

ASSESSING EMERGING TECHNOLOGY FROM A HEALTHCARE EXECUTIVE ECONOMICS PERSPECTIVE: A Case Study in New Technology for Osteoporosis

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ABSTRACT:

New medical technology is attributed as bearing a large responsibility for our ongoing rise in health care costs. They are one of the most nagging reasons for hospital expenses being driven up and profit margins dwindling away. The cost of health care, however, serves as motivation for healthcare executives to demand medical technology that not only enhances quality of care, but also lowers the costs of managing each patient's health condition. Healthcare executives have an opportunity to identify and extract substantial economic gains from new medical interventions and emerging technology. This article presents a case study in the use of evidenced-based management control of healthcare delivery costs relative to the adoption of new technology. It provides a model for hospital executive decisions to adopt and manage the costs, economic returns and quality of care implications relative to new medical technology. New technology for osteoporosis is used as the case study example.

Technology for the diagnosis and treatment of osteoporosis has received substantial attention for clinical research because the disease is growing at almost "epidemic" proportions worldwide.¹ It is a disease likewise creating a large economic burden on healthcare. The clinical and economic significance of osteoporosis rests with the fractures that arise as a consequence of the condition and their attendant morbidity. Thus if physicians can reliably identify fracture risk in patients early, clinical intervention can be commenced with the objective of reducing the risk and, by extension, the occurrence of fractures and its associated high costs. The reduction of costs does not come about entirely, however, as a result of early detection. Diagnostic accuracy, therapy effectiveness, and patient adherence to treatment management throughout the entire course of patient care also play a role according to published clinical findings.

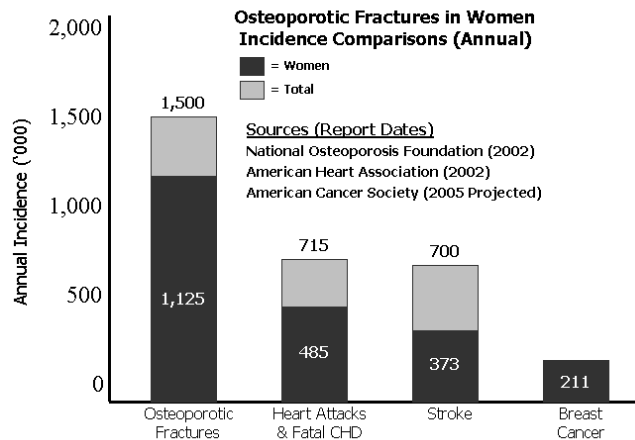
Our Study: We analyzed the cost effectiveness of biochemical bone markers, using a Technology Economic Impact model², relative to their clinically determined roles within standard patient screening, diagnosis, and treatment for osteoporosis. Bone marker cost effectiveness was analyzed relative to its identified capacity to influence the reduction of fractures and associated healthcare costs pertinent to the course of treatment and clinical outcomes. Specific points of evaluation covered their use for (1) the prediction of fracture risk, (2) patient diagnosis, (3) monitoring therapy efficacy, and (4) managing patient adherence to prescribed therapy. Healthcare resource consumption and costs used for this analysis were based upon a review of clinical studies published during the years 1995 – 2005 inclusive plus samples of regional hospital cost reports. From the review of published clinical studies, a report on a cohort of 668 postmenopausal women followed prospectively over nine years was selected for our analysis.³

Conclusion: The selected clinical study reported that of 115 (from a cohort of 668) postmenopausal women sustaining an osteoporotic fracture, 54 episodes occurred in women who had been identified as "normal" by a bone mineral density test (BMD) test. The addition of a biochemical marker test of bone resorption to bone mineral density (BMD) and clinical factor (prior frailty fracture) screening tests for fracture risk prediction – raising test sensitivity by 70% to 100% - enables the identification of the 54 women for fracture prevention therapy. Antiresorption agent therapy for the prevention and treatment of osteoporosis decreases turnover, increases bone density and reduces fracture risk by as much as 50% thereby developing the possibility that 21 of the 54 women may avoid having a fracture. The economic value of 21 avoided fractures was determined to be \$151,230 given conditions of 100% patient adherence to prescribed treatment. Patient adherence to medication has been shown to be about 50% throughout a period of twelve months, however, thereby reducing the savings potential added by bone markers to an estimated \$75,615. The deployment of bone markers for therapy monitoring and patient adherence management has been shown to reduce the rate of fracture occurrence by 16% thus increasing avoided costs to \$90,100 for the patient cohort (13 fractures avoided from the original 54 "non-osteoporotic" women). The prospective incremental economic implications of bone marker testing for fracture risk screening, monitoring for therapy efficacy and management of patient adherence may be significant for large patient populations. The application of these findings to the average annual occurrence of osteoporotic fractures in the United States infers a potential savings of \$225 million - \$300 million from a current \$15 - \$19 billion annually spent for direct healthcare expenses on osteoporosis (a 1%–2.5% reduction in costs) while improving clinical outcomes relative to the added capital and operating costs of intervening a new technology into an established patient management process.

