Management of Distressing Symptoms in Children with Life-Threatening Illness

Linda D. Pegram, MD and Melissa S. Mark, MD

October 2, 2012
My pain is gone but…

- Nausea/Vomiting
- Constipation
- Dyspnea/Air Hunger
- Anxiety
- Bleeding
- Fatigue and Sleep issues
- Psychosocial aspects of care/Preparing and Empowering the caregivers
Distressing Symptoms will be addressed separately, however…

“Increasing knowledge of the complex symptom experiences of pediatric oncology patients provides the scientific basis for new directions in symptom intervention”

“This cluster analysis increases awareness of sickness behavior symptoms, patterns, interaction, and synergy”

Nausea and Vomiting: Assessment

- **Pattern**
  - timing, duration, frequency, volume/description, severity

- **GI status**
  - early satiety, constipation, poor motility, mechanical obstruction, diarrhea

- **Triggers**
  - anxiety/depression, motion/change in position, odors/foods, pain

- **Medications**

- **Other causes**
  - increased ICP, gastritis, metabolic causes, infection
BARF Nausea scale


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Nausea and Vomiting: Non Pharm!

- Set realistic **goals** and discuss treatment options
- **Distraction** and **social support**
- Good oral hygiene
- Eliminate **offensive** foods, tastes or smells
- **Visualization/relaxation** techniques
- Hypnosis/acupuncture
- Slow, **controlled breathing**
- Calm, *quiet* environment, *comfortable* temperature
More Non Pharmacologic therapies:

- Drink **clear liquids** for 24 hours
- Avoid eating or drinking for 1-2 hours after vomiting
- **Sip** liquids *slowly* but *frequently*
  - off spoon or from a syringe to prevent gulping
- **Diet** changes: small frequent meals, low fat, bland foods, experiment
- Peppermint or ginger
Which **NEURAL PATHWAY** is involved?

- **GUT**
  - motility problems, reflux, NSAID use, microbial infection, inflammation, *chemotherapy*

- **VESTIBULAR**
  - motion, positional changes, *opioids*

- **CHEMORECEPTOR TRIGGER ZONE** **CTZ**
  - *Chemotherapy* or any toxin, metabolic, sepsis, myocardial, *opioids, cerebral metastases*

- **CNS**
  - increased intracranial pressure, meningeal irritation, *cerebral metastases, anxiety*
Vomiting Center: in Medulla

CTZ: in the area postrema at base of 4th ventricle

5-HT₃R & D₂R

substance P & opioid

H₁R = Histamine receptors

vestibular-labyrinthine apparatus

ACh = acetylcholine

Motion sickness
Poorly understood

GUT

5-HT₃R

H₁R & ACh (visceral mechanoreceptors)

5-HT₃R = Serotonin Receptors
D₂R = Dopamine Receptors

smell, taste, psychological distress, anticipation, pain

Motion sickness

Visceral afferent nerves
GUT: Dopaminergic or Serotonergic

Dopamine (D2) Receptor Antagonists

- **Prochlorperazine** (Compazine®): antihistamine, weak anticholinergic
- **Haloperidol** (Haldol®): minimal anticholinergic/antihistamine effects
- **Droperidol** (Inapsine®): some histamine and serotonin antagonist activity
- **Metoclopramide** (Reglan®): gastroprokinetic, mixed serotonin antagonist/agonist. **Avoid using with anticholinergic antiemetics!**
- **Metopimazine**, widely used in Europe, not reported to cause extrapyramidal reactions

Serotonin (5-HT3) Receptor Antagonists

- **Ondansetron** (Zofran®)
- Antacids and proton pump inhibitors (PPIs)
- Antibacterials, virals or fungals

- **Erythromycin**, a macrolide antibiotic, as a *prokinetic* agent

- **Scopolamine**, *anticholinergic*, inhibition of secretion of saliva and sweat, decreases GI motility and secretions

- **Glycopyrrolate** (Robinul®) for reducing secretions

- **Dicyclomine** (Bentyl®), *anticholinergic*, antispasmodic
- **Hyoscyamine** (Levsin®), *anticholinergic*, antispasmodic
- **Promethazine** (Phenergan®): antihistamine, *anticholinergic* effects (weak dopamine receptor binding)
VESTIBULAR: **Cholinergic or Histaminergic**

- **Meclizine** (Antivert®, Bonine®, Dramamine®), *antihistamine*, central *anticholinergic* action and CNS depressant activity
  - Decreases excitability of the middle ear labyrinth and blocks conduction in the middle ear vestibular-cerebellar pathways

