Health Related Quality of Life and Health Status

Robert M. Kaplan
Stanford University
Dennis G. Fryback
University of Wisconsin (Retired)

Prepared for
State of the Science: Medical and Social Care Integration
Portland
February 4, 2019
Measuring Effectiveness

What is the meaning of life?
Tell me old wise one...
What is the meaning of life?
AH YESSS... THE MEANING OF LIFE...
LIFE, MY BOY, IS DOIN' STUFF!!
Life is "Doin' Stuff"??
...That's it???
...as opposed to death, which is NOT doin' stuff!!
...it's a more elementary theory than I had expected, but one you can't argue with!
Our Primary Goal: Improve Quality-Adjusted Life

Overall Goals of DHHS Healthy People 2000, 2010, 2020

• #1 Overall Objective for Health People 2000
  – To increase the span of healthy life (quality-adjusted life expectancy)

• #1 Overall Objective for Healthy People 2010
  – Increase the quality and years of life

• Healthy People 2020:
  4 overall goals, including
  – Promote quality of life, healthy development, and healthy behaviors across all life stages
New Mission of the American Heart Association

• To be a relentless force for a world of longer, healthier lives
  – Note: Does not mention heart disease
NIH: Steward of Medical and Behavioral Research for the Nation

“Science in pursuit of fundamental knowledge about the nature and behavior of living systems and the application of that knowledge to extend healthy life and reduce the burdens of illness and disability.”
What Methods Can Be Used to Measure Health?
40 years of making the same argument

- **Kaplan, Bush & Berry, 1976**
  - Argued that health outcome has just two major components
    - Length of life
    - Quality of life
  - Other physiological measures gain their validity through evidence of association with these two constructs
  - Demonstrated validity of general health measures

- **Kaplan & Bush (1982)**
  - Offered model for estimating the cost/effectiveness of health care using the using these methods and proposed cost/utility methods using QALY

- **Kaplan (1990)**
  - Behavior as the central outcome in health care
What Do Our Colleagues Prefer to Measure?

- Blood pressure
- Weight
- Glycosylated Hemoglobin
- Cortisol
- Avoid self report

- Information is meaningful if it comes from your veins
- Not from your mouth

Information is meaningful if it comes from your veins.
The Surrogate Marker Problem

USPSTF focuses on health outcomes rather than on intermediate markers
What is a surrogate endpoint?


- Examples of surrogate endpoints
  - Blood pressure
  - Serum Cholesterol
  - Blood glucose
  - HbA1C
  - Cortosol
  - FEV 1.0
  - FMRI
  - EEG
Median Glycated Hemoglobin Levels at Each Study Visit ACCORD Trial (NEJM, 358:2545-2559)

<table>
<thead>
<tr>
<th>Years</th>
<th>Intens</th>
<th>1</th>
<th>3</th>
<th>5</th>
<th>7</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>5109</td>
<td>3186</td>
<td>1744</td>
<td>455</td>
</tr>
<tr>
<td></td>
<td></td>
<td>5119</td>
<td>4768</td>
<td>4585</td>
<td>3165</td>
</tr>
</tbody>
</table>
Kaplan-Meier Curves for the Primary Outcome and Death from Any Cause ACCORD Trial (NEJM, 358:2545-2559)
**Meta Analysis of Glucose Lowering on CVD Mortality (Top) and All Cause Mortality (Bottom)**