Osteoporosis: Deployment of New Technology to Halt a “Fracture Epidemic”

Osteoporosis is defined by the National Institutes of Health Consensus Development Panel on Osteoporosis Prevention as a skeletal disorder characterized by compromised bone strength. This in turn predisposes a person to an increased risk of fracture.⁴ It is prevalent among women over the age of 50. Osteoporosis affects over 10 million individuals in the United States.⁵ Only 10% to 20% of persons within this demographic group are diagnosed and treated. An additional 34 million are afflicted with osteopenia.⁶ Every year about 1.5 million people in the U.S. suffer an osteoporotic-related fracture, which in turn leads to declines in health, both physically and mentally (Figure 1 displays the annual incidence of osteoporotic fractures relative to

Figure 1: Annual Incidence Comparison



heart failure, stroke and breast cancer occurrences). Twenty percent (20%) – 25% of persons who suffer a hip fracture die within one year. These numbers may double or triple by the year 2020 due the country’s aging population. About 600,000 individuals were diagnosed with

osteoporosis in 1990. In 2003, that number was 3.6 million. The number of patient visits to U.S. physicians (92% of osteoporosis visits occur in outpatient settings.) likewise increased five-fold from 1994 – 2003.⁷ Annual aggregate direct expenditures in the United States for these fractures range from about \$15 - \$19 billion in estimated 2004 dollars. Hip fractures are the most overwhelming type in terms of hospitalizations (about 300,000 per year) and direct healthcare costs. Of the above-mentioned aggregate direct expenditures, between \$8.5 billion and \$12.5 billion are attributed to hip fractures. Table 1 shows the

Table 1: Growth in patient Volume; Costs of Care

**OSTEOPOROSIS:
 Diagnoses & Patient Visits (1994 – 2004)**

	1994	2004
Patients (Millions)	0.5	3.7
Patient Visits (Millions)	1.3	6.4
Patient Age (%)		
≤ 39 Years	1.5%	0.8%
40 – 59 Years	19.7	19.3
60 – 64 Years	9.7	11.3
≥ 65 Years	70.8	68.6
Women (%)	91%	94%

Estimates: 2004	Hip	Spine	Forearm	Other
Hospitalizations	289,725	47,300	17,735	236,510
Direct Costs of Care	-	-	-	-
Range (Low)	\$8.5 BL -	\$0.75 BL -	\$0.38 BL -	\$3.8 BL -
Range (High)	\$12.5 BL	\$1.08 BL	\$0.56 BL	\$5.7 BL
Total Cost per Fracture	\$47,750	\$30,845	\$38,075	\$31,585
Aggregate Est. Lifetime Cost	\$82,500	\$54,525	\$67,775	\$56,225

Source: Randall S. Stafford, MD et al. "National Trends in Osteoporosis Visits and Osteoporosis Treatment, 1988 – 2003", *Archives of Internal Medicine* (2004); 164: pp. 1525 – 1530; Data extracted from the Diagnosis Reference File 1988 – 2003 of the National Disease and Therapeutic Index (NDTI), IMS Health; Data adjusted to 2004 estimates

most recent report of U.S. hospitalizations and direct costs per osteoporotic fracture.

Osteoporosis imposes a large economic burden in other countries as well. Sweden reports over 17,000 fractures per year and the costs to treat them exceed 300 million (U.S.) dollars annually. In Canada, approximately 1 in 4 women and 1 in 8 men have osteoporosis. 25% of the Canadian population will be over 65 years of age by 2041 and the incidence of this disease

is thereby expected to have risen sharply.⁸ In aggregate, more than 75 million persons are afflicted with osteoporosis in the United States, Europe and Japan and the resulting treatment and management costs are high.⁹

Included in these costs are the effects of sub-optimal screening and diagnostic testing, unproductive patient therapy monitoring, and poor patient adherence to medication therapy (defined as compliance with dosing regimen and instructions and persistency in staying the course through treatment completion). While current data suggest that not enough bone mineral density (BMD) tests are provided to patients within defined high-risk groups, at the same time BMD tests have been shown to possess very low sensitivity whereby about half of all osteoporotic fractures occur in women whose BMD test results were negative (low risk of fracture). Likewise the efficacy of treatment provided to high fracture-risk patients can not be measured for 24 months based upon the limitations inherent with BMD tests that capture a static measurement of bone quality rather than a derivative calculation of bone “turnover”: the rate at which the bone is either building up and breaking down. Finally, several studies have also assessed the high clinical and cost effects of poor patient compliance with prescribed dosing regimen and persistence with medication throughout the entire prescribed course of treatment. Lombas et al., for example, report that 50% of patients stop taking medication nine months after commencement of therapy. As a result, 16% of occurring osteoporotic fractures may have been avoided in their study if patients had adhered to their medication treatment and instructions. Of consequence to a society’s healthcare costs, lack of adherence and the resultant fractures add about 15% to direct medical expenditures.¹⁰

Biochemical Bone Markers as a Cost Effective Technology Innovation

Bone derived biochemical tests that have been extensively researched and tested over the past ten years provide clinicians with an index of the rate of bone remodeling. Identified “markers” reflect the rates at which our bones break down and build up. Bones are continuously remodeled in a process called “turnover” whereby old bone is removed and replaced by new bone. The breaking down of bones is referred to as “resorption”. The build up of bone is called “formation”. Resorption and formation occur throughout our skeletons at different locations and at varying rates.

