



**CENTER FOR
VALUE BASED
MEDICINE®**

**Pharmaceutical
Value Index®**

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Executive Summary

- The *Pharmaceutical Value Index*[®] is a groundbreaking, health economic instrument which objectively measures the: 1) *comparative effectiveness* and 2) *cost-effectiveness* associated with a drug or medical device.
- The *Pharmaceutical Value Index*[®] quantifies the *human value gain* (improvement in length-of-life and/or quality-of-life) conferred by any drug or device.
- The *Pharmaceutical Value Index*[®] uses a novel, societal cost perspective demonstrating the remarkable *financial value gain*, or return-on-investment, many drugs and devices accrue to society for the direct medical costs expended.
- The *Pharmaceutical Value Index*[®] is applicable for a drug or device which is: 1) under consideration for development, 2) under development in clinical trials, or 3) already in the marketplace.
- The *Pharmaceutical Value Index*[®] is directed by physicians with the clinical & business acumen to appreciate: 1) market need, 2) market pricing, 3) market penetration and 4) net present value (NPV) analysis.
- The *Pharmaceutical Value Index*[®] gives manufacturers a more effective tool to promote their drug/device to their most sophisticated markets: regulatory agencies, payers, and physicians who prescribe their products.
- The *Pharmaceutical Value Index*[®] quantifies the quality-of-life gain conferred by a drug or device using the *Quality-of-Life Utility Database*[®], a proprietary, validated, information system comprised of over 50,000 patient utility estimates.
- The *Pharmaceutical Value Index*[®] integrates the best, evidence-based medicine (EBM), clinical trial outcomes with patient quality-of-life data, thus establishing a more *accurate measure of the total patient benefit* conferred by a drug or device than possible with EBM data alone.

**Comments on the Value-Based Medicine® methodology utilized
in the *Pharmaceutical Value Index*®**

Thomas Scully, JD, Former Administrator, Centers for Medicare and Medicaid Services

“Drs. Brown visited with me at CMS in 2002. I liked their work then, and I like it now.”

“No matter the system of healthcare delivery, value-based medicine provides an extraordinary return on investment. In essence, it gives us an information system that identifies healthcare interventions of the highest quality for the most reasonable cost. By doing so, value-based medicine allows healthcare dollars to be directed to services that return the greatest value.”

From the Foreword of Brown MM, Brown GC & Sharma S. *Evidence-Based to Value-Based Medicine*, Chicago, American Medical Association Press, 2005.

Mark McClellan, MD, PhD, Former Administrator, Centers for Medicare and Medicaid Services

“I will do anything I can to make this go”

Referent to a Value-Based Medicine®, cost-utility, healthcare information system for clinical practice during a meeting at CMS with principals from the Center for Value-Based Medicine®, 1-05.

Carmen Puliafito, MD, MBA, Dean, University of Southern California School of Medicine

“The authors are to be congratulated for their path-breaking work.”

During a formal discussion of a Center for Value-Based Medicine paper®, AAO, 2000

Amit K. Ghosh, MD, on behalf of the American College of Physicians

“Value-based medicine fills a void in applying evidence-based medicine to patients.”

ACP Journal Club, 2006, Discussion of *Evidence-Based to Value-Based Medicine*, Chicago, AMA Press, 2005

RxPG

“Medical research and practice is currently evolving from evidence-based medicine to an even higher quality of patient care: value-based medicine.”

Review of *Evidence-Based to Value-Based Medicine*, which received the coveted ***** rating by RxPG, the Internet’s largest community website for medical students and physicians

ChiroCode

“This guidebook is to the nation’s current health care revolution like the Federalist Papers were to the American Revolution.”

DH Leavitt, ChiroCode Institute, 2009, review of the text, *Evidence-Based to Value-Based Medicine*

Current and/or former clients of Center for Value-Based Medicine[®] services include:

Allergan, Inc.