### Cardiovascular Mortality

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Intervention</th>
<th>Control</th>
<th>Risk Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Events</td>
<td>Total</td>
<td>Weight</td>
</tr>
<tr>
<td>Chiasson, 2002*</td>
<td>1</td>
<td>682</td>
<td>0.50 [0.05, 5.53]</td>
</tr>
<tr>
<td></td>
<td>Events</td>
<td>Total</td>
<td>Weight</td>
</tr>
<tr>
<td>DPP, 2002*</td>
<td>1</td>
<td>1073</td>
<td>0.25 [0.03, 2.25]</td>
</tr>
<tr>
<td></td>
<td>Events</td>
<td>Total</td>
<td>Weight</td>
</tr>
<tr>
<td>DREAM, 2006*</td>
<td>12</td>
<td>2635</td>
<td>1.20 [0.52, 2.77]</td>
</tr>
<tr>
<td></td>
<td>Events</td>
<td>Total</td>
<td>Weight</td>
</tr>
<tr>
<td>NAVIGATOR, 2010</td>
<td>126</td>
<td>4645</td>
<td>1.07 [0.84, 1.37]</td>
</tr>
<tr>
<td></td>
<td>Events</td>
<td>Total</td>
<td>Weight</td>
</tr>
<tr>
<td>Ramachandran, 2009</td>
<td>2</td>
<td>204</td>
<td>4.98 [0.24, 103.00]</td>
</tr>
</tbody>
</table>

Total (95% CI) 9239 9266 100.0%

Total events 142 134

Heterogeneity: Tau² = 0.00; Chi² = 3.11, df = 4 (P = 0.54); I² = 0%

Test for overall effect: Z = 0.53 (P = 0.60)

### All Cause Mortality

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Intervention</th>
<th>Control</th>
<th>Risk Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Events</td>
<td>Total</td>
<td>Weight</td>
</tr>
<tr>
<td>Chiasson, 2002*</td>
<td>6</td>
<td>682</td>
<td>2.01 [0.51, 8.01]</td>
</tr>
<tr>
<td></td>
<td>Events</td>
<td>Total</td>
<td>Weight</td>
</tr>
<tr>
<td>DeFronzo, 2011</td>
<td>3</td>
<td>303</td>
<td>2.96 [0.31, 28.30]</td>
</tr>
<tr>
<td></td>
<td>Events</td>
<td>Total</td>
<td>Weight</td>
</tr>
<tr>
<td>DREAM, 2006*</td>
<td>30</td>
<td>2635</td>
<td>0.91 [0.56, 1.49]</td>
</tr>
<tr>
<td></td>
<td>Events</td>
<td>Total</td>
<td>Weight</td>
</tr>
<tr>
<td>Kawamori, 2009</td>
<td>6</td>
<td>897</td>
<td>12.77 [0.72, 226.31]</td>
</tr>
<tr>
<td></td>
<td>Events</td>
<td>Total</td>
<td>Weight</td>
</tr>
<tr>
<td>NAVIGATOR, 2010</td>
<td>310</td>
<td>4645</td>
<td>1.00 [0.86, 1.16]</td>
</tr>
<tr>
<td></td>
<td>Events</td>
<td>Total</td>
<td>Weight</td>
</tr>
<tr>
<td>Nijpels, 2008</td>
<td>1</td>
<td>60</td>
<td>0.32 [0.03, 3.01]</td>
</tr>
<tr>
<td></td>
<td>Events</td>
<td>Total</td>
<td>Weight</td>
</tr>
<tr>
<td>Ramachandran, 2006*</td>
<td>1</td>
<td>262</td>
<td>0.51 [0.05, 5.63]</td>
</tr>
<tr>
<td></td>
<td>Events</td>
<td>Total</td>
<td>Weight</td>
</tr>
<tr>
<td>Ramachandran, 2009</td>
<td>2</td>
<td>203</td>
<td>2.00 [0.18, 21.88]</td>
</tr>
</tbody>
</table>

Total (95% CI) 9687 9691 100.0%

Total events 359 355

Heterogeneity: Tau² = 0.00; Chi² = 6.66, df = 7 (P = 0.46); I² = 0%

Test for overall effect: Z = 0.04 (P = 0.97)
Measures of Health – a quick typology

• Mortality-based measures
  – death rates, life expectancies, etc.

• All the familiar stuff
Measures of Health – a quick typology

- **Mortality-based measures**
  - death rates, life expectancies, etc.

