Improving Patient-Centered Outcomes in Cancer Care: Leveraging Insights Derived from Big Data

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Big Data in Biomedicine and Health: Trends

• Increasing availability and accessibility of huge and complex databases resulting from:
  – research
  – routinely collected sources (eg. EHR, claims)
  – passively collected sources (eg. GPS, twitter, sensors)
• Advances in genome sequencing technology and digital imaging
• Growth of clinical data warehouses
• Routine data collection for quality assessment and clinician performance metrics
• Expanding role of patients in managing their own health information
• Technological advances:
  – Cloud computing
  – Electronic data capture of patient-reported outcomes
  – Interconnectivity via social media and the web
  – Information-sensing devices (eg. mobile and wearable technologies such as FitBit, smartphone-based GPS)
Big Data in Biomedicine and Health: Trends

• Researchers face challenges in recruiting participants to studies
• Fewer extramural resources and greater emphasis on data sharing, particularly for expensive studies
• Increasing emphasis on outcomes-oriented research to improve the performance of health systems and to guide management and clinical decision-making
• Increasing emphasis on externally valid research findings derived from representative samples, collected in real-world settings and under usual care conditions
• Expanded funding for:
  – Electronic Health-Related Datasets (EHRDs) (Appari et al. 2013)
  – Meaningful Use of Health IT approaches
Strengths and Limitations of Big Data

**Strengths**
- Real-world
- Large sample size
- Often longitudinal
- Unobtrusive; low burden
- Timely

**Limitations**
- Interoperability
- Cost
- Governance/Data Access
- Privacy and consent
- Missing data
- Sampling bias
- Lack of standards for data quality
- Underrepresentation of constructs of interest to nursing science

Selected examples of large investments in data infrastructure: PCORnet, Mini-sentinel, SEER, CancerLinQ, Improvement Science Research Network
The **FOUR V’s** of Big Data

**Volume**

- 40 zettabytes (4 quintillion gigabytes) of data will be created by 2020, an increase of 300 times from 2005.
- 6 billion people have cell phones.
- World population: 7 billion.
- 6.7 million people have cell phones.
- The New York Stock Exchange captures 1 TB of trade information during each trading session.

**Variety**

- Different forms of data.
- 420 million wearable, wireless health monitors.
- 4 billion+ hours of video are watched on YouTube each month.
- 400 million tweets are sent per day by about 200 million monthly active users.

**Velocity**

- Analysis of streaming data.
- Modern cars have close to 100 sensors that monitor items such as fuel level and tire pressure.
- By 2015, 4.4 million IT jobs will be created globally to support big data, with 1.9 million in the United States.

**Veracity**

- Uncertainty of data.
- 27% of respondents in one survey were unsure of how much of their data was inaccurate.

**Sources:** McKinsey Global Institute, Twitter, Cisco, Gartner, EMC, SAS, IBM, MEPTEC, GfK.
BIOMEDICAL BIG DATA EXPLOSION

NIH National Center for Biotechnology Information

DATA STORAGE

In **1990** fit on 3 floppy disks

In **1993** fit on 1 CD-ROM

In **2014** could fill **400 MILLION** 4-drawer filing cabinets

Types of BD2K Awards
- Enabling Data Utilization
- Analysis Methods and Software
- Enhancing Training
- Centers of Excellence

NIH Big Data to Knowledge (BD2K) is an initiative of the National Institutes of Health
What is the NIH Doing to Fulfill That Promise?
Big Data to Knowledge (BD2K)

• Goal: address the opportunities and challenges faced by researchers in accessing, managing, analyzing and integrating diverse data, including biomedical, biological, and behavioral data

• Data Sharing
  • Genomic data sharing announced
    – Data sharing plans on all research awards
    – Data sharing plan enforcement
      • Machine-readable plan
      • Repository requirements to include grant numbers

• Data Citation
  – Goal: legitimize data as a form of scholarship
    • Machine readable-standard for data citation
    • Endorsement of data citation for inclusion in NIH biosketch, grants, reports, etc.
    • Introduce into NLM/NCBI workflow
Big Data: A Definition

- Formal definition: ‘datasets with sizes beyond the ability of commonly used software tools to capture, curate, manage and process the data within a tolerable elapsed time’ (Freedman, Pisani & Purvis, 2004)

- Size, complexity, technology (Ward & Barker 2013 ‘Undefined by Data: A Survey of Big Data Definitions)

- Pose technical, conceptual, and operational challenges
Disparate Data are Linked Together at Varying Levels for Use in Health Care Delivery Research: Size, Complexity, Technology

From: Finding the Missing Link for Big Biomedical Data; JAMA. 2014();. doi:10.1001/jama.2014.4228
Improving Patient-Centered Outcomes Using Big Data

- Provide an overview of selected measurement systems and data resources relevant to patient-centered research using big data
- Illustrate the use of some of those resources and measurement systems to generate new insights about patient-centered outcomes important to the delivery of nursing care
NCI SURVEILLANCE, EPIDEMIOLOGY AND END RESULTS PROGRAM (SEER)
Linkage studies example: Data Systems linked to the Surveillance, Epidemiology and End Results Program (SEER) cancer incidence, mortality, and survival data
Common Themes

– Large number of records and amount of information per record
– Mix of types of data and sources
– Multilevel (individuals nested within organizations within systems)
– Longitudinal
– Contains personally identifiable and proprietary info
– Linkage across federal and state governments, delivery systems, and academic institutions
– Common needs across federal and state governments, delivery systems, and academic institutions
– Often made publicly or semi-publically available
CMS conducts two important surveys of its Medicare beneficiaries annually

- The Medicare Health Outcomes Survey (MHOS) assesses illness burden and quality of life
- The Consumer Assessment of Healthcare Providers and Systems (CAHPS) survey assesses care experiences

Building on the success of SEER-Medicare, NCI has collaborated with the SEER program and CMS to create the SEER-MHOS and SEER-CAHPS linked datasets
Why SEER-CAHPS & SEER-MHOS?

These datasets provide unique national data that emphasize the patient’s perspective in assessments of the quality of cancer care and patient health outcomes.
What is MHOS?

- The MHOS is a questionnaire administered to a random sample of ~1,000 beneficiaries in each managed care plan participating in Medicare.

- The MHOS survey includes:
  - Activities of Daily Living (ADLs)
  - HEDIS effectiveness of care questions
  - Health problems (eg. Cardiovascular disease, diabetes, etc.)
  - Health-Related Quality of Life (SF-36 & VR-12)


- A new cohort is selected each year for baseline measurement and a 2-year follow-up assessment.
What is SEER-MHOS?

- The SEER-MHOS dataset contains linked records for beneficiaries with both SEER and MHOS data (n=95,723) as well as those without a reported cancer diagnosis but with MHOS data (n=1,510,127).

- Includes MHOS data for the years 1998-2013.
Potential Uses of SEER-MHOS

• Evaluate HRQOL before/after a cancer diagnosis and compare cancer survivors with beneficiaries never diagnosed with cancer

• Evaluate HRQOL and receipt of initial cancer treatment, especially with respect to surgical interventions and radiation

• Assess the effects of different types of cancers on HRQOL and other patient-reported outcomes
SEER-MHOS Public Use Data Resource

• The SEER-MHOS data are currently publicly available
  – 17 data use agreements
  – 12 publications

• For more information, please contact:
  – Erin Kent, PhD
    SEER-MHOS and SEER-CAHPS Scientific Lead
    Erin.Kent@nih.gov
### Variables available in SEER-MHOS