Diagnosis of osteoporosis is based upon a measurement of bone skeletal mass, as assessed by calculations of bone mineral density (BMD). Current diagnostic technology such as single and dual X-ray absorptiometry (DXA) is used to assess mineral content of the skeleton and specific sites vulnerable to fracture. Bone mineral content is the amount of mineral in the skeletal site scanned. BMD is calculated by dividing the site’s mineral content by the area measured. The World Health Organization and the International Osteoporosis Foundation have defined four diagnostic categories of BMD: Normal, Low Bone Mass, Osteoporosis, and Severe Osteoporosis, classified in the form of a “*T score*” statistic.¹¹

Tests looking at specific blood and urine markers enable clinicians to determine the rates of turnover in a patient. Bone markers, because of their linkage to bone quantity and quality, have been determined to be valuable for assessing a patient’s risk in sustaining a future fracture, monitoring a patient’s response to osteoporosis therapy, and testing for patient adherence to treatment.¹² Several recent clinical studies have resulted in the determination that

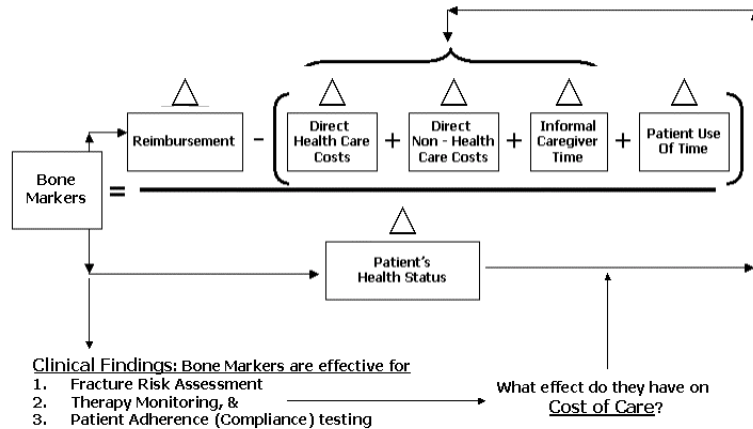
the addition of bone marker testing to BMD testing and physician assessment of various clinical factors (a combined patient assessment approach) substantially improves fracture prediction in postmenopausal women.

Based upon its reported clinical value, healthcare stakeholders considering the adoption of bone marker testing will benefit from knowing its economic efficacy in association with its impact on quality of care. To learn the prospective economic value of biochemical bone marker tests, we began our evaluation by establishing a *Technology Economic Impact* template (displayed in Figure 2) for assessing new diagnostic and therapeutic technology. This formula presents the financial value derived from a new technology relative to its clinical benefits. It enables a hospital executive to analyze the use of a new diagnostic test, device or therapy, which require the consumption of both direct healthcare resources (such as medical supplies and a pathologist’s or clinician’s time) and non-healthcare resources (such as transportation). The new technology may also require the use of caregiver time and time expended by the patient for treatment. The Δ symbol denotes that we are interested in determining the relative changes in resource consumption resulting from the intervention, compared with the resources consumed for existing or alternative processes.

The reimbursement received by the hospital is a reflection of the payer mix of net revenue secured in relation to costs of utilized resources. The numerator then portrays the change in net cash flow or operating income depending upon financial vehicles used to acquire the technology. For the purposes of this case study, derivation of the hospital’s mean cost of care relative to its reimbursement mix pertains to reimbursement minus direct hospital costs only.

The denominator – the patient’s health status – represents the change in clinical outcome based upon the technology’s use relative to results from current or alternative clinical

Figure 2: Blending Economic Efficacy with Clinical Impact
Are Bone Markers Cost Effective?



processes. While the avoidance of fractures is the primary patient objective, there may be a blend of objectives, including reductions in morbidity, mortality, length-of-stay, unnecessary referrals, hospital admissions and readmissions.

Another health status metric may be a patient’s quality-adjusted life years (QALY) remaining after the new technology intervention. The clinical outcome, in turn, affects subsequent healthcare costs. The arrows indicate this relationship.