- **Morbidity-based measures**
  - indicators

- **Indicators:**
  - Single, countable things
    - TB rate
    - C-section rates
    - % population who exercise

- **Examples:**
  - Healthy People 2010 “Leading Indicators”
  - WHO “Core Health Indicators”
  - America’s Health Rankings
  - Wisconsin County Health Rankings
<table>
<thead>
<tr>
<th>Mobility</th>
<th>Physical Activity</th>
<th>Social Activity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Drove car and used bus or train</td>
<td>Walked without physical problems</td>
<td>Did work, school, or housework</td>
</tr>
<tr>
<td>without help (5)</td>
<td>(4)</td>
<td>and other activities (5)</td>
</tr>
<tr>
<td>Did not drive, or had help to use</td>
<td>Walked with physical limitations</td>
<td>Did work, school, or housework but</td>
</tr>
<tr>
<td>bus or train (4)</td>
<td>(3)</td>
<td>other activities limited (4)</td>
</tr>
<tr>
<td>In house (3)</td>
<td>Moved own wheelchair without help</td>
<td>Limited in amount or kind of work,</td>
</tr>
<tr>
<td>In hospital (2)</td>
<td>(2)</td>
<td>school, or housework (3)</td>
</tr>
<tr>
<td>In special care unit (1)</td>
<td>In bed or chair (1)</td>
<td>Performed self-care but not work,</td>
</tr>
<tr>
<td></td>
<td></td>
<td>school or housework (2)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Had help with self-care (1)</td>
</tr>
</tbody>
</table>
Measures of Health – a quick typology

- Mortality-based measures
  - death rates, life expectancies, etc.
- Morbidity-based measures
  - indicators
  - health status measures
    - disease-, organ-specific

Health Status Measures: point in time summaries of state of a person’s health

Disease-, organ-specific....

Created to be sensitive to changes in symptoms or functional impairment due to a particular disease process

Examples:
- Arthritis Impact Measurement System (AIMS)
- Vision Function Questionnaire (VFQ-25)
- McGill Pain Questionnaire
- NY Heart Association Classification

Some physician-reported, others patient-reported

*Many of these are scored by summing across questions in a questionnaire*
Measures of Health – a quick typology

- Mortality-based measures
  - death rates, life expectancies, etc.
- Morbidity-based measures
  - indicators
  - health status measures
    - disease-, organ-specific
    - “Generic” health status

**Generic Health Status Measures**

Most famous: SF-36 health profile

- One questionnaire with 36 questions
- Several questions about each of 8 different domains of health

**KEY:** multiple scales to cover broad scope of health, not tied to one disease or organ system

**Scoring:**

Psychometric scales based on summing responses to multiple questions

Separate scores for each subscale or health concept

- PF, RP, BP, GH, VT, SF, RE, MH
- PCS, MCS
Measures of Health – a quick typology

- Mortality-based measures
  - death rates, life expectancies, etc.
- Morbidity-based measures
  - indicators
  - health status measures
    - disease-, organ-specific
    - “generic”
  - health-related quality-of-life (HRQoL) indexes

HRQoL indexes

Like generic health status – try to comprehensively cover conceptual basis of health with multiple questions about health

Scoring

- not simple sums--these are not psychometric scales!
- econometric methods used to elicit utility weights (“preferences”) for health states
- 0 = dead, 1= perfect health
- average preference weights from community sample of people
Data Pyramid for Population Health (after Wolfson)

more aggregated = summarization, evaluation

HRQoL Indexes
preference-weighted aggregate scores summarizing overall health

Generic Health Status Profiles
Vector of health status domain scales

Disease-specific Scales
Do not necessarily cover all health domains

more disaggregate = explanation, description

Multitude of health indicators
Survival Analysis

• Alive 1.0
• Dead 0.0
Problem with Survival Analysis

• Tennis player 1.0
• Man in coma 1.0
The concept of a QALY

QALYs = 2x1 + 1.5x0.7 + 1x0.3 + 2.5x0.9 = 5.6

from Peter Neumann, Tufts Medical Center
US Norms for Six Generic Health-Related Quality-of-Life Indexes From the National Health Measurement Study