<table>
<thead>
<tr>
<th>SEER Variables</th>
<th>MHOS Variables</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Cancer incidence and survival</td>
<td>• HRQOL: SF 36 v2, VR 12</td>
</tr>
<tr>
<td>• Month/year of diagnosis, site of cancer, histology, grade, and stage</td>
<td>• Activities of daily living</td>
</tr>
<tr>
<td>• Initial surgical and radiation treatment within 12 months of diagnosis</td>
<td>• Comorbidities</td>
</tr>
<tr>
<td>• Follow-up vital status</td>
<td>• Depressive symptoms</td>
</tr>
<tr>
<td>• Demographics</td>
<td>• Urinary incontinence</td>
</tr>
<tr>
<td></td>
<td>• Number of unhealthy days</td>
</tr>
<tr>
<td></td>
<td>• Health behaviors: Smoking</td>
</tr>
<tr>
<td></td>
<td>• HEDIS effectiveness of care measures</td>
</tr>
<tr>
<td></td>
<td>• Urinary incontinence</td>
</tr>
<tr>
<td></td>
<td>• Physical activity management</td>
</tr>
<tr>
<td></td>
<td>• Bone Mineral Density</td>
</tr>
<tr>
<td></td>
<td>• Fall risk management</td>
</tr>
<tr>
<td></td>
<td>• Demographics</td>
</tr>
</tbody>
</table>

N=98,000 patients in SEER who have completed at least one MHOS survey
<table>
<thead>
<tr>
<th>Cancer Site</th>
<th>N</th>
<th>Age Mean(SD)</th>
<th>Median</th>
<th>Gender Female(%)</th>
<th>Mean(SD)</th>
<th>Median</th>
</tr>
</thead>
<tbody>
<tr>
<td>No history of cancer</td>
<td>1,224,549</td>
<td>74.8(6.7)</td>
<td>74</td>
<td>59.7</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Bladder</td>
<td>3195</td>
<td>70.1(8.9)</td>
<td>70</td>
<td>23.1</td>
<td>86.2(76.7)</td>
<td>65</td>
</tr>
<tr>
<td>Melanoma</td>
<td>3019</td>
<td>68.8(9.4)</td>
<td>69</td>
<td>40.3</td>
<td>90.7(81.3)</td>
<td>69</td>
</tr>
<tr>
<td>Uterus</td>
<td>2558</td>
<td>65.8(9.3)</td>
<td>66</td>
<td>100</td>
<td>131.9(98.5)</td>
<td>113</td>
</tr>
<tr>
<td>Non-Hodgkin Lymphoma</td>
<td>1563</td>
<td>69.7(9.1)</td>
<td>70</td>
<td>50.9</td>
<td>75.9(74.2)</td>
<td>53</td>
</tr>
<tr>
<td>Kidney</td>
<td>1120</td>
<td>68.9(8.7)</td>
<td>69</td>
<td>42.3</td>
<td>76.7(75.0)</td>
<td>52</td>
</tr>
<tr>
<td>Cervix</td>
<td>1016</td>
<td>55.5(11.7)</td>
<td>55</td>
<td>100</td>
<td>216.7(110.4)</td>
<td>214</td>
</tr>
<tr>
<td>Oral cavity &amp; Pharynx</td>
<td>942</td>
<td>67.7(9.0)</td>
<td>68</td>
<td>40.0</td>
<td>92.9(83.7)</td>
<td>71</td>
</tr>
<tr>
<td>Thyroid</td>
<td>586</td>
<td>63.0(10.8)</td>
<td>64</td>
<td>72.9</td>
<td>132.9(110.0)</td>
<td>106</td>
</tr>
<tr>
<td>Ovary</td>
<td>568</td>
<td>65.7(10.2)</td>
<td>66</td>
<td>100</td>
<td>113.0(98.0)</td>
<td>88</td>
</tr>
<tr>
<td>Upper Gastrointestinal</td>
<td>530</td>
<td>71.1(8.2)</td>
<td>70</td>
<td>40.4</td>
<td>63.7(69.5)</td>
<td>37</td>
</tr>
<tr>
<td>Chronic Leukemia</td>
<td>505</td>
<td>71.8(8.2)</td>
<td>72</td>
<td>44.8</td>
<td>65.6(66.5)</td>
<td>42</td>
</tr>
<tr>
<td>Multiple Myeloma</td>
<td>302</td>
<td>72.4(7.8)</td>
<td>73</td>
<td>48.7</td>
<td>43.7(50.4)</td>
<td>24</td>
</tr>
<tr>
<td>Pancreas</td>
<td>191</td>
<td>72.4(8.5)</td>
<td>71</td>
<td>56.5</td>
<td>37.2(55.6)</td>
<td>13</td>
</tr>
</tbody>
</table>
Covariate-Adjusted Physical (PCS) and Mental (MCS) Component Summary Scores; SEER-MHOS Participants, diagnosed 1998-2009

Kent, Ambs, Mitchell et al., Health-related quality of life in older adult survivors of selected cancers: Data from the SEER-MHOS linkage. *Cancer, 2015; 121 (5), p. 758-765*
# Number of SEER-MHOS Respondents Age 65+ by First Cancer Site, 1998-2009

<table>
<thead>
<tr>
<th>First Cancer</th>
<th>Total # of linked Patients</th>
<th>Baseline Survey</th>
<th>Baseline and Follow-up Surveys</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>N</td>
<td>%</td>
</tr>
<tr>
<td>Prostate</td>
<td>19,727</td>
<td>19,598</td>
<td>99.35</td>
</tr>
<tr>
<td>Breast</td>
<td>16,388</td>
<td>16,264</td>
<td>99.24</td>
</tr>
<tr>
<td>Colorectal</td>
<td>11,127</td>
<td>11,061</td>
<td>99.41</td>
</tr>
<tr>
<td>Lung and bronchus</td>
<td>7,823</td>
<td>7,756</td>
<td>99.14</td>
</tr>
<tr>
<td>Gynecological Cancers</td>
<td>5,171</td>
<td>5,134</td>
<td>99.28</td>
</tr>
<tr>
<td>Bladder</td>
<td>4,757</td>
<td>4,723</td>
<td>99.29</td>
</tr>
<tr>
<td>Melanomas</td>
<td>4,338</td>
<td>4,302</td>
<td>99.17</td>
</tr>
<tr>
<td>Kidney and Renal pelvis</td>
<td>1,874</td>
<td>1,859</td>
<td>99.20</td>
</tr>
<tr>
<td>Non-Hodgkin's lymphomas - nodal</td>
<td>1,893</td>
<td>1,877</td>
<td>99.15</td>
</tr>
<tr>
<td>Stomach</td>
<td>1,029</td>
<td>1,026</td>
<td>99.71</td>
</tr>
<tr>
<td>Pancreas</td>
<td>1,294</td>
<td>1,284</td>
<td>99.23</td>
</tr>
</tbody>
</table>
Changes in adjusted health-related quality of life (over two years) for men with and without prostate cancer, by time since diagnosis

Reeve et al., 2012 Cancer
Measurement Systems will Make Patient-Centered Big Data Increasingly Available

• Currently Available Measurement Systems such as PROMIS, NIH Toolbox, NeuroQOL, and PRO-CTCAE:
  – Integrated into EHRs, registries, and patient-portals/kiosks
  – Need to become more familiar with interpretation of these and other commonly used measures (eg. CES-D, PHQ)
  – Does measurement science receive adequate contemporary attention in nursing? Are we falling behind as a discipline?
    • Modern measurement theory
    • Electronic data capture
  – Nurse scientists should seek greater engagement in instrument development and testing so that constructs (and covariates) of importance to our science are captured in a timely way relative to informative events (eg. admission and discharge), and are coded in ways that are meaningful for our science
What is PROMIS?

Patient/Person Reported Outcomes Measurement Information System

• Flexible system of highly reliable, precise health outcome assessment tools that measure

• PROMIS measures person-reported health by asking people how they feel (pain, fatigue, depression, etc.) and what they can do (mobility, activities of daily living, social function, etc.)

• Questions are categorized on 3 main domains (physical, mental and social health)
Comparability

• Common domains and metrics of self-reported health provide health measurement that is relevant to patients regardless of chronic health condition
• All PROMIS measures, for every health concept apply the T score method:
  • A score of 50 is the average score in the US general population on every PROMIS measure
  • A deviation of 10 from the average score is equivalent to one standard deviation unit healthier or less healthy than the US population on every PROMIS measure
Comparability - What is the value?

