Using Patient-reported Outcomes Throughout the Product Lifecycle
Today’s presenter…

Gus Gardner  
Group President | Life Sciences

Gus’s experience spans operations, finance, mergers and acquisitions, IT, sales, and marketing. He is currently Group President within the Life Sciences segment at Optum where he leads the Patient Insights (Patient Reported Outcomes, electronic data capture technologies [EDC], and Medication Adherence Analytics) business unit, as well as the Epidemiology Group.

He joined Optum via acquisition of QualityMetric in 2010, a transaction he led for the QualityMetric founders and investors.
Agenda

1. PROs in context
2. PRO uses throughout the product life cycle
3. Questions
How do stakeholders define health?

REGULATORS
“…improvement in survival and how patients feel and function …”

~ FDA ~

PAYERS
“Societal, humanistic and/or economic burden.”

~ AMCP ~

POLICY-MAKERS
“a state of complete physical, mental, and social well-being not merely the absence of disease and infirmity”

~ WHO ~

“The best measure of quality is not how well or how frequently a medical service is given, but how closely the result approaches the fundamental objectives of prolonging life, relieving distress, restoring function and preventing disability.”

~ Paul Anthony Lembcke, MD, MPH ~
Healthcare reform drives demand for outcomes measures

Pay for performance

Accountable Care Organizations

Comparative Effectiveness Research

Patient-centered Medical Homes

Value-based Reimbursements
The SF Health Surveys

The most reliable, rigorously validated, and widely used health status measures in the world

The surveys measure eight health domains and offer summary scores for physical and mental health

A score of 50 is considered average health, and all scores are age, gender, and disease specific

The scores are standardized so that outcomes are comparable across groups, time frames, and populations
The SF Surveys are widely used in Research and published in peer reviewed journals...

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The product life cycle

- **Identify Markets**: What is the next big opportunity? Where are the patients?
- **Develop Evidence**: Is our drug safe, effective and economically viable?
- **Navigate Regulation**: Have all processes been followed? Are we prepared for contingencies?
- **Differentiate Products**: How do we establish value? What about pricing?
- **Realize Potential**: How do we reach consumers? Where do we focus marketing?

**Is our drug safe, effective and economically viable?**
Identify markets

Humanistic burden:

- PROs can be used to understand met and unmet needs in the market, allowing the client to develop products where the need and economic demand is greatest.
- Example: Six inflammatory conditions were investigated using the SF Health Surveys to identify targets for a new biologic therapy.
Identify markets

Humanistic burden of disease: Ankylosing Spondylitis

“Societal, humanistic and/or economic burden.”

Brkham, 2005
Bodur, 2010
Davis, 2005
Ertenli, 2010
Salaffi, 2009
Singh, 2009
Braun, 2007
Cho, 2013
Ozdemir, 2010
Ozgul, 2006
Machado, 2011
Morck, 2013
Ovayolu, 2010
Optum internal data
Develop evidence

PRO evidence strategy for regulators and payers:

1. Martin et al. Translation of health-related quality of life scores to projected annual health plan expenses utilizing data from a study of opioids in chronic non-cancer low back pain. Presented at the 4th Congress of the EFIC, Prague, 2–6 September 2003
Develop evidence

Standard metric:

- The SF tools are the most frequently used PROs in clinical trials according to a study published in “Contemporary Clinical Trials”
- According to the SF bibliography, they have been used 3,291 times since 1992
- PROs are used when accepted clinical endpoints are not available or reliable, e.g. antimigraine, antiinflammatory, asthma and allergy, and gastrointestinal agents.

“The SF-36 is the most frequently used PRO instrument in clinical trials today.”
Navigate Regulation:
Start with the end in mind: “feel and function”

Treatment Benefit

- Treatment benefit is demonstrated by evidence that the treatment has a positive impact on a concept of interest:
  - How long a patient lives
  - How a patient feels or functions in daily life
- Treatment benefit can be demonstrated as either:
  - A comparative advantage in how patients survive, feel or function
  - A comparative reduction in treatment-related toxicity
Types of Outcome Assessments