Emmes Corporation

Eye Research Institute

Genaera Pharmaceuticals

Genentech, Inc.

Lippincott, Wilkins and Williams

Merck, Inc.

National Eye Institute, National Institutes of Health

National Institute on Aging, National Institutes of Health

NeoVista, Inc.

Novartis

Pennsylvania Department of Public Assistance

Pfizer

US Cochrane Center, Cochrane Collaboration

Vision Care Ophthalmic Technologies, Inc.

List incomplete



CENTER FOR VALUE BASED MEDICINE[®]

Pharmaceutical Value Index[®]

A. Pharmacoeconomic Background

In 1980, the annual prescription drug expenditure in the U.S. was \$12 billion.¹ Projections for 2010 by actuaries at the Centers for Medicare and Medicaid Services (CMS) estimate an expenditure of \$291.5 billion.¹ In inflation-adjusted real dollars, the cost of prescription drugs per capita in 2010 has increased to approximately 3-4 times what it was in 1980.²

Critics emphasize rising pharmaceutical costs, but typically ignore the astonishing costs of drug development. Even more importantly, they fail to take into account the fact that drugs and devices greatly improve length-of-life and/or quality-of-life.

Detractors also uniformly fail to recognize that drugs and devices effect what the Center for Value-Based Medicine[®] refers to as “The Disregarded Dozen Costs” (Table), largely unrecognized costs which accrue a considerable financial return-on-investment (ROI) to society.

Table. The “Disregarded Dozen Costs”

Pharmaceuticals and medical devices save society money by:

- 1) making expensive, invasive interventions unnecessary**
- 2) increasing the incidence of patient employment**
- 3) increasing patient salaries**
- 4) decreasing depression costs**
- 5) decreasing injuries**
- 6) decreasing Skilled Nursing Facility (SNF) admissions,**
- 7) decreasing nursing home admissions**
- 8) decreasing other Medicare costs**
- 9) decreasing caregiver costs**
- 10) decreasing disability payments**
- 11) allowing patients to volunteer, and**
- 12) freeing up unpaid caregivers to pursue gainful employment**

The Pharmaceutical Value Index[®] addresses and integrates each of these financial parameters. The financial ROI referent to drug and device direct medical costs can be enormous.³

While not yet formal policy in the U.S., countries such as Canada, Great Britain, the Baltic States, Australia and others require an economic analysis, in addition to sound evidence-based data,^{4,5} before a new drug is added to a formulary or a medical device put into clinical practice. Recent federal legislation establishing the Patient-Centered Outcomes Research Institute makes it almost certain that economic analyses in the U.S. will also soon be required. *Thus, pharmaceutical and device companies should prepare for the economic analyses that will be required for new drugs and devices, as well as for those already on the market. Failing to do so could be very costly, depending upon who in the bureaucracy quantifies the comparative effectiveness and cost-effectiveness of their drugs and devices.*

Pharmaceutical Value Index[®] analyses are performed in user-friendly fashion by clinical physicians experienced in medical economic modeling. These analyses give pharmaceutical and device manufacturers a powerful information system and marketing tool to let stakeholders know the great human capital gains their products confer to patients, and the considerable financial capital gains they accrue for society.

Pharmaceutical companies should prepare for the economic analyses the Patient Centered Outcomes Research Institute will surely require for drugs and devices. Relying solely upon those performed by the bureaucracy could be very costly.

The *Pharmaceutical Value Index*[®] provides a standardized, validated information system, created by clinician researchers, to allow drug and device manufacturers to: 1) quantify the patient-perceived value conferred by their drugs or devices in user-friendly format, 2) strategically use the data in regard to pricing, and 3) utilize the information in marketing their

product(s) to stakeholders in healthcare, including physicians, other providers, patients, policymakers regulatory agencies, employers and insurers.

B. Value-Based Medicine[®] (VBM)

Evidence-based medicine is the practice of medicine based upon the highest level of scientific evidence available.^{4,5} Regrettably, evidence-based medicine generally focuses on one outcome and often ignores the quality-of-life parameters associated with an intervention.