- Ability to compare the health burden of different chronic conditions to answer the questions such as:
  - Which disease is associated with the most suffering and disability?
  - How does the depression of chronic pain patients compare to the clinically depressed?
  - How does the health burden of obesity compare to that of other chronic conditions?
  - Ability to compare the benefits of different treatments for a given disease
PROMIS®: Developing Instruments for use in Clinical Research and Practice

- Publicly available, adaptable and sustainable system that will provide:
  - Brief, precise, valid fixed instruments (Short Forms)
  - Individually “tailored” questionnaires (Computerized-Adaptive Testing, CAT)

- Advantages:
  - ↓ response burden
  - ↑ scale precision to detect group differences
  - Standardized measures offer the capacity to compare or combine results from multiple studies

More information available at nihpromis.org
PROMIS® Domain Framework

Self-Reported Health

Physical Health

Mental Health

Social Health

Symptoms

Function

Affect

Behavior

Cognition

Relationships

Function

For more information: www.nihpromis.org
Physical Health Banks

Physical Health

**Adult**
- Pain Behavior
- Pain Interference
- Fatigue
- Physical Function
- Sleep Disturbance
- Sleep-related Impairment
- Sexual Function

**Pediatric**
- Pain Interference
- Fatigue
- Upper Extremity Function
- Mobility
- Asthma Impact
Mental Health Banks

**Adult**
- Anxiety
- Depression
- Anger
- Illness Impact - Negative
- Illness Impact - Positive
- Applied Cognition - Concerns
- Applied Cognition - Abilities

**Pediatric**
- Anxiety
- Depression
- Anger
- Illness Impact - Negative
- Illness Impact - Positive
- Applied Cognition - Concerns
- Applied Cognition - Abilities
Social Health Banks

**Adult**
- Ability to Participate in Roles & Activities
- Satisfaction with Roles & Activities
- Companionship
- Emotional Support
- Informational Support
- Instrumental Support
- Social Isolation

**Pediatric**
- Peer Relationships

**Social Health**
Physical Functioning

Are you able to get in and out of bed?

Are you able to stand and walk without losing your balance for 1 minute?

Are you able to walk a block on flat ground?

Are you able to run or jog for two miles?

Are you able to run five miles?
Physical Functioning Item Bank

- Are you able to walk a block on flat ground?
- Are you able to run or jog for two miles?
- Are you able to run five miles?
Physical Functioning Item Bank

- Item 1
- Item 2
- Item 3
- Item 4
- Item 5
- Item 6
- Item 7
- Item 8
- Item 9
- Item n

- Are you able to walk a block on flat ground?
- Are you able to run or jog for two miles?
- Are you able to run five miles?
Physical Functioning Item Bank

1. Are you able to get in and out of bed?
2. Are you able to stand without losing your balance for 1 minute?
3. Are you able to walk from one room to another?
4. Are you able to walk a block on flat ground?
5. Are you able to run or jog for two miles?
6. Are you able to run five miles?
Computerized Adaptive Testing (CAT)

Question #1

high physical function

Question #2

Question #3

low physical function

Questionnaire with a high precision - AND a wide range
PROMIS® Contribution to the Future of Clinical Research

- **Precision** – Improved measurement precision across the full range of patient-reported outcomes
- **Efficiency** – less respondent burden
- **Standardization** – more interpretable research with standard terminology and metrics
- **International** collaborations & trial applications
- **Common metric** across studies and between research and practice
National Cancer Institute
Patient-Reported Outcomes
version of the Common Terminology Criteria for Adverse Events

PRO-CTCAE
• Treatment-related toxicity (safety and tolerability)
  • Fundamental outcome when drawing conclusions about therapeutic effectiveness, including comparative effectiveness
  • Currently evaluated by clinicians using Common Terminology Criteria for Adverse Events (CTCAE)
1 of 8 of the adverse events listed in CTCAE is a symptom outcome.

- Evidence indicates that the validity of reporting symptom outcomes is eroded when those reports are filtered through research staff and clinicians.
- Staff-based adverse event reporting occurs at clinic visits; adverse events that occur between visits may be missed.
- Real-time ascertainment of symptomatic adverse events using PROs could improve the precision and reproducibility of adverse event reporting.
NCI’s PRO-CTCAE is a new measurement system designed to complement the CTCAE:

- capture the patient’s perspective of symptoms and treatment toxicity in cancer clinical trials
- improve the validity of adverse event reporting in cancer clinical trials
- support improved care quality for patients participating in trials
# PRO-CTCAE Measurement System

<table>
<thead>
<tr>
<th>1. Symptom Library</th>
<th>2. System for Survey Administration</th>
</tr>
</thead>
<tbody>
<tr>
<td>• 78 symptomatic adverse events drawn from CTCAE</td>
<td>• Web-based system to customize surveys and manage survey administration</td>
</tr>
<tr>
<td>• PRO-CTCAE questions evaluate symptom occurrence, frequency, severity, interference, and amount</td>
<td>• Patient responds to surveys using web, tablet or interactive voice response (IVRS) telephone system</td>
</tr>
<tr>
<td></td>
<td>• Conditional branching (skip patterns)</td>
</tr>
<tr>
<td></td>
<td>• Write-ins with automatic mapping to standardized terminology</td>
</tr>
</tbody>
</table>

For more information about PRO-CTCAE visit: [http://healthcaredelivery.cancer.gov/pro-ctcae/](http://healthcaredelivery.cancer.gov/pro-ctcae/)
## CTCAE vs. PRO-CTCAE Item Structures

### CTCAE

<table>
<thead>
<tr>
<th>Adverse Event</th>
<th>Grade</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1</td>
</tr>
<tr>
<td>Mucositis oral</td>
<td></td>
</tr>
<tr>
<td>Asymptomatic or mild symptoms; intervention not indicated</td>
<td>Moderate pain; not interfering with oral intake; modified diet indicated</td>
</tr>
</tbody>
</table>

### PRO-CTCAE

Please think back over the past 7 days:

**What was the severity of your MOUTH OR THROAT SORES at their WORST?**
None / Mild / Moderate / Severe / Very severe

**How much did MOUTH OR THROAT SORES interfere with your usual or daily activities?**
Not at all / A little bit / Somewhat / Quite a bit / Very much
## Patient-Reported Outcomes version of the Common Terminology Criteria for Adverse Events (PRO-CTCAE) Item Library

### Attributes

<table>
<thead>
<tr>
<th>Presence/Absence</th>
<th>Severity</th>
<th>Frequency</th>
<th>Interference</th>
</tr>
</thead>
<tbody>
<tr>
<td>P</td>
<td>S</td>
<td>F</td>
<td>I</td>
</tr>
</tbody>
</table>

### Categories

#### Attention/Memory
- Concentration (SI)
- Memory (SI)

#### Cardio/Circulatory
- Swelling (FSI)
- Heart palpitations (FS)

#### Neurological
- Numbness & tingling (SI)
- Dizziness (SI)

#### Sleep/Wake
- Insomnia (SI)
- Fatigue (SI)

#### Sexual
- Achieve and maintain erection (S)
- Ejaculation (F)
- Desire (S)
- Orgasm (P)
- Pain w/sexual intercourse (S)

#### Cutaneous
- Rash (P)
- Skin dryness (S)
- Acne (S)
- Hair loss (P)
- Itching (S)
- Hives (P)
- Hand-foot syndrome (S)
- Nail loss (P)
- Nail ridging (P)
- Nail discoloration (P)
- Sensitivity to sunlight (P)
- Pressure sores (P)
- Radiation skin reaction (S)
- Skin darkening (P)
- Stretch marks (P)

#### Pain
- General pain (FSI)
- Headache (FSI)
- Muscle pain (FSI)
- Joint pain (FSI)

#### Mood
- Anxious (FSI)
- Discouraged (FSI)
- Sad (FSI)

#### Respiratory
- Shortness of breath (SI)
- Cough (SI)
- Wheezing (S)

#### Cardio/Circulatory
- Swelling (FSI)
- Heart palpitations (FS)
- General pain (FSI)
- Headache (FSI)
- Muscle pain (FSI)
- Joint pain (FSI)