- Survival
- Biomarkers
  - A physiologic, pathologic, or anatomic characteristic that is objectively measured and evaluated as an indicator of some normal or abnormal biologic function, process or response to a therapeutic intervention
- Clinical outcome assessments (COAs)
  - Performance outcomes (PerfOs)
  - Clinician-reported outcomes (ClinROs)
  - Observer-reported outcomes (ObsROs)
  - Patient-reported outcomes (PROs)
FDA and Labeling

“Although the SF-36 is not an optimal assessment … it is a legacy measure of general health status that has been used across many rheumatologic conditions… Its prior acceptance and usage has provided an extensive experiential basis to support its comparative utility due to a long tradition of use as a general measure of health status … CDER made the decision that there was adequate justification to begin to again include SF-36 in RA labeling.” ~FDA: “SF-36 and RA Talking Points”

Disease-specific PROs are favored  BUT  Generic Scales are Making a Comeback
Navigate regulation: Xeljanz

“General health status was assessed by the Short Form health survey (SF-36). … patients receiving XELJANZ … demonstrated greater improvement from baseline compared to placebo in physical component summary (PCS), mental component summary (MCS) scores and in all 8 domains of the SF-36 at Month 3.” (XELJANZ Package Insert)
Differentiate products

Are PROs relevant to US Payers?

- PROs are relevant **outside of the US** in Payers’ access decisions, but US payers have traditionally not included PROs data in access decisions

**HOWEVER...**
- US payer perspectives may be **changing** along with the Affordable Care Act’s linking of payment to quality standards
- At the state and federal level
  1. National Quality Forum white paper on PRO performance measures
  2. NCQA’s PRO metric for implementation in EHRs
  3. Medicare’s “HOS” rating metric based on the SF-12 Health Survey metric
  4. Medicaid plans require reporting of PRO data

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2. aspe.hhs.gov/health/reports/2014/HealthCarePurchasing/rpt_vbp_summary.pdf
Differentiate products

Why would payers care about health status?

• Patient health status directly impacts utilization
  1. 1-point improvement on 100-point well-being scale reduces likelihood of hospitalization by 2.2% and ER visit by 1.7%\(^1\)
  2. Low well-being triples overall cost for a patient\(^1\)
  3. SF-12\(^\text{®}\) Health Survey results improve the prediction of subsequent medical expenditures.\(^2\)


2. Fleishman et al

3. SF=36 Manual
Differentiate products

Optum’s 2014 study of payers’ use of PRO evidence:

**Objective**: Identify U.S. payers’ current and future insights regarding the use of PRO* evidence in making patient access decisions for pharmaceuticals.

**Methods**: One hour, double blind telephone interviews

**Sample**: n=12: Commercial (Nat’l and Regional), ACO, VA, DOD, PBM, SEI, Actuary

* We define PROs *broadly* as a patient’s experience with a disease and its treatment.

Differentiate products

Payer perspective: Current and future use of PROs

10-point rating scales

- How relevant (now): 3.7
- How relevant (future): 6.3
- Would you like to see more (now): 6.1
- Would you like to see more (future): 6.6
- Should Pharma invest more (now): 5.6
- Should Pharma invest more (future): 6.3

Future = PROs used in quality assessment
Differentiate products

Know your audience:

There IS Payer Interest in PROs – But It Varies

- Department of Defense: 58
- Accountable Care Organization #1
- Actuary
- Veteran's Affairs
- Accountable Care Organization #2
- Pharmacy Benefit Manager (PBM)
- Commercial Payer - Regional / Local
- Commercial Payer - Regional / Local
- Self-Insured Employer
- Pharmacy Benefit Manager
- Commercial Payer - National
- Commercial Payer - National: 15

Current and Future Opinions (10-point scales):
- "How relevant"?
- "Would you like more"?
- "Should Pharma invest more"?