- **Scopolamine** (Transderm Scōp®), *anticholinergic*, antagonizes *histamine and serotonin*

- **Promethazine** (Phenergan®), *blocks histamine* receptors, *anticholinergic* effects

- **Diphenhydramine** (Benadryl®), *antihistamine*, labeled for motion sickness

Motion sickness... Poorly understood!
CHEMORECEPTOR TRIGGER ZONE: CTZ
Seratonergic or Dopaminergic

- Serotonin 5-HT3 Receptor Antagonists (5-HT3 RA): 1st generation:
  - Ondansetron (Zofran®)
  - Granisetron (Kytril®)
  - Dolasetron (Anzemet®), po only for CINV (Chemotherapy Induced N/V)

- 2nd generation:
  - Palonosetron (Aloxi®), half life 36-42 hrs, higher affinity and selectivity to 5-HT(3) receptor

- Dopamine receptor antagonists:
  - Prochlorperazine (Compazine®)
  - Metoclopramide (Reglan®)
  - Haloperidol (Haldol®)
  - Droperidol (Inapsine®)
  - Promethazine (Phenergan®), weak

CTZ: in the area postrema at base of 4th ventricle
5-HT₃R & D₂R substance P & opioid
CHEMORECEPTOR TRIGGER ZONE: Other

- Steroids (Dexamethasone)
  - proven effective in combination with 5-HT3 RA
  - mechanism of antiemetic activity unknown

- Add 2nd generation 5-HT3 RA, Palonosetron (Aloxi®)
  - enables decrease from 3 days to 1 day of dexamethasone treatment (data in breast cancer patients)

- Aprepitant (Emend®), inhibits substance P/neurokinin 1 (NK₁) receptor
  - augments antiemetic activity of 5-HT3 RA and corticosteroids
  - inhibits acute and delayed phases of chemotherapy-induced emesis
  - Fosaprepitant (Emend® IV), lack of data/dosing for children
CNS/Other

- **Corticosteroids**
  - cerebral metastases, meningeal irritation, increased ICP

- **Short** or long acting **benzodiazepines**
  - anxiety or anticipatory
  - **Lorazepam** (Ativan®), should be used as an *adjunct* for N/V, works well for anticipatory N/V

- **Dronabinol** (Marinol®)
  - principal psychoactive substance found in *Cannabis sativa* (marijuana)
  - mechanism of action as antiemetic not well defined
  - probably inhibits vomiting center in medulla oblongata
  - complex effects on CNS, including central sympathomimetic activity
- **Nabilone** (Cesamet™), antiemetic activity may be due to effect on cannabinoid receptors (CB1) within CNS

- **Medical Marijuana** (limited by state)

- **BAD** (Diphenhydramine/Benadryl®, Lorazepam/Ativan®, Dexamethasone), patient controlled pump
  - some include metoclopramide/Reglan®, BADR 😊

- **ABHR** (Ativan®, Benadryl®, Haldol®, Reglan®)
  - used widely in adult hospice programs, generally well tolerated
  - compounded into capsules, troches, suppositories, suspension
  - 0.5mg/12.5mg/0.5mg/10mg per unit or 5ml or topical gel at higher doses
  - also used as ABH, ABR and BDR (D=dexamethasone)
Recommended Review Article on CINV


- The Hospital for Sick Children and University of Toronto, Toronto, Ontario, Canada
Constipation: back to basics

Prevention

- History/PE
- Imaging

Assessment

- Postprandial stooling
- Behavior strategies
- Activity

Rx

- Fluid/fiber
- Toilet access
- Massage

Medication management

- Laxatives/Stimulants

Ddx:
- Medication
- Electrolytes
- Disease progression
  - Neurologic
  - Physical obstruction