#### Gastro-Intestinal
- Taste changes (S)
- Decreased appetite (SI)
- Nausea (FS)
- Vomiting (FS)
- Heartburn (FS)
- Gas (P)
- Bloating (FS)
- Hiccups (FS)
- Constipation (S)
- Diarrhea (F)
- Abdominal pain (FSI)
- Fecal incontinence (FI)

#### Gynecologic/Urinary
- Vaginal bleeding (P)
- Missed menstrual periods (P)
- Vaginal discharge (P)
- Vaginal dryness (S)
- Painful urination (S)
- Urinary urgency (FI)
- Urinary frequency (PI)
- Change in usual urine color (P)
- Urinary incontinence (FI)

#### Miscellaneous
- Breast swelling and tenderness (S)
- Bruising (P)
- Chills (FS)
- Increased sweating (FS)
- Decreased sweating (P)
- Hot flashes (FS)
- Nosebleed (FS)
- Pain and swelling at injection site (P)
- Body odor (S)

#### Oral
- Dry mouth (S)
- Difficulty swallowing (S)
- Mouth/throat sores (SI)
- Cracking at the corners of the mouth (cheilosis/cheilitis) (S)
- Voice quality changes (P)
- Hoarseness (S)
• Psychometrically robust library of items
• Electronic system fits data collection smoothly into trials workflow and offers favorable user-experience
• Accommodate patients with limited English proficiency/digital literacy
• Supply meaningful data to improve understanding of symptomatic AEs

2009

Develop Items

Cognitive Testing

Validation Study

Implement telephone reporting (IVRS)

Usability testing

Electronic system for survey mgmt

2016

Spanish Validation

Feasibility, Acceptability & Cost

Evaluate utility for decision-making
Early Adopters

- >100 early adopters in 12 countries are testing PRO-CTCAE in therapeutic trials and observational studies, including registry studies
- Collaboration agreements established between NCI and investigators:
  - Ensure continuing integrity of the PRO-CTCAE tool
  - Stimulate efficient and coordinated testing of PRO-CTCAE
  - Allow for sharing of data and collaborative analysis
  - Generate evidence about best approaches for data interpretation and reporting in particular study contexts and in specific patient populations
Measurement Systems for PROs

• Advantages of Currently Available Measurement Systems:
  – Harmonized measures
  – Robust psychometric properties
  – Interpretive guidance in form of norms, cut-scores, and MID in development
  – Free to users with agreement to share data/contribute to further development of the measurement system

• Caveats:
  – May be less sensitive to unique population-specific issues
  – Capacity to detect treatment effects not yet established
  – Constructs of interest for particular study designs may not be captured within current domain structure for the instruments
Big Data-Driven Consensus on Core Outcome Measures in Adult Cancer Treatment Trials

Recommended Patient-Reported Core Set of Symptoms to Measure in Adult Cancer Treatment Trials


Manuscript received May 24, 2013; revised April 1, 2014; accepted April 11, 2014.

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Background

The National Cancer Institute’s Symptom Management and Health-Related Quality of Life Steering Committee held a clinical trials planning meeting (September 2011) to identify a core symptom set to be assessed across oncology trials for the purposes of better understanding treatment efficacy and toxicity and to facilitate cross-study comparisons. We report the results of an evidence-synthesis and consensus-building effort that culminated in recommendations for core symptoms to be measured in adult cancer clinical trials that include a patient-reported outcome (PRO).

Methods

We used a data-driven, consensus-building process. A panel of experts, including patient representatives, conducted a systematic review of the literature (2001–2011) and analyzed six large datasets. Results were reviewed at a multistakeholder meeting, and a final set was derived emphasizing symptom prevalence across diverse cancer populations, impact on health outcomes and quality of life, and attribution to either disease or anticancer treatment.

Results

We recommend that a core set of 12 symptoms—specifically fatigue, insomnia, pain, anorexia (appetite loss), dyspnea, cognitive problems, anxiety (includes worry), nausea, depression (includes sadness), sensory neuropathy, constipation, and diarrhea—be considered for inclusion in clinical trials where a PRO is measured. Inclusion of symptoms and other patient-reported endpoints should be well justified, hypothesis driven, and meaningful to patients.

Conclusions

This core set will promote consistent assessment of common and clinically relevant disease- and treatment-related symptoms across cancer trials. As such, it provides a foundation to support data harmonization and continued efforts to enhance measurement of patient-centered outcomes in cancer clinical trials and observational studies.

Reeve BB, Mitchell SA et al. (2014). Recommended patient-reported core set of symptoms to measure in adult cancer treatment trials. Journal of the National Cancer Institute, 106(7)
Evidence-Based Process for Selecting Core Domains

- Literature Review
  - Items Proposed
    - Rank ordered within the top 10 symptoms based on prevalence, severity, and/or importance ratings in at least two data sources.
    - Present across diverse cancer populations
    - Attributable to either disease or to anti-cancer treatment
    - Sensitive to change
    - Measurable from the patient perspective