This *Technology Economic Impact*

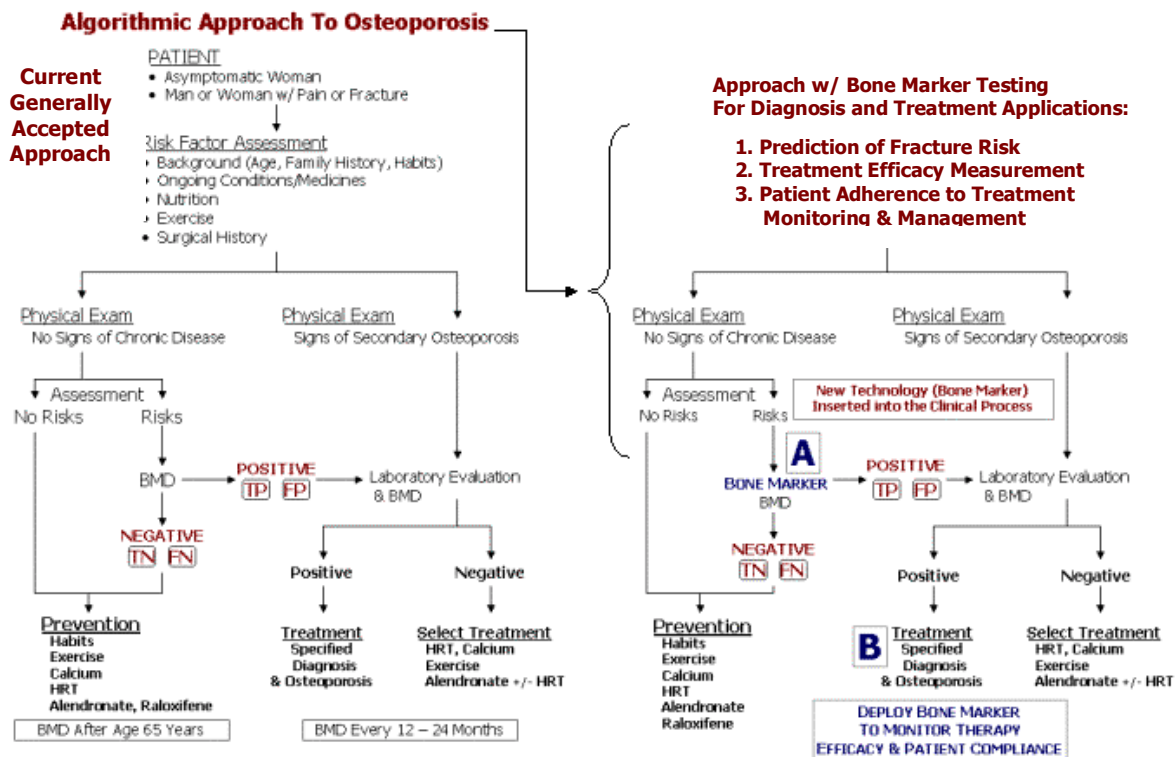
model can be used to evaluate four areas of bone marker clinical and economic impact: (1) Fracture risk assessment and prevention, (2) diagnosis, (3) calculation of treatment efficacy, and (4) patient adherence monitoring and management. Of the above four areas, studies over the past several years have established that bone markers are not clinically useful for diagnosis of osteoporosis, but they add value to bone mineral density testing for fracture risk assessment,

and they offer a superior means to monitor therapy efficacy and patient adherence to medication and instructions.

Determining The Economic Benefit of Biochemical Markers: Setting The Stage

Bone marker tests have specific “intervention locations” within a standard clinical approach to osteoporosis patient management. The following dual clinical algorithm (Figure 3) displays a patient management approach to osteoporosis. The left algorithm presents the generally accepted management process beginning with patient screening through therapy specific to clinical findings.¹³ The right algorithm reflects the insertion of bone marker technology into the process in accordance with recommended roles. In this algorithm, bone marker tests are deployed in concert with BMD (A) to determine the patient’s risk of sustaining an osteoporotic fracture. Secondly they are inserted as tools to monitor therapy efficacy and patient adherence to prescribed treatment (B). The designations “**POSITIVE**” and “**NEGATIVE**” indicate the results of fracture risk assessment tests. **TP** and **FP** under “**POSITIVE**” indicate that the findings may be True Positive as well as False Positive, reflections of the fact that BMD tests are not 100% accurate. Likewise for **TN** (“True Negative”) and **FN** (“False Negative”) under “**NEGATIVE**”.

Figure 3: Inserting Bone Markers Into Patient Management Protocol



Resource: South-Paul, Jeanette E., “Osteoporosis: Evaluation & Assessment”, *American Family Physician* (2001; 63: 5)

The optimal blended clinical and economic values of markers are derived when (1) fracture risk is accurately detected and managed early enough in the patient management process to prevent the fracture and the related occurrence of high individual and societal costs, (2) the

most effective treatment is determined via early testing, and (3) patients are effectively managed for their adherence to prescribed therapy.

In addition to bone markers, a number of clinical factors provide information on fracture risk. Several of these factors (such as age, a prior fragility fracture, family history, low bodyweight, patient use of glucocorticoid therapy, and cigarette smoking) offer information that is independent from that provided by a BMD test. The physician may opt to use any of these or other clinical factors in combination with biochemical markers and BMD to determine a patient's fracture risk. Clinical factors are considered by the physician at the beginning of the process and serve as a partial determinant of whether a bone mineral density test should be administered for diagnosis. Treatment intervention is prescribed if the BMD falls below a given standard deviation statistic (T-score) threshold.¹⁴