Value-Based Medicine[®] (VBM) is the practice of medicine based upon the standardized *value* (improvement in length-of-life and/or quality-of-life) conferred by healthcare interventions.^{2,3,6} The term *value* does not imply cost, but rather the total *benefit* conferred by an intervention. Value-Based Medicine[®] incorporates patient *utilities* which objectively measure the quality-of-life associated with any health state and the improvement in quality-of-life conferred by a drug, device or other intervention.

Value-based medicine[®] integrates the best evidence-based medicine data (Level 1^{4,5} data derived from randomized clinical trials) with quality-of-life utilities obtained from patients to provide a more accurate representation of the overall benefit of a drug or device to a patient than possible with evidence-based data alone.² By assimilating quality-of-life improvement with evidence-based outcomes such as increased life expectancy, the patient *value gain* conferred by a drug can improve considerably compared to that demonstrable with evidence-based data alone. And when providers understand which interventions convey the greatest value, they can deliver the highest quality care.

Value-Based Medicine[®] data allow higher quality medical care than possible with evidence-based medicine data alone.

C. Utility Analysis

--A Measure of Quality-of-Life--

The improvement in length-of-life conferred by a healthcare intervention can generally be acquired from the evidence-based literature, but the improvement in quality-of-life is more difficult to measure. The quality-of-life associated with any health state can, however, be objectively measured using *utility analysis*.⁷⁻¹³

The variant of utility analysis incorporated in the *Pharmaceutical Value Index*[®] is the established time tradeoff method.^{2,6} The utilities themselves are derived from patients who have lived in a health state, since patients are best able to appreciate to what degree the diseases they live with on a daily basis diminish their quality-of-life.²

Patient utilities often differ substantially from those of experts, the community and other surrogate respondents.² The patient utilities used in the *Pharmaceutical Value Index*[®] are reproducible and validated across adult age strata, level of education, ethnicity, geographical borders, gender and income levels (see Validation References).² In essence, they are unaffected by each of these variables.

The utilities employed herein have been demonstrated to be similar in the U.S., Canada and Europe.^{2,8,14} It appears that utilities are innate to human nature.²

***Utility analysis* very effectively quantifies
the great improvement that drugs &
medical devices confer in *quality-of-life*.**

Utility value anchors. By convention, utilities vary from the anchors of 1.0 (perfect health permanently) to 0.0 (death).² The more desirable a health state, the closer its associated utility is to 1.00. Conversely, the poorer the

health state, the closer its associated utility is to 0.00. As examples, the utility associated with treated systemic arterial hypertension is 0.98, while that associated with a severe stroke is 0.34. If a severe stroke can be converted to a mild stroke by a drug, the utility improves from 0.34 to 0.84, a gain of 0.50, or a 147% improvement in quality-of-life.

Decision analysis. Decision analysis² combines all benefits and all adverse events associated with the use of a drug or device. The resultant utility associated with drug or device therapy can be compared to the utility outcome associated with no treatment or with another intervention.^{2,3}

**The *total value gain* conferred by drugs
and devices is a measure of their
comparative effectiveness.**

Total value. The *total value* gained conferred by an intervention, also known as the *comparative effectiveness*, is calculated by multiplying the (utility gain) x (duration of benefit in years) to yield an outcome measured in quality-adjusted life-years (QALYs) or percent value gain.² Thus, a drug or device which converts a severe stroke (utility of 0.34) to a mild stroke (utility of 0.84) for 10 years, confers a total value gain of (+0.50 x 10 =) **5.0 QALYs**. Length-of-life gains can also be integrated. If that same drug or device also adds another year of life, an additional (0.84 x 1 =) **0.84 QALY** is accrued, for a total of **5.84 QALYs**.