- Items Finalized Through Data-Driven Consensus Process
<table>
<thead>
<tr>
<th>Characteristic</th>
<th>CDUS/AdEERS</th>
<th>EORTC</th>
<th>SOAPP</th>
<th>PRO-CTCAE</th>
<th>FACT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Data Type</td>
<td>Clinician-reported adverse events in NCI clinical trial systems database (CDUS and AdEERS)</td>
<td>Patient-reported symptom data from EORTC trials and other research studies. These data were also used to derive QLQ-C30 reference values</td>
<td>Patient-reported symptom data from cooperative group study</td>
<td>Patient-reported symptom data from instrument validation study in cancer</td>
<td>Patient-reported symptom importance for monitoring</td>
</tr>
<tr>
<td>Measure Type</td>
<td>CTCAE</td>
<td>EORTC-QLQ-C30</td>
<td>MDASI</td>
<td>PRO-CTCAE</td>
<td>FACT-G and other HRQOL questions</td>
</tr>
<tr>
<td>Measure</td>
<td>Clinician-reported</td>
<td>Patient-reported</td>
<td>Patient-reported</td>
<td>Patient-reported</td>
<td>Patient-reported</td>
</tr>
<tr>
<td>Sample Size</td>
<td>449,672 AE reports</td>
<td>23,553 patients</td>
<td>3,123 patients</td>
<td>595 patients</td>
<td>533 patients</td>
</tr>
<tr>
<td>Cancer Site</td>
<td>Multiple cancer sites (details not available)</td>
<td>14% lung, 14% prostate, 12% breast, 12% other, 8% colorectal, 8% esophagus/stomach, 5% gynecological, 5% melanoma, 5% unknown, 4% myeloma, 3% head &amp; neck, 2% leukemia, 2% liver, 2% lymphoma, 2% testicular, 1% brain, 1% kidney, 1% pancreas; &lt; 1% each of bladder, bone, and sarcoma</td>
<td>50% breast, 23% colorectal, 17% lung, 10% prostate</td>
<td>21% breast, 20% lung, 17% head or neck, 12% prostate, 7% colorectal, and 23% other cancer types</td>
<td>10% - breast, 10% ovarian, 9% brain, 9% colorectal, 9% head and neck, 9% hepatobiliary, 9% kidney, 9% lung, 9% lymphoma, 9% prostate, 6% bladder</td>
</tr>
<tr>
<td>Disease stage</td>
<td>Not available</td>
<td>20% stage 1-II; 34% stage III-IV; 20% recurrent/metastatic disease</td>
<td>38% advanced disease</td>
<td>Not available</td>
<td>100% stage III-IV</td>
</tr>
<tr>
<td>ECOG PS Rating</td>
<td>Not available</td>
<td>Not available</td>
<td>ECOG 0: 57%</td>
<td>ECOG 0-1: 77%</td>
<td>ECOG 0: 23%</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>ECOG 1: 36%</td>
<td>ECOG 2-4: 23%</td>
<td>ECOG 1: 48%</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>ECOG 2-4: 7%</td>
<td>ECOG 2: 25%</td>
<td>ECOG 2: 25%</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>ECOG 3: 4%</td>
<td>ECOG 3: 4%</td>
</tr>
<tr>
<td>Gender</td>
<td>Not available</td>
<td>46% female</td>
<td>70% female</td>
<td>53% female</td>
<td>48% female</td>
</tr>
<tr>
<td>Age</td>
<td>Not available</td>
<td>&gt; 54% 60 years or older</td>
<td>Median 61 years</td>
<td>Mean 59 years</td>
<td>mean 59 years</td>
</tr>
<tr>
<td>Symptom</td>
<td>CDUS/AdEERS</td>
<td>EORTC</td>
<td>SOAPP</td>
<td>PRO-CTCAE</td>
<td>FACT</td>
</tr>
<tr>
<td>---------------------</td>
<td>-------------</td>
<td>-------</td>
<td>-------</td>
<td>-----------</td>
<td>------</td>
</tr>
<tr>
<td></td>
<td>Prevalence</td>
<td>Prevalence</td>
<td>Prevalence</td>
<td>Prevalence</td>
<td>Prevalence</td>
</tr>
<tr>
<td>Fatigue</td>
<td>%</td>
<td>rank</td>
<td>%</td>
<td>rank</td>
<td>%</td>
</tr>
<tr>
<td></td>
<td>6.2</td>
<td>2</td>
<td>32</td>
<td>2</td>
<td>34</td>
</tr>
<tr>
<td>Insomnia</td>
<td>0.6</td>
<td>17</td>
<td>25</td>
<td>4</td>
<td>27</td>
</tr>
<tr>
<td>Pain</td>
<td>7.7</td>
<td>1</td>
<td>25</td>
<td>3</td>
<td>19</td>
</tr>
<tr>
<td>Anorexia</td>
<td>2.2</td>
<td>5</td>
<td>18</td>
<td>6</td>
<td>17</td>
</tr>
<tr>
<td>Dyspnea</td>
<td>1.8</td>
<td>7</td>
<td>15</td>
<td>7</td>
<td>19</td>
</tr>
<tr>
<td>Cognitive problems</td>
<td></td>
<td>14</td>
<td>10</td>
<td>17</td>
<td>9</td>
</tr>
<tr>
<td>Anxiety</td>
<td></td>
<td>32</td>
<td>1</td>
<td>19</td>
<td>5</td>
</tr>
<tr>
<td>Nausea</td>
<td>3.3</td>
<td>3</td>
<td>9</td>
<td>12</td>
<td>22</td>
</tr>
<tr>
<td>Depression</td>
<td></td>
<td>19</td>
<td>5</td>
<td>17</td>
<td>9</td>
</tr>
<tr>
<td>Neuropathy</td>
<td>1.9</td>
<td>6</td>
<td>19</td>
<td>5</td>
<td>19</td>
</tr>
<tr>
<td>Constipation</td>
<td>1.4</td>
<td>11</td>
<td>14</td>
<td>9</td>
<td>30</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>3.1</td>
<td>4</td>
<td>6</td>
<td>13</td>
<td>25</td>
</tr>
<tr>
<td>Dry mouth</td>
<td></td>
<td></td>
<td>19</td>
<td>5</td>
<td>32</td>
</tr>
<tr>
<td>Irritability</td>
<td></td>
<td></td>
<td>15</td>
<td>8</td>
<td></td>
</tr>
<tr>
<td>Drowsiness</td>
<td>1.0</td>
<td>13</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Coughing</td>
<td></td>
<td></td>
<td>22</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>Taste alteration</td>
<td>0.6</td>
<td>19</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Itching</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dizziness</td>
<td>0.5</td>
<td>20</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vomiting</td>
<td>1.7</td>
<td>8</td>
<td>5%</td>
<td>14</td>
<td></td>
</tr>
<tr>
<td>Alopecia</td>
<td>1.5</td>
<td>9</td>
<td></td>
<td>20</td>
<td>4</td>
</tr>
<tr>
<td>Headache</td>
<td></td>
<td></td>
<td>20</td>
<td>14</td>
<td></td>
</tr>
</tbody>
</table>
Recommended Core Set

- Identify a standard core set of 12 symptoms to be collected in all patients across trials where a PRO is included:
  - Nausea, vomiting, anorexia, diarrhea, sensory neuropathy, dyspnea, pain, fatigue, impaired mental concentration, anxiety, depressed mood, insomnia
CDC-NCI Healthstyles PROMIS Collaboration

• Data license costs were jointly funded by Centers for Disease Control and National Cancer Institute
• Objective: Assess measurement issues related to HP2020 HRQOL and Well-Being objectives
• 2010 HealthStyles Study
  – N=4,184 respondents (67% response rate)
  – Weighted responses to achieve population representativeness
• Items added to the 2010 survey
  – PROMIS-Global Scale (10 items)
  – CDC Core Healthy Days Items (4 items)
  – Diener Satisfaction With Life Scale (4 of the 5 items)
• Additional data included about comorbid conditions, BMI, behavior (tobacco use, exercise guideline adherence)
• Data became available Spring, 2011
Psychometric Evaluation of the NIH PROMIS Global Health, CDC Healthy Days, and Satisfaction with Life Instruments

• Background and Aims
  – Few studies have examine the reliability and validity of the NIH PROMIS Global Health Scale and CDC Healthy Days Measure using large, representative, community-dwelling populations
  – Extend previous work in 3 ways:
    • Determine if the previously identified factor structures for the PROMIS Global Health Scale fit data from another sample of the US general population
    • Assess whether the CDC Healthy Days items reflect latent constructs comparable to those that underlie the PROMIS physical and mental health subscales
    • Determine whether the factor structures of the PROMIS subscales combined with relevant CDC Health Days indicators are equivalent across age (<64 vs. ≥65 years), gender, and the presence/absence of comorbidities
Psychometric Evaluation of the NIH PROMIS Global Health, CDC Healthy Days, and Satisfaction with Life Instruments

• Methods
  – N=4184 (66.9% response rate)
  – Survey data weighted to match U.S. population estimates
  – Confirmatory factor analyses
    • confirm the factor structures
    • test for measurement invariance across demographic groups (age, gender and chronic condition status)
    • evaluate latent mean differences between groups
### Means and distributions of the items included in the CDC, PROMIS, and Satisfaction with Life Measures (N = 4,184)

<table>
<thead>
<tr>
<th>CDC Items</th>
<th>Mean</th>
<th>Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0 Days</td>
<td>1-10 Days</td>
</tr>
<tr>
<td># of Physically Unhealthy Days (0-30)</td>
<td>3.24</td>
<td>69%</td>
</tr>
<tr>
<td># of Mentally Unhealthy Days (0-30)</td>
<td>2.51</td>
<td>73%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>PROMIS® Physical Health Items</th>
<th>Better Health*</th>
<th>Worse Health*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>5</td>
<td>4</td>
</tr>
<tr>
<td>PROMIS/CDC General health</td>
<td>3.38</td>
<td>10%</td>
</tr>
<tr>
<td>Physical health</td>
<td>3.33</td>
<td>8%</td>
</tr>
<tr>
<td>Physical function</td>
<td>4.44</td>
<td>66%</td>
</tr>
<tr>
<td>Pain</td>
<td>3.85</td>
<td>27%</td>
</tr>
<tr>
<td>Fatigue</td>
<td>3.80</td>
<td>23%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>PROMIS® Mental Health Items</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Quality of life</td>
<td>3.62</td>
</tr>
<tr>
<td>Mental health</td>
<td>3.71</td>
</tr>
<tr>
<td>Social discretionary</td>
<td>3.44</td>
</tr>
<tr>
<td>Emotional problems</td>
<td>3.57</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Satisfaction With Life Scale Items</th>
<th>Strongly Agree*</th>
<th>Strongly Disagree *</th>
</tr>
</thead>
<tbody>
<tr>
<td>In most ways my life is close to my ideal</td>
<td>3.29</td>
<td>10%</td>
</tr>
<tr>
<td>The conditions of my life are excellent</td>
<td>3.32</td>
<td>11%</td>
</tr>
<tr>
<td>I am satisfied with my life</td>
<td>3.58</td>
<td>20%</td>
</tr>
<tr>
<td>So far I have gotten the important things I want in life</td>
<td>3.63</td>
<td>21%</td>
</tr>
</tbody>
</table>