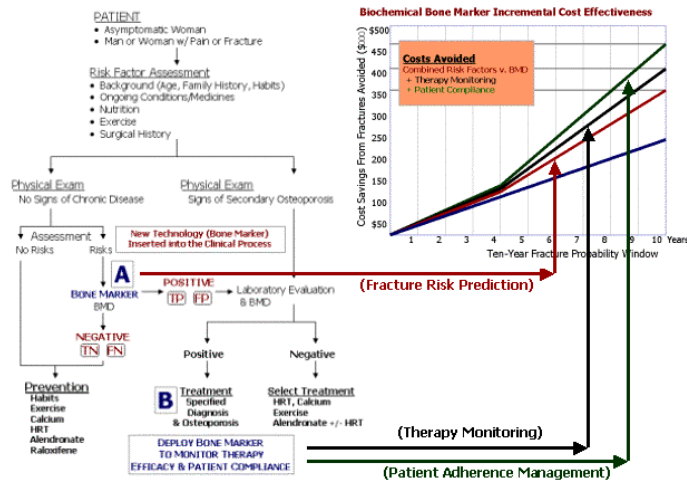
An economic rationale for use of bone marker technology may be initially explored from results of published clinical studies. We reviewed findings from 133 studies published during the years 1995 – 2005. Our selected studies were categorized in accordance with clinical guidelines for the use of bone turnover biochemical markers; patient screening, diagnosis and treatment of osteoporosis; fracture risk assessment; comparative efficacy analyses of biochemical bone markers with BMD tests; osteoporosis prevention and treatment; and patient management throughout therapy, including patient adherence to prescribed regimen.

A variety of studies conducted in the past five years have examined the performance of bone markers in the role of a prediction tool for patient fractures. The overall results are that they do predict fractures wherein the effectiveness of different markers varies depending upon fracture type.¹⁵ The general finding of these clinical studies has been that bone markers add predictive value to bone mineral density (BMD) tests for assessing a patient's future fracture risk. Additional studies examined bone marker contribution to treatment effectiveness assessments and the impact of varied patient adherence to prescribed therapy.¹⁶ From those studies we gleaned a clinical consensus that bone markers play three important roles in osteoporosis. These roles, respectively, have a measurable economic impact on patient care (Figure 4).

- 1) They are effective for prediction of fracture risk: When patients are evaluated for the risk of bone loss & fracture risk, the high consensus among the studies that we reviewed noted that increased bone resorption marker levels correlate strongly with bone loss. Conversely, the findings of studies on the relationship of bone formation markers and fracture were not as conclusive.¹⁷ The value inherent in this finding is that approximately 50% of osteoporotic fractures occur in individuals who are identified as non-osteoporotic (BMD > 2.5). Thus while BMD tests alone are not sufficient for the prediction of fractures, their use in concert with biochemical markers has been determined to enhance testing sensitivity and specificity.
- 2) Biochemical bone markers are effective tools for therapy monitoring. In particular, studies have shown that markers may be used as early as 3 months after the start of therapy for testing of a drug's effectiveness. This is considered an important clinical breakthrough because previously physicians had to wait for at least two years to assess the efficacy of a drug therapy when testing for a meaningful change in bone mass density alone. Further, the studies showed that gains in bone mineral density explain only a small proportion of fracture risk reduction.

3) Bone markers also display clinical value when used for adherence testing, i.e. testing to confirm that patients are both complying with prescribed therapy regimen and persistent in taking their medication throughout the entire course of therapy. Studies have shown that 50% of patients stop taking medication nine months after therapy. As a result, treatment is compromised and fracture risk potentially increases for these patients. The benefits of improving patient adherence are a significant decrease in fracture risk combined with a lowering of hospital costs.¹⁸

Figure 4: Evaluating The Economic Impact of Bone Markers



Calculating Bone Marker Cost Utility

Biochemical bone markers have been shown to have clinical usefulness. But are they cost effective? What incremental economic value does the use of biochemical bone marker testing create relative to their use for fracture risk evaluation, treatment efficacy assessment, and patient adherence management? What is their economic impact on fracture prevention?

The clinical and economic significance of osteoporosis rests with the fractures that arise as a consequence of the condition and their attendant morbidity and mortality. Thus if physicians can reliably identify fracture risk in patients early, clinical intervention can be commenced with the objective of reducing the risk and, by extension, the occurrence of fractures.

Clinical intervention for the prevention of fractures and care upon its occurrence encompasses the deployment of a wide array of healthcare resources. To understand the prospective economic value of bone marker technology, we need to understand what resources are deployed and their associated costs.

Table 2 displays the resources used and the respective costs of care at the individual patient level for hip failure. The template and thought process is from a 1997 prospective cohort study of 759 patients who sustained hip fractures, reported by a team from the University of Pennsylvania lead by Ada Brainsky MD.¹⁹ The University of Pennsylvania team’s cost analysis template covers five time periods of per patient/per month cost: 1) a six-month period preceding the patient’s fracture, 2) the time of hospital admission, 3) the first two months after patient discharge, 4) the four month period comprising the third through sixth months, and the six month period (months 7 – 12) after that. The team’s time window for analysis thereby encompassed 18 months. Cost figures were adjusted for patient mortality occurring during the 12-month period after fracture. Study findings compared patient healthcare resource

consumption among surviving patients in the six months preceding the fracture with resource consumption following the fracture.

While the team reported cost findings from 1995, the displayed resource and cost data are our estimates for the year 2004 reflecting additional published studies of osteoporotic fractures in various community settings and our analysis of sample southern California regional cost data in the summer of 2005.²⁰ The table showcases the variance in annualized patient management costs prior to and following the occurrence of an osteoporotic fracture.