Quality-of-Life Utility Database[®]. The Center for Value-Based Medicine[®] database of over 50,000 validated patient utilities, the *Quality-of-Life Utility Database[®]* was created and assembled, under direction of the Center[®] principals, by more than 30 physician researchers at medical specialty offices and hospitals over a decade.

Designed specifically for use in pharmacoeconomic analyses, the *Database[®]* allows the best evidence-based data from pharmaceutical clinical trials to be converted to utility form. This reliable and validated database parallels the

general population of the United States and Canada in ethnic makeup, as well as educational and economic strata. *Currently, the majority of published cost-utility analyses use utilities from experts, researchers, physicians, caregivers, the general community and others, in large part because of the lack of access to patients, as well as the time-consuming and resource-consuming process of obtaining patient utilities.*

The Qualify-of-Life Utility Database[®] is a compendium of over 50,000 patient, quality-of-life estimates which are applicable across all medical specialties.

The database is singularly unique and integral to the *Pharmaceutical Value Index[®]*.² It allows consistency and reproducibility across all Value-Based Medicine[®] analyses performed at the Center for Value-Based Medicine[®]. If additional patient utilities are needed, the Center[®] has the capability of sending teams into the field to expeditiously acquire and collate these data.

D. Cost-Utility Analysis

Cost-utility analysis, also referred to by some researchers as cost-effectiveness analysis,⁹ is the healthcare economic instrument that correlates the value of a medical intervention with its incremental costs. Its unit of measure is the \$/QALY (cost expended per quality-adjusted life-year gained). The *Pharmaceutical Value Index[®]* uses cost-utility analysis, in conjunction with standardized inputs and outcomes, to assess a drug or device.

The *Pharmaceutical Value Index[®]* is comprised of the: 1) *comparative effectiveness (value gain)* and 2) *cost-effectiveness* of a drug or device.

Comparative effectiveness is measured in both: a) percent improvement in value and b) QALYs gained.

The *Index*[®] is unaffected by gender, age, ethnic, educational or socioeconomic strata. It employs population-based, health-related quality-of-life estimates that mirror a cross-section of the U.S. and Canadian populations. The *Index*[®] is applicable across North America and Europe.^{2,8,14}

Index[®] data are typically calculated for the *base case*, or average case, versus no treatment to allow a standardized comparison across all interventions. This helps to eliminate bias against age or any specific cohort. Incremental cost-utility analyses are also performed, when appropriate, to compare one intervention with another

The costs used in the *Index*[®] are the average, national Medicare reimbursements to acute hospitals, ambulatory surgical centers, providers and for durable goods.¹⁵ The Medicare Average Sales Price (ASP) is utilized for pharmaceutical costs.

**Pharmaceutical Value Index[®] analyses are performed
by physicians to maximize *translational medicine*
applications into the clinical arena.**

Most importantly, the *Pharmaceutical Value Index*[®] includes all benefits conferred by a drug or device, all associated adverse events, and all relevant costs, including those obviated by use of the intervention.

Cost-Effectiveness Standards

Standards for cost-utility analysis outcomes are not formally set by any agency in the U.S. at the current time. Nonetheless, most researchers in the U.S. consider interventions costing less than \$50,000/QALY to be very cost-effective, while those costing more than \$100,000/QALY are not considered to be cost-effective.¹⁶⁻¹⁹

In the United Kingdom, NICE (National Institute for Health and Clinical Excellence) has set standards and advises the National Health Service (NHS) as to which drugs, devices and other interventions are cost-effective and should or should not be used.²⁰ Interventions costing less than £20,000/QALY (~ U.S. \$31,700) are generally accepted as cost-effective, while those costing more than £30,000/QALY (~ U.S. \$47,500) are only accepted as cost-effective for increasingly strong reasons.