*Note. The general health item is part of the CDC Healthy Days measure as well as the PROMIS® Global Health scale. The headings for the PROMIS® item response categories have been altered from those that appeared in the survey in order to simplify the table. Please see the Appendix for the exact wording and response corresponding response categories for each item.
Standardized factor loadings from a multi-group confirmatory factor analysis of physical health and mental health factors, by gender, age, and number of comorbidities

<table>
<thead>
<tr>
<th>Indicators</th>
<th>Gender Model</th>
<th>Age Model</th>
<th>Medical Conditions Model</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Fully</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Constrained</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Model (N=4184)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Physical Health Factor</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PROMIS/CDC General health</td>
<td>.83</td>
<td>.81</td>
<td>.85</td>
</tr>
<tr>
<td>PROMIS Physical health</td>
<td>.90</td>
<td>.89</td>
<td>.92</td>
</tr>
<tr>
<td>PROMIS Physical function</td>
<td>.63</td>
<td>.63</td>
<td>.64</td>
</tr>
<tr>
<td>PROMIS Pain</td>
<td>.62</td>
<td>.58</td>
<td>.66</td>
</tr>
<tr>
<td>PROMIS Fatigue</td>
<td>.63</td>
<td>.64</td>
<td>.63</td>
</tr>
<tr>
<td>CDC Physically Healthy Days</td>
<td>.54</td>
<td>.52</td>
<td>.53</td>
</tr>
<tr>
<td>Mental Health Factor</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PROMIS Quality of life</td>
<td>.93</td>
<td>.92</td>
<td>.95</td>
</tr>
<tr>
<td>PROMIS Mental health</td>
<td>.79</td>
<td>.80</td>
<td>.79</td>
</tr>
<tr>
<td>PROMIS Social discretionary</td>
<td>.80</td>
<td>.79</td>
<td>.81</td>
</tr>
<tr>
<td>PROMIS Emotional problems</td>
<td>.56</td>
<td>.57</td>
<td>.55</td>
</tr>
<tr>
<td>CDC Mentally Healthy Days</td>
<td>.51</td>
<td>.49</td>
<td>.51</td>
</tr>
</tbody>
</table>

Measurement invariance is examined by fitting a multi-group confirmatory factor analysis model of physical health and mental health factors, by gender, age, and number of comorbidities. The models fit as well (based on TLI, RMSEA, and CFI) as when the loadings were free to vary across gender or age.

These differential loadings suggest these measures (CDC Health Days measure and the PROMIS Fatigue scale) may perform differentially in those with chronic conditions compared to those without.

Patterns of Multimoribidity: Associations between Chronic Conditions, Behaviors and HRQL

• **Background and Aims**
  
  – Chronic conditions can act cumulatively and synergistically to adversely affect health outcomes, caregiver burden and treatment costs, and are associated with symptoms, functional limitations and impaired HRQL
  
  – Comorbidities or multiple chronic conditions are often assessed through broad summary indices such as the Charlson Comorbidity Index and little is known about patterns of co-occurrence
  
  – **Aims:**
    
    • Examine patterns of co-occurrence among 27 chronic conditions within a large, diverse sample of adults;
    
    • Determine whether these patterns were associated with sociodemographic factors, patterns of tobacco use, physical activity, and body mass index (BMI), and differences in self-assessed health status and well-being

Barile, Mitchell et al. *Preventing Chronic Disease* (accepted for publication)
Patterns of Multimorbidty: Associations between Chronic Conditions, Behaviors and HRQL

• Methods
  – 2010 HealthStyles Survey is a mail panel survey; sampling design with stratification by region, household income, population density, age and household size
  – N=4184 (66.9% response rate)
  – Survey data weighted based on demographic factors to match U.S. population estimates
  – Measures included:
    • 24 Chronic Conditions Listed: During the past year, have you had (or do you currently have) any of these health conditions?
    • PROMIS Global Health Scale, CDC Healthy Days Measures, Satisfaction with Life Scale
    • Behavioral Risk Factors: BMI; Current or Past Tobacco Use; Minutes of Physical Activity Per Week

Barile, Mitchell et al. Preventing Chronic Disease (accepted for publication)
Patterns of Multimorbidty: Associations between Chronic Conditions, Behaviors and HRQL

• Analysis
  – Latent class analysis using Mplus version 7
  – LCA is a person-centered, rather than variable-centered statistical approach for identifying groups of individuals who share similar characteristics.
  – LCA was used to divide the population into subgroups that share a distinct, interpretable pattern of relationships among the chronic health conditions
  – LCA models estimated representing two, three or four latent classes
  – 4 class model resulted in the best fit (129 parameters):
    • AIC=52375, sample-size adjusted BIC=52783, and entropy (.79)

Barile, Mitchell et al. Preventing Chronic Disease (accepted for publication)
Frequencies for the chronic conditions included in the latent class analyses (N = 4,184)

<table>
<thead>
<tr>
<th>Condition</th>
<th>Sample Prevalence</th>
<th>Weighted</th>
</tr>
</thead>
<tbody>
<tr>
<td>Atrial fibrillation</td>
<td>98</td>
<td>3%</td>
</tr>
<tr>
<td>Heart disease (angina or heart attack)</td>
<td>158</td>
<td>3%</td>
</tr>
<tr>
<td>Congestive heart failure</td>
<td>70</td>
<td>1%</td>
</tr>
<tr>
<td>Other heart disease</td>
<td>155</td>
<td>3%</td>
</tr>
<tr>
<td>High blood pressure</td>
<td>1468</td>
<td>31%</td>
</tr>
<tr>
<td>High cholesterol</td>
<td>1148</td>
<td>25%</td>
</tr>
<tr>
<td>Diabetes</td>
<td>645</td>
<td>14%</td>
</tr>
<tr>
<td>Arthritis</td>
<td>1153</td>
<td>24%</td>
</tr>
<tr>
<td>Osteoporosis</td>
<td>203</td>
<td>5%</td>
</tr>
<tr>
<td>Chronic pain</td>
<td>659</td>
<td>15%</td>
</tr>
<tr>
<td>Sciatica</td>
<td>222</td>
<td>5%</td>
</tr>
<tr>
<td>Asthma</td>
<td>386</td>
<td>10%</td>
</tr>
<tr>
<td>Emphysema/COPD</td>
<td>131</td>
<td>3%</td>
</tr>
<tr>
<td>Eczema</td>
<td>180</td>
<td>6%</td>
</tr>
<tr>
<td>Ulcers</td>
<td>105</td>
<td>3%</td>
</tr>
<tr>
<td>Irritable Bowel Syndrome (IBS)</td>
<td>214</td>
<td>5%</td>
</tr>
<tr>
<td>Overactive bladder or incontinence</td>
<td>329</td>
<td>7%</td>
</tr>
<tr>
<td>Skin cancer</td>
<td>156</td>
<td>3%</td>
</tr>
<tr>
<td>Cancer other than Skin Cancer</td>
<td>175</td>
<td>3%</td>
</tr>
<tr>
<td>Multiple sclerosis</td>
<td>39</td>
<td>1%</td>
</tr>
<tr>
<td>Epilepsy or seizure disorder</td>
<td>52</td>
<td>1%</td>
</tr>
<tr>
<td>Hearing impairment</td>
<td>393</td>
<td>8%</td>
</tr>
<tr>
<td>Migraine headaches</td>
<td>532</td>
<td>14%</td>
</tr>
<tr>
<td>Insomnia/sleep disorder</td>
<td>464</td>
<td>12%</td>
</tr>
<tr>
<td>Depression</td>
<td>631</td>
<td>16%</td>
</tr>
<tr>
<td>Anxiety</td>
<td>593</td>
<td>16%</td>
</tr>
<tr>
<td>Other mental health condition</td>
<td>116</td>
<td>3%</td>
</tr>
</tbody>
</table>

Note. 26.2% of the sample reported no chronic conditions.
Frequencies for the chronic conditions included in the latent class analyses (N = 4,184)