Dennis G. Fryback, PhD,* Nancy Cross Dunham, PhD,* Mari Palta, PhD,* Janel Hanmer, PhD,* Jennifer Buechner, AB,* Dasha Cherepanov, BS,* Shani A. Herrington, MS,* Ron D. Hays, PhD,†‡§ Robert M. Kaplan, PhD,‡ Theodore G. Ganiats, MD,¶ David Feeny, PhD,¶¶** and Paul Kind, MPhil††

**Background:** A number of indexes measuring self-reported generic health-related quality-of-life (HRQoL) using preference-weighted scoring are used widely in population surveys and clinical studies in the United States.

**Objective:** To obtain age-by-gender norms for older adults on 6 generic HRQoL indexes in a cross-sectional US population survey and compare age-related trends in HRQoL.

**Methods:** The EuroQol EQ-5D, Health Utilities Index Mark 2, Health Utilities Index Mark 3, SF-36v2™ (used to compute SF-6D), Quality of Well-being Scale self-administered form, and Health and Activities Limitations index were administered via telephone interview to each respondent in a national survey sample of 3844 noninstitutionalized adults age 35–89. Persons age 65–89 and telephone exchanges with high percentages of African Americans were oversampled. Age-by-gender means were computed using sampling and poststratification weights to adjust results to the US adult population.

**Results:** The 6 indexes exhibit similar patterns of age-related HRQoL by gender; however, means differ significantly across indexes. Females report slightly lower HRQoL than do males across all age groups. HRQoL seems somewhat higher for persons age 65–74 compared with people in the next younger age decade, as measured by all indexes.

**Conclusions:** Six HRQoL measures show similar but not identical trends in population norms for older US adults. Results reported here provide reference values for 6 self-reported HRQoL indexes.

**Key Words:** health-related quality-of-life, health status, EQ-5D, SF-6D, QWB-SA, SF-6D, Health Utilities Index, HUI2, HUI3, SF-36, population survey, adults, aging, patient-reported outcomes, health outcomes measures, comparative studies

(Med Care 2007;45: 1162–1170)
Data from the NHMS – population sample (n=3844) in US

Women

Men

The Health Measurement Research Group
www.healthmeasurement.org
NHMS: Relation between summary health and 6 HRQoL indexes

The Health Measurement Research Group
www.healthmeasurement.org
Summary

- Surrogate markers are not health outcomes. Sometimes they offer misleading guidance.
- Common metrics are needed to make comparisons between studies and between competing approaches to improve health outcomes
  - Prevention vs treatment
  - Investments in medical treatment vs social determinants
- Many generic measures appear to capture the same or very similar information
- We need more effort to identify standardized approaches to health status measurement
Released Today by Harvard University Press

Robert M. Kaplan

More Than Medicine

The Broken Promise of American Health
• EXTRA SLIDES
Examples of Symptom/Problem Complexes and Linear Weights to Adjust

<table>
<thead>
<tr>
<th>Symptom/Problem Complex</th>
<th>Adjustment</th>
</tr>
</thead>
<tbody>
<tr>
<td>19. Pain, stiffness, numbness, or discomfort of neck, hands, feet, arms, legs, or several joints.</td>
<td>- .034</td>
</tr>
<tr>
<td>20. One hand or arm missing, deformed (crooked), paralyzed (unable to move), or broken (includes wearing artificial limbs or braces).</td>
<td>- .061</td>
</tr>
<tr>
<td>27. Burn over large areas of face, body, arms or legs.</td>
<td>- .110</td>
</tr>
</tbody>
</table>
Evolution

• Items used in RAND Health Insurance Experiment
  – Evolved into SF-36/SF-12/VF-12
• Similar structure used for EQ-5D
• Provided basis for PROMIS