MUSH
- Polyethylene glycol
- Lactulose

PUSH
- Senna
- Bisacodyl
### Victoria Hospice Bowel Performance Scale

<table>
<thead>
<tr>
<th>BPS Score</th>
<th>Constipation</th>
<th>Characteristics</th>
<th>Normal</th>
</tr>
</thead>
<tbody>
<tr>
<td>-4</td>
<td>Impacted or Obstructed +/- small leakage</td>
<td>Formed Hard with pellets</td>
<td>Formed Hard</td>
</tr>
<tr>
<td>-3</td>
<td>Formed Hard</td>
<td>Formed Solid</td>
<td>Formed Semi-solid</td>
</tr>
<tr>
<td>-2</td>
<td>Formed Hard</td>
<td>Formed Solid</td>
<td>Formed Semi-solid</td>
</tr>
<tr>
<td>-1</td>
<td>Formed Hard</td>
<td>Formed Solid</td>
<td>Formed Semi-solid</td>
</tr>
<tr>
<td>0</td>
<td>Normal</td>
<td>Formed Soft</td>
<td>Formed Soft</td>
</tr>
<tr>
<td>+1</td>
<td>Normal</td>
<td>Formed Soft</td>
<td>Formed Soft</td>
</tr>
</tbody>
</table>

- **No stool produced**
- **Delayed ≥ 3 days**
- **Patient’s Usual Pattern**
- **Patient’s Usual Pattern**
- **Unable to defecate despite maximum effort or straining**
- **Major effort or straining required to defecate**
- **Moderate effort or straining required to defecate**
- **Minimal or no effort required to defecate**
- **Control Minimal or no effort to defecate**
- **Minimal or no effort required to control urgency**

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Downing, Watson, Carter © Victoria Hospice Society  
## Modified Bristol Stool Form Scale

<table>
<thead>
<tr>
<th>Number</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Separate hard lumps, like nuts (hard to pass)</td>
</tr>
<tr>
<td>2</td>
<td>Sausage-shaped but lumpy</td>
</tr>
<tr>
<td>3</td>
<td>Like a sausage or snake, smooth and soft</td>
</tr>
<tr>
<td>4</td>
<td>Fluffy pieces with ragged edges, a mushy stool</td>
</tr>
<tr>
<td>5</td>
<td>Watery, no solid pieces.</td>
</tr>
</tbody>
</table>

http://dx.doi.org/10.1016/j.jpeds.2011.03.002
Constipation

Diarrhea, abdominal pain, nausea, bloating, cramping...

Opioid Antagonist
- methylnaltrexone
- alvimopan

Back to Basics Management

Enemas
- surfactant rectal laxatives

Suppositories
- glycerine bisacodyl

Low dose oral/ultra low dose IV naloxone

Opioid induced constipation
Dyspnea: Assessment

- **Patient description**
  - Exactly what they feel (caregiver describe what they see)

- **Triggers**
  - Increased secretions, difficulty handling secretions
  - Difficulty swallowing, coughing, choking
  - Pleural effusion, pneumothorax, pneumonia, lung metastases
  - Fluid overload (puffiness, edema, gallop)
  - Abdominal distension, constipation
  - Anxiety or severe pain

- Assess **position** of patient

- Assess respiratory rate and **work** of breathing (accessory muscle use, nasal flaring)

- Assure \(O_2\) hooked up properly/flowing properly

- **Overall goals of care**
  - If comfort, encourage removal of pulse oximetry monitoring, discontinuation of blood gases, etc.
Dyspnea: Non Pharm management!

- **Positioning** of patient key!
  - Sitting up, head of bed semi-upright helpful
  - Assure proper chin lift, support of head

- **Increased air flow** is comforting
  - **Fan**, open window, cool mist humidifier

- Visualization/relaxation techniques, distraction

- **Slow**, controlled breathing

- Calm, quiet environment, comfortable temp

- **Oxygen** (humidified if possible) for comfort
  - blow by, nasal cannula, face mask, tent, etc.
  - **blowing air may be as effective as O\textsubscript{2}**

- Suction, chest PT
Dyspnea management

- Review overall goals of care
  - with patient/caregivers and staff
- Review meds, fluids, TPN, enteral feeds, bowel regimen, etc.
  - assure not causing harm
- Consider reducing rate/discontinuation IV fluids/TPN/enteral feeds, etc.
- Reduce volume/concentrate required IV/PO meds, flushes
- Aggressively treat constipation if abdominal distension
- Decompress bowel if indicated by venting G-tube, using suction, etc.