<table>
<thead>
<tr>
<th>Condition</th>
<th>Sample Prevalence</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
</tr>
<tr>
<td>Atrial fibrillation</td>
<td>98</td>
</tr>
<tr>
<td>Heart disease (angina or heart attack)</td>
<td>158</td>
</tr>
<tr>
<td>Congestive heart failure</td>
<td>70</td>
</tr>
<tr>
<td>Other heart disease</td>
<td>155</td>
</tr>
<tr>
<td><strong>High blood pressure</strong></td>
<td>1468</td>
</tr>
<tr>
<td><strong>High cholesterol</strong></td>
<td>1148</td>
</tr>
<tr>
<td><strong>Diabetes</strong></td>
<td>645</td>
</tr>
<tr>
<td><strong>Arthritis</strong></td>
<td>1153</td>
</tr>
<tr>
<td>Osteoporosis</td>
<td>203</td>
</tr>
<tr>
<td>Chronic pain</td>
<td>659</td>
</tr>
<tr>
<td>Sciatica</td>
<td>222</td>
</tr>
<tr>
<td>Asthma</td>
<td>386</td>
</tr>
<tr>
<td>Emphysema/COPD</td>
<td>131</td>
</tr>
<tr>
<td>Eczema</td>
<td>180</td>
</tr>
<tr>
<td>Ulcers</td>
<td>105</td>
</tr>
<tr>
<td>Irritable Bowel Syndrome (IBS)</td>
<td>214</td>
</tr>
<tr>
<td>Overactive bladder or incontinence</td>
<td>329</td>
</tr>
<tr>
<td>Skin cancer</td>
<td>156</td>
</tr>
<tr>
<td>Cancer other than Skin Cancer</td>
<td>175</td>
</tr>
<tr>
<td>Multiple sclerosis</td>
<td>39</td>
</tr>
<tr>
<td>Epilepsy or seizure disorder</td>
<td>52</td>
</tr>
<tr>
<td>Hearing impairment</td>
<td>393</td>
</tr>
<tr>
<td><strong>Migraine headaches</strong></td>
<td>532</td>
</tr>
<tr>
<td><strong>Insomnia/sleep disorder</strong></td>
<td>464</td>
</tr>
<tr>
<td>Depression</td>
<td>631</td>
</tr>
<tr>
<td>Anxiety</td>
<td>593</td>
</tr>
<tr>
<td>Other mental health condition</td>
<td>116</td>
</tr>
</tbody>
</table>

Note. 26.2% of the sample reported no chronic conditions.
Class-specific probabilities of reporting each of the 27 chronic conditions
Mean differences on measures of health-related quality of life and well-being by latent class (N = 4,184)

<table>
<thead>
<tr>
<th>Latent Class</th>
<th>Physically Unhealthy Days (0-30)</th>
<th>Mentally Unhealthy Days (0-30)</th>
<th>Activities Limitation Days (0-30)</th>
<th>PROMIS Physical Health T-Score</th>
<th>PROMIS Mental Health T-Score</th>
<th>Well-being Score (1-5)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Class 1: Healthy (n = 2321)</td>
<td>Mean*: 93 95% CI: .7-1.1</td>
<td>Mean*: 1.39 95% CI: 1.2-1.6</td>
<td>Mean*: .39 95% CI: .21-.57</td>
<td>Mean*: 52.31 95% CI: 52.1-52.6</td>
<td>Mean*: 49.96 95% CI: 49.7-50.2</td>
<td>Mean*: 3.61 95% CI: 3.6-3.7</td>
</tr>
<tr>
<td>Class 2: Physical Health Conditions (n = 1072)</td>
<td>Mean*: 4.80 95% CI: 4.1-5.5</td>
<td>Mean*: .83 95% CI: 2-1.5</td>
<td>Mean*: 3.81 95% CI: 3.2-4.4</td>
<td>Mean*: 47.02 95% CI: 46.3-47.8</td>
<td>Mean*: 49.42 95% CI: 48.7-50.2</td>
<td>Mean*: 3.57 95% CI: 3.5-3.7</td>
</tr>
<tr>
<td>Class 3: Mental Health Conditions (n = 418)</td>
<td>Mean*: 5.82 95% CI: 5.4-6.3</td>
<td>Mean*: 6.22 95% CI: 5.8-6.7</td>
<td>Mean*: 5.15 95% CI: 4.7-5.6</td>
<td>Mean*: 43.23 95% CI: 42.7-43.8</td>
<td>Mean*: 43.74 95% CI: 43.2-44.3</td>
<td>Mean*: 2.98 95% CI: 2.9-3.1</td>
</tr>
<tr>
<td>Class 4: Physical and Mental Health Conditions (n = 329)</td>
<td>Mean*: 23.36 95% CI: 22.7-24.0</td>
<td>Mean*: 5.19 95% CI: 4.3-6.0</td>
<td>Mean*: 21.06 95% CI: 20.5-21.7</td>
<td>Mean*: 38.44 95% CI: 37.7-39.2</td>
<td>Mean*: 43.48 95% CI: 42.7-44.2</td>
<td>Mean*: 2.60 95% CI: 2.5-2.7</td>
</tr>
</tbody>
</table>

Note. *Estimated marginal means. All analyses controlled for age, race/ethnicity, gender and income.

Overall means: physically unhealthy days = 3.24 (SD = 7.49); mentally unhealthy days = 2.51 (SD = 6.23); activities limitation days = 2.22 (SD = 6.29); PROMIS physical health = 49.86 (SD = 8.29), PROMIS mental health = 49.47 (SD = 7.89), well-being score = 3.46 (SD = .914).
### Behavioral risk factors by latent class membership

<table>
<thead>
<tr>
<th></th>
<th>Total (N = 4,184)</th>
<th>Class 1: Healthy (n = 2321)</th>
<th>Class 2: Physical Health Conditions (n = 1072)</th>
<th>Class 3: Mental Health Conditions (n = 418)</th>
<th>Class 4: Physical and Mental Health Conditions (n = 329)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tobacco use</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nonsmoker</td>
<td>2308 (57.5%)</td>
<td>1464 (65.9%)</td>
<td>516 (48.1%)</td>
<td>212 (52.4%)</td>
<td>116 (36.7%)</td>
</tr>
<tr>
<td>Smoker</td>
<td>712 (17.7%)</td>
<td>359 (16.1%)</td>
<td>148 (13.9%)</td>
<td>137 (33.8%)</td>
<td>68 (21.6%)</td>
</tr>
<tr>
<td>Former smoker</td>
<td>994 (24.8%)</td>
<td>399 (18.0%)</td>
<td>408 (38.0%)</td>
<td>56 (13.7%)</td>
<td>131 (41.7%)</td>
</tr>
<tr>
<td>BMI</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Underweight BMI &lt; .18.4</td>
<td>67 (1.6%)</td>
<td>44 (1.9%)</td>
<td>16 (1.5%)</td>
<td>4 (0.9%)</td>
<td>3 (0.8%)</td>
</tr>
<tr>
<td>Normal weight BMI 18.5-24.9</td>
<td>1212 (29.0%)</td>
<td>787 (34.7%)</td>
<td>264 (24.2%)</td>
<td>116 (28.6%)</td>
<td>45 (14.1%)</td>
</tr>
<tr>
<td>Overweight BMI 25-29.9</td>
<td>1354 (32.4%)</td>
<td>758 (33.4%)</td>
<td>372 (34.1%)</td>
<td>125 (30.9%)</td>
<td>99 (31.1%)</td>
</tr>
<tr>
<td>Obese BMI &gt; 30</td>
<td>1448 (34.6%)</td>
<td>677 (29.9%)</td>
<td>438 (40.2%)</td>
<td>161 (39.7%)</td>
<td>172 (53.9%)</td>
</tr>
<tr>
<td>Leisure Time Aerobic Activity</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sedentary</td>
<td>670 (16.8%)</td>
<td>286 (12.8%)</td>
<td>226 (21.5%)</td>
<td>63 (15.7%)</td>
<td>95 (31.4%)</td>
</tr>
<tr>
<td>Low aerobic activity/below guidelines</td>
<td>1072 (26.8%)</td>
<td>542 (24.2%)</td>
<td>321 (30.5%)</td>
<td>108 (26.8%)</td>
<td>101 (33.1%)</td>
</tr>
<tr>
<td>Meets minimal aerobic guidelines</td>
<td>796 (19.9%)</td>
<td>485 (21.6%)</td>
<td>190 (18.1%)</td>
<td>79 (19.7%)</td>
<td>42 (14.0%)</td>
</tr>
<tr>
<td>Meets maximal aerobic guidelines</td>
<td>1463 (36.5%)</td>
<td>930 (41.4%)</td>
<td>315 (29.9%)</td>
<td>153 (37.8%)</td>
<td>65 (21.5%)</td>
</tr>
<tr>
<td>Strength Training</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low or None (0 or 1 time a week)</td>
<td>2257 (57.1%)</td>
<td>1209 (54.7%)</td>
<td>631 (61.1%)</td>
<td>214 (53.2%)</td>
<td>203 (67.1%)</td>
</tr>
<tr>
<td>Moderate (2 or more times a week)</td>
<td>1693 (42.9%)</td>
<td>1003 (43.2%)</td>
<td>402 (38.9%)</td>
<td>189 (46.8%)</td>
<td>99 (32.9%)</td>
</tr>
<tr>
<td>Combination Aerobic and Strength Training</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sedentary (No aerobic or strength training)</td>
<td>615 (16.0%)</td>
<td>262 (12.1%)</td>
<td>206 (20.7%)</td>
<td>59 (14.9%)</td>
<td>88 (30.5%)</td>
</tr>
<tr>
<td>Strength Training Only</td>
<td>1038 (27.0%)</td>
<td>530 (24.5%)</td>
<td>302 (30.3%)</td>
<td>107 (27.0%)</td>
<td>99 (34.3%)</td>
</tr>
<tr>
<td>Low aerobic Only</td>
<td>395 (10.2%)</td>
<td>230 (10.6%)</td>
<td>102 (10.2%)</td>
<td>43 (10.9%)</td>
<td>20 (6.8%)</td>
</tr>
<tr>
<td>Min/Max Aerobic w/o Strength Training</td>
<td>924 (24.0%)</td>
<td>587 (27.1%)</td>
<td>204 (20.5%)</td>
<td>79 (20.0%)</td>
<td>54 (18.6%)</td>
</tr>
<tr>
<td>Min/Max Aerobic with Strength Training</td>
<td>874 (22.7%)</td>
<td>556 (25.7%)</td>
<td>183 (18.3%)</td>
<td>107 (27.2%)</td>
<td>28 (9.7%)</td>
</tr>
</tbody>
</table>