Expectations and Timing

- Payers expect functional status evidence in certain contexts
  - Physical functioning in Multiple Sclerosis, Rheumatoid Arthritis
- Coverage decisions based on Pivotal Trial results, Phase IV is too late
- Do the PRO results need to be on the label to be considered by payers?
  - No. It helps, but payers will consider all data from Phase III.
Realizing Potential: Foster engagement

- Embed smart PROs in consumer-facing programs
  - Branded or unbranded
  - Real-time feedback
  - Calls to action

Other examples
- Advate.com (Baxter)
- BTforAsthma.com (Boston Scientific)
Finding the target patients

- **Statin Myalgia Clinical Index**
  - Risk stratification and case-finding
  - Patient experience of statin-associated myalgia
  - Facilitate prescribing: use in prior authorization

### Statin Myalgia Clinical Index V3

**Instructions:**
- Use with patients who have had muscle symptoms that were new or increased after starting a statin regimen.
- A **statin regimen** includes any statin at any dose or frequency, including a statin the patient has used previously, at the same or a different dose.
- Muscle symptoms may include aches, cramps, heaviness, discomfort, weakness, or stiffness.
- Interpret overall score in light of other possible causes of the muscle symptoms, such as:
  - Recent physical exertion
  - Hypothyroidism
  - Changes in exercise patterns
  - Drug interaction with statin
  - Concurrent illness
  - Underlying muscle disease
- See reverse for Frequently Asked Questions.

#### How many statin regimens has the patient that involved new or increased muscle symptoms?

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<th>Two or more Complete the questions on the right side of this page.</th>
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#### Regarding this statin regimen:

- **A. Location and pattern of muscle symptoms**
  - If more than one category applies, record the highest number.
  - Symmetric, hip or thighs: 3
  - Symmetric, calves: 2
  - Symmetric, proximal upper extremity: 2
  - Asymmetric, intermittent, or not specific to any area: 1

- **B. Timing of muscle symptom onset in relation to starting statin regimen**
  - < 4 weeks: 3
  - 4 - 12 weeks: 2
  - > 12 weeks: 1

- **C. Timing of muscle symptom improvement after withdrawal of statin**
  - If patient is still taking statin, stop regimen and monitor symptoms.
  - < 2 weeks: 2
  - 2 - 4 weeks: 1
  - No improvement after 4 weeks: 0

#### Rechallenge the patient with a statin regimen, even if same statin compound or regimen as above then complete final questions:

- **D. Timing of recurrence of similar muscle symptoms in relation to starting second regimen**
  - < 4 weeks: 3
  - 4 - 12 weeks: 1
  - > 12 weeks or similar symptoms did not recur: 0

#### Total:

- All four scores above must be entered before totaling.

#### Interpretation:

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Clinically Meaningful Improvements in Physical Health-Related Quality of Life

Reduced levels of pain and improvements in the limitations of work due to pain.

Improvements in the ability to perform work or other daily activities.

Changes not observed in limitations to a range of minor and major physical activities.

Changes not observed in the views and expectations of overall health.

Overall improvement in physical functioning, well-being, general health, and/or energy level, based on Physical Component Score.

ADVATE [Antihemophilic Factor (Recombinant)] is the only recombinant factor VIII with physical health-related quality of life results for people with hemophilia A.

After 12 months of prophylactic treatment, physical health-related quality of life improved in patients, mainly due to clinically meaningful improvements in:

- The amount of pain experienced by a patient and how much pain interferes with normal work
- The impact physical health can have on performing work or other daily activities

Clinically meaningful changes were not seen in the physical health-related sub-categories of General Health and Physical Functioning and the mental health-related component score and sub-categories of Mental Health, Role Emotional, Social Functioning, and Vitality.

Based on a list of other drugs and biologics approved with health-related quality of life data in the labeling, as of January 2014.
The Take-Away

Patient centricity is here to stay:

• Our study\(^1\) found that:
  – Payers’ reliance on PRO data will increase in the next five years, focused on symptomatic conditions with few objective measures.
  – PRO evidence is valued as a predictor of clinical and economic outcomes
• Zagadailov et al.\(^2\) recommend that:
  – “… novel payer-industry-FDA collaborations may be necessary to heighten the relevance and importance of PROs.”
• What can we all do:
  – Sponsors should be ready with data that aligns with patient-centered initiatives of both FDA and payers
  – Instrument developers and sponsors educate payers and regulators about interpretation and meaning of PRO data
  – Broader interpretation of results from traditional PROs can enrich the value proposition without added burden/cost to trials

2. Zagadailov E, Duhig A, Denno M. The Current State of Patient-Reported Outcomes in Managed Care: Payer Perceptions of PROs and Other Measures of Benefit. Academy of Managed Care Pharmacy | October 8, 2014, Boston, MA