- Use of non-invasive positive pressure ventilation (depending on underlying disease process and overall goals of care), beyond scope of this presentation
Medications for Dyspnea

- **OPIOIDS** are the drug of choice for dyspnea!
- Educate patient/care providers on how and why
- Dispel *myths and fears* of opioid use in this setting
  - to patient, caregivers and staff
- Route depends on patient status
  - all routes of systemic administration should help
  - often **low doses are effective** for dyspnea
  - 25% of usual dose for pain, if pain is not contributing to dyspnea
  - may require more frequent dosing
- Limited data regarding **nebulized** morphine or fentanyl but helps some patients
  - *J-type stretch receptors in lungs are thought to be involved in sensation of dyspnea, and output from these receptors is attenuated by opioids*
- If severe, **continuous infusion of opioid with frequently available PCA doses**
  - activated by the patient, caregivers or staff
- **Frequent reassessment with timely and aggressive adjustment of dosing is key**
Dyspnea management

- **Dyspnea** is one of the most feared, terrifying and **anxiety** provoking symptoms a person can suffer
  - Need **strong social support** and often **spiritual support** as well
  - Power of human contact, **touch**

- **Anxiolytics** very helpful as **adjunct** treatment
  - Lorazepam (Ativan®), widely used in this setting, can be given IV/PO

- In severe cases, consider use of a **continuous infusion**
  - (e.g., **midazolam**) with bolus doses still available

- **Terminal sedation** for severe symptoms refractory to other treatments
  - beyond scope of this presentation
Dyspnea management: simple things

- Good mouth and nose care
- **Anti-tussives** (opioid preparations) to reduce coughing
- **Mucolytics** (e.g., guaifenesin) and **nasal decongestants** (e.g., oxymetazoline nasal spray)
- **Antimicrobials** for infection
  - if consistent with overall goals of care given status
- **Medications to reduce secretions**
  - e.g., scopolamine, glycopyrrolate, hyoscyamine, if indicated
  - use with **caution**, may make dyspnea worse if develop **thick**, difficult to handle secretions
- **Diuretics** if fluid overload cause of dyspnea
- **Bronchodilators** if reactive airway component
- Corticosteroids, **only** if helps underlying disease process leading to dyspnea

**Recommended reading**: Christina K. Ullrich, MD, Oscar H. Mayer, MD *Assessment and Management of Fatigue and Dyspnea in Pediatric Palliative Care* Pediatr Clin N Am 54 (2007) 735–756
Anxiety

Management

- Share Control
- Separation

Parent

ADL

Pain

Distract

Child life

Physician

Sx

Relax

Chaplaincy

Clinical SW

Assessment and Considerations
- Symptom vs. disorder
- Communication
- Parental anxiety

Therapy modalities
- CBT
- Bibliotherapy
- Art therapy
- Writing
- Music therapy
Bleeding that is *not seen* may be unavoidable, may provide for a peaceful death
- e.g., CNS hemorrhage, distal GI hemorrhage, if pain well managed

Visible Bleeding
- very scary to patients/caregivers
- often looks like more volume than it is

Use of dark towels, wash cloths and linens

Preparation and prevention is key!
Bleeding

- Blood vessel, platelet or coagulation disorder
- Platelet and coagulation disorders common in hematologic malignancies
- Solid tumors, risk of bleeding related to tumor location

For MAJOR BLEEDING:

- Local pressure!!!
- Endoscopic hemostasis techniques may be appropriate
- Angiographic embolization procedures may be indicated
- If major bleeding at end of life (e.g., pulmonary hemorrhage) and goal is comfort only, terminal sedation may be required
- Consider use of recombinant Factor VIIa in hospital setting

3 common bleeding problems
Epistaxis

- Avoid **trauma** to nose!
- **Demonstrate** how to hold pressure properly
  - avoid tilting head back, avoid blowing nose to dislodge clots
- If on O₂ use **humidification**, use the **least amount of flow** possible
- **Cool mist humidifier** in room where patient sleeps

- Petroleum jelly at night in nares, other type of **nasal moistener** (nasal gels, etc.)
- Have **Oxymetazoline HCl (Afrin®) nasal spray** available!
  - Can use more liberally/frequently than directed per routine of ENT specialists for epistaxis
  - If thrombocytopenia, consider **transfusion with platelets** on a schedule
- Ask ENT if **nasal cautery** would help (as friable/prominent nasal vessels common)
- Avoid packing
Mouth Bleeding

- **Good oral hygiene**
  - if friable mucosa, use **soft** tooth brushes or foam “toothettes”, use mouthwash *without alcohol* to keep bacterial contamination down

- **Keep lips, mouth moist**
  - petroleum jelly, lip balm, vitamin E
  - mouth moisturizers

- **Avoid trauma** to mucosal surfaces, gentle with suction devices

- **Keep diet soft**

- **Aminocaproic acid (Amicar®)**
  - difficult to find at local pharmacies (many have to order)
  - keep a supply at home (just in case)