While the higher utilization of resources after fracture were hardly a surprise, the University of Pennsylvania team was impressed with the variance in annualized costs. Findings from the variety of studies that we had examined indicated the aggregate cost of care over a 12-month time frame for patients sustaining a hip fracture fell within a range of \$44,250 and \$61,725 (adjusted to 2004 dollars; data is not shown). Overall lifetime costs attributable to a hip fracture could be greater than \$85,000.²¹ Our 2004 cost estimates, displayed in Table 2 following in accordance with the Brainsky team's calculation process, were that the twelve-month mean per-patient cost of care following a fracture was \$47,650 compared with \$23,155 before the fracture occurred, a difference of \$24,495. Therefore, an economic justification for improved fracture risk prediction and event avoidance was established.

Table 3 displays our comparable estimates for the direct healthcare costs of hip, spine (vertebral), forearm and all other fracture types. Overall, when we took into account all fractures (that is, hip, spine, forearm and all other types), our estimated weighted average per fracture cost is \$35,765 (comprising the first twelve months of treatment) with an estimated average lifetime cost of \$60,000. Our weighted average pre-fracture annualized cost was determined to be \$16,865. We used these weighted average numbers for our economic impact analysis.

To validate the reasonableness of these costs, we examined billing report samples from hospitals located in San Diego and Los Angeles, California. The samples contained between 25 to 50 patient episode-specific costs covering a 24-month period, 12 months preceding the fracture and twelve months following the incidence (all names and other proprietary

Table 2: Healthcare Resource Consumption (Hip Failure)

Service	Before Fracture	Months After Fracture		
		0 - 2	3 - 6	7 - 12
Hospital (Days)	0.47	1.15	0.57	0.56
Nursing Home (Days)	0.04	7.20	1.10	0.20
Rehabilitation Center (Days)	NM	1.40	0.10	0.01
Informal Care (Hours)	292.80	326.70	294.00	273.40
Formal Assistance (Hours)	26.00	54.40	23.70	40.70

Estimated for Year 2004	Pre-Fracture 6 Months	(\$/Month/Patient)		
		0 - 2	3 - 6	7 - 12
Hospital Admissions	\$319	\$854	\$415	\$375
Nursing Home Stays	8	909	171	30
Rehabilitation	5	789	63	4
Physician Visits	30	75	54	36
Nurse Home Visits	6	29	19	6
Nurse Aid Visits	6	30	19	5
Physical Therapy	10	46	26	8
Equipment	14	79	60	38
Meal Service	5	5	6	5
Home Aid Services	166	331	225	175
Transportation	21	30	24	18
Informal Care	1,555	1,656	1,490	1,234
Miscellaneous Support & Services	35	99	73	30
TOTAL PER MONTH	\$2,180	\$4,931	\$2,644	\$1,963
Survival in the Period	1.00	0.95	0.91	0.85

12-Month Cost of Care After Fracture: \$47,650

Annualized Cost Of Care Prior to Fracture: \$23,155

Variance: \$24,495

Resource: Ada Brainsky, MD et al., "The Economic Costs of Hip Fractures in Community Dwelling Older Adults: A Prospective Study", *Journal of The American Geriatrics Society* (1997: 45: 281-287); Numbers have been adjusted to 2004 estimates.

information were protected). From this data we developed an understanding of the resources deployed throughout the patient's course of care during this period of time. In aggregate we studied 225 cases. While not statistically derived samples, we consider the information derived as a fair representation. Published study costs were estimated to 2004 levels via consumer price indices and Medicare annual reimbursement adjustments.

Table 3: Mean Estimated Direct Healthcare Costs Per Fracture Type

<u>Estimates: 2004</u>	<u>Hip</u>	<u>Spine</u>	<u>Forearm</u>	<u>Other</u>
Hospitalizations	289,725	47,300	17,735	236,510
Direct Costs of Care	-	-	-	-
Range (Low)	\$8.5 BL -	\$0.75 BL -	\$0.38 BL -	\$3.8 BL -
Range (High)	\$12.5 BL	\$1.08 BL	\$0.56 BL	\$5.7 BL
Cost per Fracture	\$47,650	\$22,835	\$31,575	\$24,100
Lifetime Cost	\$85,000	\$33,755	\$46,675	\$35,625

Sources: Randall S. Stafford, MD et al. "National Trends in Osteoporosis Visits and Osteoporosis Treatment, 1988 - 2003", *Archives of Internal Medicine* (2004; 164: pp. 1525 - 1530); 2004 Surgeon General Report
Data adjusted to 2004 estimates

Studies over the past ten years have been generally in agreement and consistent in terms of osteoporotic fracture treatment resources utilized and reporting of costs per episode over fixed periods of time. Hospital costs are based upon room and board, nursing care, laboratory

services, medications and other supplies. Physician services encompass surgery, medical management, physical therapy, radiology and anesthesia. Outpatient care services for discharged patients comprise skilled nursing (SNF) and intermediate care facilities (ICF) about 98% of the time.