The World Health Organization (WHO) utilizes with the DALY (disability-adjusted life-year), an entity similar to the QALY in measuring quality-of-life gain or loss. WHO has suggested that interventions costing less than 1 x GDP per capita for a DALY (~ U.S. \$4700/QALY) are *very cost-effective*, while those costing less than 3 x GDP per capita for a DALY (~ U.S. \$141,000/QALY) are *cost-effective*.²¹

Cost-Utility Analysis Standardization

Twenty-eight million cost-utility variants. Researchers at the Center for Value-Based Medicine[®] estimate that the multiple utility instruments (time tradeoff, standard gamble, willingness-to-pay, multi-attribute, etc.), utility respondents (patients, experts, administrators, general community, physicians, nurses, caregivers etc.), costs (Medicare, Medicaid, commercial, blended, etc.), discount rates (0%, 3%, 5%, 10%), cost perspectives (third party insurer, societal, governmental, patient etc.), currency, year of analysis, and other features allow for 28 million possible cost-utility input variants. Unfortunately, even one can make a cost-utility analysis significantly dissimilar from others, thus explaining why the vast majority of cost-utility analyses in the literature are not comparable.

Value-Based Medicine[®] cost-utility analyses are standardized in that they utilize time tradeoff utilities, patient utility respondents, and average national Medicare costs (all insurers apply the Medicare Fee Schedule in some fashion). These analyses typically utilize the third party insurer and societal cost perspectives, but can assess others as well. Purposefully, the sensitivity analyses performed on variables with the greatest uncertainty allow an increased chance of valid comparability with other published, cost-utility analyses.

E. Drug & Device Manufacturer Benefits

Pharmaceutical companies and device manufacturers have long had difficulty demonstrating the considerable human value conferred and the striking financial value accrued by their products to stakeholders in healthcare. The *Pharmaceutical Value Index*[®] allows them to do just this.

Potential *Pharmaceutical Value Index*[®] (*Index*[®]) benefits are listed below:

Human Value Gain for a Drug or Device

- The *Index*[®] integrates the total human value gain, including quality-of-life improvement, conferred by drugs and devices.
- Unlike the vast majority of published cost-utility analyses, VBM analyses are comparable due to the standardization of utilities, utility respondents, costs, decision analyses, net present value (NPV) analyses and outcomes.
- The *Index*[®] provides drug and device manufacturers with an objective measure of their product's maximum, human value gain referent to other interventions.
- The *Index*[®] analyses are unique in that they are performed under the direction of clinical physician researchers who are expert in healthcare economic modeling and *translational analyses* into the clinical arena.
- The *Index*[®] utilizes the validated, proprietary *Quality-of-Life Utility Database*[©], which has supplied data to decide public policy and set healthcare standards for over 100 million people in the U.K., Canada and elsewhere.
- Among the principals and Senior Research Fellows, there are unmatched crossover experiences in clinical medicine, nursing, research, managed care, business, economics and healthcare public policy.

E. Manufacturer Benefits (cont.)

The Financial Return-on-Investment (ROI)

- The *Index*[®] allows drug and device companies to strategically use the information to maximize their internal ROI, justify their products' favorable pricing compared to other interventions, and demonstrate the sizeable financial return their products give back to society.
- The *Index*[®] identifies the heretofore typically unrealized, yet considerable, financial return-on-investment (ROI) which drugs and devices return to society.
- The *Index*[®] aids companies in determining the price their drug or device will support in the market and still remain *cost-effective*.
- The *Index*[®] incorporates expensive interventions and hospitalizations obviated by the use of a drug or device.
- The *Index*[®] takes into account public & private disability payments which drugs & devices save.
- The *Index*[®] integrates the increased incidence of employment and salary gains of patients made possible by drugs and devices.
- The *Index*[®] takes into account the fact that drugs and devices improve patient function to the point that unpaid caregivers (70% - 80% of all caregivers) are freed-up so they can enter the paid workforce.
- These cost savings can be readily demonstrated to all stakeholders in healthcare, especially governmental agencies, insurers, employers and others who allocate healthcare resources.