Note: Sedentary = 0 minutes/week, low aerobic activity/below guidelines = 1-149 minutes, meets minimal aerobic guidelines = 150-299 minutes, or meets maximal aerobic guidelines = 300 or more minutes. Federal guidelines also recommend muscle strengthening activities on two or more days per week. Individuals meeting both aerobic and strength training criteria are included in the Min/Max Aerobic with Strength Training group.
Big Data and Large Samples: Some Cautionary Notes

• Tendency to overemphasize sample size in relationship to other aspects of study design

• Problems with data quality and sampling bias may be more prominent in big studies in which investigators are not involved in the original data collection

• Consider/evaluate/manage potential biases
  – Are variables being measured in different ways being transformed into a single variable (hypertension measured by BP reading vs. taking an antihypertensive on medication record vs. patient report)
  – If using claims data, is there missingness that is systematic, is there upcoding or under/over-use of specific diagnostic codes?
  – When outcome is reported by patients, is it a construct that they can report without prominent measurement error?

Big Data and Large Samples: Some Cautionary Notes

• Ascertainment biases that are operative, particularly when using health system encounter data
  – Event-drive visitation creates bias towards overestimation of illness/disability
  – Follow-up intervals may be event-driven and/or at time-varying intervals, but many of our analysis strategies use fixed-effects designed for assessment at defined intervals or random-effects models that assume follow-up is on a random time schedule

• Much of the variance in health outcomes is driven by behavioral, environmental and social factors yet these are rarely recorded, or their capture may be non-uniform
  – Results in a tendency to estimate determinates of health outcomes based on the variables included in the record

Big Data and Large Samples: Some Cautionary Notes

• Even in very large studies conclusions can be inaccurate because the most important variables are:
  – Not measured or not included in the analysis model
  – Measured with error or with measures that have low reliability and validity
  – Measured in different ways or at different times within data waves/data sources
  – Missing not at random

• Are the settings that provided the data representative of the group to whom you wish to generalize?

• Expect that the effect sizes for interventions will shift as populations become more heterogeneous and complex (ie. outside of a clinical trial)

• Consider multiple comparisons bias; sensitivity analysis can be helpful
Increasing sample size is not a remedy for basic model specification problems

- Begin analysis only after you have a well-developed data analytic plan and data dictionary
- Screen data for sample size drop-offs, missingness patterns, and heterogeneity in measurement timepoints or measures
- Are key determinants/contextual factors related to the health outcome of interest missing/not available?
- Consider the validity and reliability of measured variables and transformed, weighted, covariate-adjusted or composite variables
- Incorporate team members with experience analyzing the data resource, and who have specific technical expertise needed for particular analysis strategies, variable types or data structures (eg. multi-level, sample weights, matching, registries, claims)
Conclusions and Perspectives

• Big data offer an unprecedented opportunity
• Pose research questions that capitalize on the strengths of large datasets
  – Nationally representative
  – Powerful analytic strategies that require large samples (eg. CFA, mixture models, multi-level models)
  – Permit subgroup analysis and study of rare events
Conclusions and Perspectives

• Develop data analytic plans that manage risks:
  – Missing data and other aspects of data quality
  – Historical effects of changing treatments or patterns of care (could the data have a stale date?)
  – Mismatch: constructs of interest vs. those measured
  – Mismatch: informative time points of measurement vs. those captured
  – Important constructs/variables not measured
  – Constructs measured differently across time or between data sets
  – Sensitivity analyses to determine that analysis is robust to flaws/limitations
  – Incorporate STROBE recommendations (Vandenbroucke et al. (2014). Strengthening the Reporting of Observational Studies in Epidemiology [STROBE])
Big Data and Nursing: New Thinking, Training and Tools

- As a discipline, we need to be sure that we are well equipped to participate in or lead the teams that are assembling and analyzing these data resources
  - Mentoring, training, capacity-building
  - Funding to acquire data and to maintain data resources
  - Science policy expertise in consent models for big data, as well as data sharing, privacy, and stewardship
  - Navigating permissions/approvals for analytic plans and clearance review of resulting manuscripts
  - Challenges of working in interdisciplinary teams (leadership, credit, autonomy, differing skills sets and conceptual frames)
NIH Opportunities: Training and Funding

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Grants, Funding and Fellowships

Links to fellowships, grants, and other funding opportunities.

- Fellowships
- Funding Opportunities: Federal | Foundation | Other
- NIH HSR Funding Notices and Requests for Application
- Health Philanthropy

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Big Data and Oncology Nursing: New Thinking, Training and Tools

- Participate in governance of data resources
- Advance the dialogue with respect of constructs, standard data elements, and measures to be collected across datasets
- Measurement science to build the evidence base for development, testing, and improved interpretation of health outcome measures based on modern measurement theory, and which employ electronic data capture, computer adaptive testing, and conditional branching to increase efficiency and reduce patient burden
Big Data and Oncology Nursing: New Thinking, Training and Tools

• Develop methodologic skills to address the technical challenges of big data:
  – Missing data and missing variables
  – Between-measure interpretive ‘cross-walk’ or common metric
  – Propensity scoring, instrumental variables for matching
  – Weighted samples
  – Multilevel data structures
  – Longitudinal analysis
  – Integrative data analysis (simultaneous analysis of multiple datasets) Curran, Hussong 2009
  – Visual analytics
Citations and Selected Readings


Citations and Selected Readings


Roski, J. et al. (2015). Creating value in health care through big data: Opportunities and policy implications. Health Affairs; 1115-1122


Westra, BL et al. (2015). A national action plan for sharable and comparable nursing data to support practice and translational research for transforming health care. JAMIA; 1-8