trials in Cancer Cachexia

• PRO not included in some, secondary measure for most
• Should outcomes be lean body mass, muscle strength, nutritional intake?
• BUT one published RCT found that HRQoL, appetite worse despite improvement in energy and protein intake?

The Role of Quality of Life in Cancer Cachexia

• Weight loss and reduced food intake affects QoL
  
  Brown CA Cancer J Clin 2003

• Nutritional intervention improves QoL
  
  Ravasco Clin Nutr 2007

• Weight gains associated with subjective improvements function and perceived strength correlated with improved QoL
  
  Parmar Supp care cancer 2013

• Weight loss of advanced colorectal patients associated with a decrease in several QoL scores
  
  Thoresen Eur J Cancer Care 2012
Megestrol Risk vs Benefit
Ruiz Garcia Cochrane Database Syst Rev 2013

**Benefit**
- Improves appetite
- Improves weight
- Improves Quality of Life

**Risk**
- Thromboembolism
- Edema
- Death
• “But I think if it’s saying that there’s an improvement in quality of life, then a breakdown as to what exactly that they’re looking at—because right now it’s a nebulous term. For me, quality of life means something different than what it means to my colleague sitting next to me, different to what my patient is going to say”