- **Soak gauze with oxymetazoline nasal spray (Afrin®)**
  - use this to stop mouth bleeding as well (another ENT trick)
GI Bleeding

- **Stress gastritis** very common
- Continue **acid blockers** and **proton pump inhibitors** if able

- **Aggressively treat constipation** to prevent mucosal tears
- **Consult GI** and/or **surgery** if reversible/fixable problem
- GI hemorrhage may be unavoidable
  - **dark** washcloths, towels, linens, and clothing (underwear)
  - most diapers for all ages lined in white

- **Consider stopping PRBC support**
- Most continue **platelet support** (if thrombocytopenia contributing) **scheduled**
  - **Stop checking blood counts**
  - If coagulopathy, FFP
    - sodium content like NS
    - **many cannot tolerate volume** required to correct coagulopathy
  - If fibrinogen low, **cryoprecipitate** (low volume, loaded with fibrinogen)
Assessment

- History
- Instruments or sleep diary
- Medication review
- Polysomnography
Fatigue
Mood
Pain
Assessment
• History
• Instruments or sleep diary
• Medication review
• Polysomnography

Management
• Sleep hygiene
• Optimize hospital setting
• Psychological support
• Respiratory support

Sleep Hygiene Hints
• Routine
• Quiet time before bed
• Cool room
• Positioning
• Lighting (day/night)
• Out of bed during day
• Co-sleeping

Patient
Respite
Caregiver

Fatigue
Pain
Mood

Sleep Hygiene Hints

Management
Sleep Hygiene Hints
• **Routine**
  - Quiet time before bed
  - Cool room
  - Positioning
  - Lighting (day/night)
  - Out of bed during day
  - Co-sleeping

• **Medication**
  - Melatonin
  - Antihistamines
  - Benzodiazepines
  - Non-benzo hypnotic
  - Clonidine
  - Chloral hydrate

CNS patient care respite
patient
fatigue mood pain
sleep
key

- **Sleep**
- **Respite**
- **Caregiver**
Fatigue

Assessment
- Ask
- Instruments
- Review medications

Cognitive
- concentration
- forgetfulness
- lack of focus

Physical
- weakness
- difficulty
- walking/running
- no energy
- tiredness
- heaviness
- lethargy
- desire to rest

Emotional
- irritability
- depressed
- non-communicative
- sad/mad

Adapted from J. Wolf, P. Hinds et al. Textbook of Interdisciplinary Pediatric Palliative Care. Table 29-2 Signs and Symptoms of Fatigue in Children. pg 277, (2011).
Fatigue Management

- Education
- Distraction
- Assistive devices
- CAM
- End of life

Additional Pearls

Lifestyle Modification
- Routine
- Exercise
- Nutrition

Pharmacotherapy
- Methylphenidate
- Modafinil
- Megesterol acetate
- Corticosteroids
- ATP infusions
- L-carnitine

Lifestyle
- Sleep
- Sleep hygiene
- Limit daytime naps*

Correct underlying factors
- Anemia
- Consider goals

Physical Factors
- Underlying illness
  - Type, site, stage
  - Treatment
- Unrelieved symptoms
- Side effects of treatment
- Changes in activity
  - Decoconditioning
  - Anemia
  - Muscle structure, function

Psychosocial Factors
- Depression
- Anxiety
- Fatigue
- Spiritual concerns
- Caregiver status
- Physical concerns

Fatigue Experience

Additional Pearls
Preparing and *Empowering* caregivers

- **Knowledge is power**

- **Hope for best, prepare patient/family for worst**

- **Give tools, teach what to do if…**
  - e.g., laminated cards

- Symptom management like storm/disaster preparation (e.g., hurricane)

- Have all necessary supplies on hand!
Preparing and **Empowering** caregivers

- Anticipate distressing symptoms that *may occur* and *empower* caregivers by having necessary items and/or medications in place “just in case”
  - like we do if a storm is coming, *teach* them how to use
- For a patient home at end of life have:
  - **concentrated liquid morphine 20mg/ml (Roxanol™)**
  - **rectal valium gel (Diastat®)**
    - pump batteries die, opioid bags leak, lines come out
    - seizures can occur unexpectedly
  - **true disasters can and do happen…**
- Try to get **O₂**, suction, etc. in place *before* there is a crisis
Psychosocial Aspects of Care
Distressing Symptoms

- Honest, clear, easy to understand information/discussion about overall clinical status, symptoms and **goals of care…** *repeat, repeat, repeat…*
- Care of pediatric oncology patient, a **team effort**
- Incorporate holistic concepts and team approach of palliative care *from diagnosis*

- **Communicate, Coordinate, Anticipate** and **Advocate**!
- Include team members in discussions with patients/families
- Remember that **patient and family are part of team**
- Try to use home care companies that also do hospice from diagnosis
- Remember that in the end… **it is not about us…**
Additional material

The following slides were not presented in the webinar, but have been included for your reference.

