CANCER-RELATED FATIGUE: CURRENT STATE OF THE SCIENCE: EVIDENCE & GAPS

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The fatigue never stopped. I still get tired…still have a lot of side effects.

The fatigue (is) overwhelming. I mean, you expect to not feel good during treatment…you expect to have problems,

But when you are done with treatment, you expect it to get better…
CRF: Current State of Research & Practice (Braun et al., 2008; Fu et al, 2009; Kuhnt et al, 2009; Meeske et al, 2007)

- Small sample sizes, effect sizes, & mixed results when fatigue levels compared to the general population
- Prevalence rates all over the map (i.e., 30-76%), consistently the most common Sx; severity & duration usually not described
- Most cross-sectional studies
CRF: Current State of Research & Practice

- HEAL Study (Health, Eating, Activity, & Lifestyle)
  - Early stage, diverse Breast Cancer Survivors
  - Longitudinal, 2-5 yrs after Dx; Baseline & 24-mos followup;
  - MOS-SF-36 & PFS-R (24 mos only; N=800)
  - 41% fatigued (≥4)(moderate-severe); several correlates (pain, inactivity, weight gain, antidepressant use, low income, not working, smoking, comorbidities, Hispanic, age [mixed]) Sx burden/clusters, lymphedema?
CRF: What are the Unanswered Questions/Gaps in The Field?

- Absence of longitudinal & intervention studies
- Survivorship & fatigue case definitions vary
- Need to set eligibility case definitions
  - To insure adequate power to detect intervention responses
- What constitutes an appropriate control group?
- Studies other than breast/lymphoma
- New QOL measures?

Braun et al, 2008; Crespi et al, 2010; Jeon et al, 2009;
CRF: What are the Unanswered Questions/Gaps in The Field?

- Need to examine fatigue in survivors while controlling for:
  - Aging
  - Comorbidity(s)
  - Response shift
  - Prior cancer therapy(s)
  - Absence/Description of current Rx
  - Onset, severity, pattern, & duration descriptions

Braun, Greenberg & Pirl (2008)
CRF: How is Research Being Translated into Practice?

- Limited translation of survivorship findings into practice;
- Limited translation of NCCN Fatigue Guidelines into practice:
  - Active treatment, survivorship, end of life/palliative care
CRF: How is Research Being Translated Into Practice?

- MASCC Fatigue Study Group Guidelines Study
  - Web-based survey
  - NCCN CRF Guidelines:
    - Awareness
    - Barriers
    - Other guidelines
    - Role of Fatigue Study Group
PASSPORT TO COMFORT

REducing Barriers to Pain & Fatigue Management

City of Hope Cancer Center

Duarte, CA

- **Re-examine data sets:**
  - Already collected to reduce costs & Compare no CRF to CRF

- **Possibly achieve consensus more quickly on:**
  - Clinical subtypes;
  - Case definitions;
  - Research questions

- **Look at existing international initiatives/groups as potential models/partners/collaborators:**
  - EORTC-PROBE (PROs & Behavioral Evidence)
  - UK’s Medical Research Council
  - NCIs of Canada & USA’s Clinical Trials Group
1st International Fatigue Conference (Montreal, 2008); MASCC Fatigue Workshop (Rome, 2009); MASCC Survivorship Workshop (Vancouver, 2010); 2nd International Conference (Montreal, 2010)
CRF: What are the Potential Benefits for International Partnerships & Funding? (Bottomley et al, 2009)

- **EORTC-PROBE:**
  - Unrestricted academic grant from Pfizer;
  - 3-day HRQOL Training program
  - 20 Travel fellowships to support attendance
  - Promotion through different medical societies (i.e., International Society of QOL Research & The European Journal of Cancer Care)

- Other International meetings/organizations
What are the Unanswered Questions/Gaps in the Field?

- **Conceptual models to guide research:**
  - Inflammation/stressor model;
  - **Genetic Model:**
    - Cytokine polymorphisms (SNPs)
    - Genome-wide micro-array analyses
  - **New symptom cluster/burden model?** (Brant, Beck & Miaskowski, 2009)
  - **ASCPRO Model** (Barsevick et al, 2010)
  - **Others**
    - HRQOL (Wilson & Cleary; COH)
    - Fatigue (Edmonton Fatigue Model: Olson et al, 2008); Integrated Fatigue Model (IFM): Piper et al.);
    - Central & Peripheral Nervous System Model (Davis et al),
NOW THE STICKY WICKET...
What are the Unanswered Questions/Gaps in the Field?

- **Measurement:**
  - **Timing:** Post Dx vs post primary Rx?
  - **Does fatigue affect survival? What defines chronic fatigue? Is CRF = Fatigue in other chronic illnesses?**
  - **Subjective measures** (Barsevick et al, 2010):
    - PRO perception & impact/interference
    - Fatigue vs SX inventories vs QOL Scales (Wang et al, 2010); PROMIS (Cella et al)
    - MOS-SF-36-Vitality Subscale
      - Effect sizes differ; Energy/vitality may not be the same as fatigue
  - **Objective measures** (Bower et al; Aoiuzerat et al, Loge et al)
    - The jury is still out (i.e., D-dimers, CRP, IL-6 increase with age [Bellizzi et al, 2008])
OBJECTIVE MEASUREMENT PRIORITIES

- Select what we think is the best biomarker (s) based on cost & the usual suspects…
- Collect & bank specimens (tissue, blood etc);
- Keep idcodes to go back & analyze as new information becomes available.
Questions & Discussion