Clinical Intervention

An average fracture cost of \$35,765 (with a lifetime cost of \$60,000) served as a baseline for measuring the economic value of a healthcare system's planned clinical outcome: the avoidance of osteoporotic fractures and their associated direct healthcare costs. "Avoided costs" are managed by a hospital system-wide clinical intervention decision policy. Intervention comprises screening, diagnosis, osteoporotic fracture risk management, and fracture treatment. Healthcare decision makers develop a clinical intervention "case finding strategy" - which includes decision guidelines regarding which members of the patient population to screen and treat based upon clinical risk factors - in order to reduce the occurrence of osteoporotic fractures and maintain disease management costs at defined optimal levels. To that end, the International Osteoporosis Foundation and World Health Organization recommend that fracture risk be expressed as an "absolute risk" or probability over ten years.

Osteoporotic Fracture Risk Factors

- Age
- Previous Fragility Fracture
- Glucocorticoid Therapy
- High Bone Turnover
- Low Bodyweight
- Cigarette Smoking
- Poor Visual Acuity*
- Neuromuscular Disorders*

The above factors provide indications of fracture risk over and above that gained bone mineral density (BMD) tests.

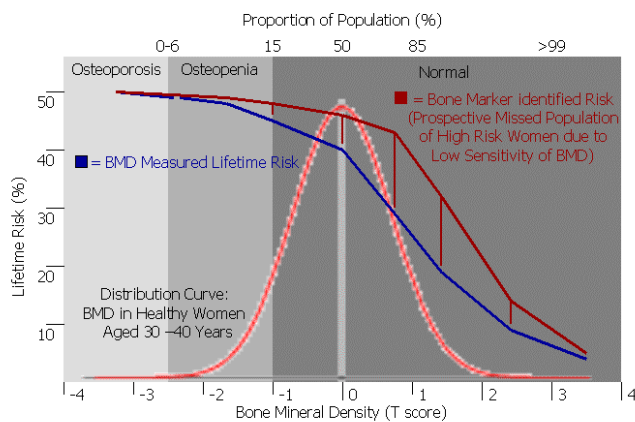
* Increases the patient's propensity to fall

Hip fractures present the greatest morbidity and economic consequences whereby when considered alone, a ten-year fracture occurrence probability of 10% or more may provide a cost effective threshold. When considering the prospective incidence of other fracture types, however, another thresholds may be feasible. So a healthcare system's "case finding strategy"

will be based upon the calculation of a patient's 10-year probability of sustaining a fracture. Determination of risk depends upon a blend of factors influencing the clinician's decision. There is no universal currently accepted policy for screening to identify individuals at a high risk of fracture threshold. Screening may comprise the consideration of age combined with a set of clinical factors as a starting point followed by BMD for diagnosis. For example, a physician may decide to select for treatment 10% of a population of women at highest risk at menopause whereby BMD is administered for confirmation.

The use of BMD however, has been shown to possess acceptable" specificity but low sensitivity.²² This means that about half of all osteoporotic fractures will occur in the women

Figure 5: Measured Lifetime Risk of Fracture (Women, 50+ Years)



Adapted from: J. A. Kanis, "Diagnosis of Osteoporosis and Assessment of Fracture Risk" (*Lancet* 2002; 359: pp. 1929-1936); Kanis et al. "Ten-Year Risk of Osteoporotic Fracture and the Effect of Risk Factors on Screening Strategies" (*Bone* 2002; 30(1): 251-8

whose BMD measurement was normal (Figure 5). The incidence of these fractures is costly, not just in terms of economics, but in terms of patient morbidity (quality of life; daily living "disutility"). To improve the system wide economic impact and clinical outcome blend, another intervention decision policy founded upon a combination of bone marker, clinical factors, and BMD tests was determined to be more effective, identifying the proportion of the patients population at risk of fracture that a BMD test could not discern alone. This combination of tests thus enhances a healthcare system's case finding strategy.²³ An example of this is noted by John Kanis, citing a study showing the independent contributions of urinary bone markers and BMD on identification of fracture risk in elderly women with a mean age of 81 years. Figure 5 displays the incremental value in risk determination and case finding through the use of bone markers and clinical risk factors independently of BMD whereby the identified 10-year risk of fracture rises from 15% to 33% on the basis of urinary markers and to 49% when using a combination of BMD and markers.²⁴