Please don’t hesitate to contact us with any questions

Linda.Pegram@chkd.org
Melissa.Mark@chkd.org
Lack of Appetite

- Lack of appetite
  - extremely common in pediatric cancer patients
  - one of most frequently reported symptoms causing distress

- Eating, mealtime and food
  - significant meaning in most cultures for patients and their families

- If patient unable to enjoy eating…
  - impacts entire family

- One of fundamental jobs as a parent is to support and feed your child
Lack of Appetite…
Do not wait for weight loss!

- Early support required from a nutritionist or dietitian

- Underlying disease contributes as does treatment
  - Nausea, vomiting, early satiety, mucositis and changes in taste, frequent side effects of chemotherapy and radiation treatments

- Increasing caloric intake is traditional approach
  - oral supplements, nasogastric tube feeding, gastric tube feeding, and parenteral nutrition
Nonpharmacologic treatments used in anorexia and cachexia

- Relaxation and imagery
- Provide favorite foods in desired amount
- Reduce portion size
- Eliminate foods with unpleasant odor
- Explore emotional and spiritual issues related to weight loss

Can use appetite stimulants

- Cyproheptadine hydrochloride (Periactin)
  - serotonin and histamine antagonist
- Megestrol acetate (Megace®)
  - synthetic progestin, antiestrogenic properties, disrupt estrogen receptor cycle
  - exact mechanism for appetite stimulation not determined
  - postulated to be due to direct effect on hypothalamus
  - now known to have an **impact on muscle protein metabolism**
  - can cause adrenal suppression!
- Dronabinol (Marinol®), discussed previously for N/V, also an appetite stimulant
- Steroids (Predisone, Dexamethasone)
- The hormone **Melatonin**
- Complimentary
  - amino acid derivative, L-carnitine
  - essential fatty acids, Omega 3; polyunsaturated fatty acids may inhibit IL-1 and TNF
Loss of appetite (anorexia), pre-cachexia, cachexia

- “Cachexia is a complex metabolic syndrome
  - associated with underlying illness and characterized by loss of muscle with or without loss of fat mass. The prominent clinical feature of cachexia is weight loss in adults (corrected for fluid retention) or growth failure in children (excluding endocrine disorders).

- Anorexia, inflammation, insulin resistance and increased muscle protein breakdown are frequently associated with wasting disease.
  - Wasting disease is distinct from starvation, age-related loss of muscle mass, primary depression, malabsorption and hyperthyroidism and is associated with increased morbidity”

Cachexia score (CASCO): a new tool for staging cachectic cancer patients (not yet validated)

- Includes **weight** and **lean body mass**
- Measures of **inflammation**, **metabolic disturbances** and **immunosuppression**
- Measure of **physical performance**
- **Anorexia** questionnaire
- A **Quality of Life** instrument
- Propose a **Pre-cachexia** Quantitative approach
  - To identify pre-cachexia **before any change in body weight or composition**

New Directions

Targeting Protein Synthesis in a Myc/mTOR-Driven Model of Anorexia Cachexia Syndrome Delays Its Onset and Prolongs Survival


- findings suggest new paradigm to treat Anorexia Cachexia Syndrome (ACS)
- strategies target protein synthesis, block production of pro cachexic factors

Reversal of cancer cachexia and muscle wasting by ActRIIB antagonism leads to prolonged survival


- ActRIIB, a high affinity activin type 2 receptor
- mediates signaling of a subset of TGF-b family ligands, including myostatin, activin, GDF11 and others (see figure)
Xiaolan Zhou, Jin Lin Wang, John Lu, Yanping Song, Keith S. Kwak, Qingsheng Jiao, Robert Rosenfeld, Qing ... 

Reversal of Cancer Cachexia and Muscle Wasting by ActRIIB Antagonism Leads to Prolonged Survival

Cell Volume 142, Issue 4 2010 531 - 543
http://dx.doi.org/10.1016/j.cell.2010.07.011