The Economic Value of Fracture Risk Prediction Using Bone Marker Technology

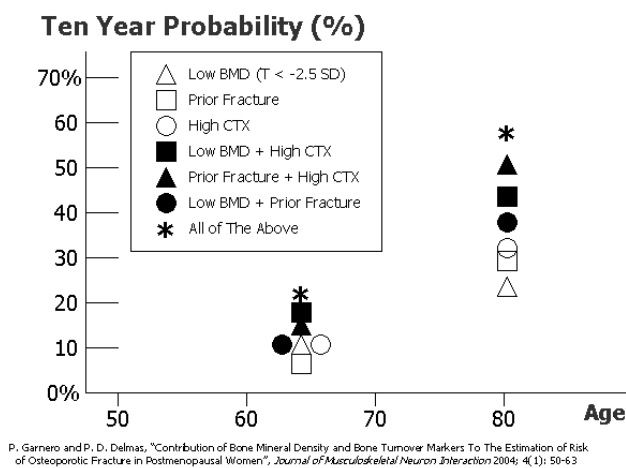
A case in point comes from data derived from a study published in 2004 by Patrick Garnero and Pierre D. Delmas of a patient population (known as the OFELY study) consisting of 668 healthy postmenopausal women.²⁵ This group of women was followed prospectively for nine years wherein a variety of test techniques and blends were studied for their fracture predictive values. Part of the study compared the incidence of fracture among the population relative to the risk identified by a BMD, a history of a previous fracture, and use of the urinary CTX (carboxy-terminal peptide of collagen I) bone marker. It was discovered that a risk factor combination of a high bone resorption marker with a history of fracture provided a predictive value equivalent to that obtained with BMD.²⁶ It was further found that a blend of tests comprising a combination of a urinary resorption marker (CTX) with BMD or a history of previous fracture resulted in a ten-year probability of hip fracture that ranged between 70% and 100% higher than what was derived from BMD alone. Figure 6 displays the findings of Garnero and Delmas for patient cohorts aged 65 years and 80 years respectively, wherein in

both age groups, the diagnostic accuracy of a urinary bone marker test exceeded that of BMD and a combination test strategy was the most clinically effective in determining the ten year probability of a fracture event.

Sensitivity to fracture risk is markedly increased when resorption markers are used to support BMD and the clinical risk factor of a previous fracture. Healthcare system executives are not, however, simply seeking to increase the hospital's capacity to detect as many at-risk patients as possible and avoid false negatives. It is also necessary to fortify the specificity of the defined

Figure 6: Prediction of Risk at ages 65 and 80

Combination of Clinical Risk Factors, BMD and Bone Turnover Measurements



women as high risk, but a test combination of bone marker and clinical history did. Prospective economic implications may thereby be derived from a hypothetical scenario wherein these 54 patients, with fracture risk predicted, undergo clinical intervention with the objective of fracture avoidance (Figure 7).

Our analysis assumed that the mean annualized cost per average fracture avoided was \$35,765 over a five-year period and \$60,000 over ten years of treatment. We assumed annual fracture prevention treatment costs at \$1,500. We compared these costs with a weighted pre-fracture per patient management costs of \$16,865. Since cost savings from fractures avoided occur later than the clinical intervention, we inserted a discount rate (thereby taking into account the time value of money).

Varying the rate used for discounting (we used 7.5%) will impact cost effectiveness as will the initial cost of clinical intervention. Treatment duration would also have an impact on cost effectiveness such that a longer time period for treatment will have an impact on efficacy (a lowered risk of fracture occurrence) as will differences in annual treatment costs. With regard to clinical intervention costs, we determined that screening and diagnosis costs (including BMD and marker testing) are sunk costs. We did not treat these costs as a part of clinical intervention for treatment. Costs included in treatment include the drug, physician follow-up visit, and treatment efficacy measurements. Since we are concentrating on direct healthcare

battery of tests in order to attain optimal cost effectiveness. The added prediction value of a urinary bone marker was identified to be between 15% and 20%.²⁷ The combined diagnostic approach of a resorption marker with BMD and pertinent history such as the prior fracture was found to increase specificity by about 40%.²⁸ With this information we can now revisit the cost utility of fracture avoidance to reach a general understanding of prospective healthcare system economic implications.

The Garnero and Delmas study of the 668 postmenopausal women cohort found that of 115 incident fractures, 54 (47%) had occurred in women identified as being non-osteoporotic. BMD alone had not picked these

system economics, the patient’s personal costs of expended time, travel costs, and related expenses are not included. Finally, we took into account an assumption of patient mortality occurrence throughout the ten years of analysis (12% in the first year and progressing to an aggregate 48% in the tenth year).

Antiresorption agent therapy for the prevention and treatment of osteoporosis decreases turnover, increases bone density and reduces fracture risk by as much as 50%.²⁹ Thus there is an opportunity for avoidance of fracture within the group of 54 women who had sustained a fracture. Given the finding by Johnell et al. and discussed by Garnero and Delmas wherein the combined diagnostic approach of a resorption marker with BMD (and pertinent history such as the prior fracture) was found to increase specificity by about 40%, approximately 20 – 25 of the above 54 may be identified as risk bearing, referred for treatment. A 50% prospective efficacy rate means that fracture risk may be reduced in 10 to 12 women. A patient treatment and management cost savings opportunity of \$151,230 (range of \$140,675 - \$175,850) is thus derived.

Figure 7: Prospective Cost Effectiveness Opportunity – “Non-Osteoporotic” Women Identified

Age	65
Cohort Population	668
Incident Fractures	115
Non-Osteoporotic Fractures	21.5
Reduction in Fracture Rate	50% 11

Sunk Cost Healthcare Expenditures	\$16,865
Clinical Intervention	\$1,500
Avoided Fracture Cost (per Episode)	\$35,765
Lifetime Fracture Cost Avoided	\$60,000

	Year 1	Year 2	Year 3	Year 4	Year 5	Year 6	Year 7	Year 8	Year 9	Year 10
Operating Cash Flow:										
Clinical Intervention	\$32,250	\$30,000	\$27,907	\$25,960	\$24,149					
"Sunk Cost"	0	0	0	0	0					
Avoided Fracture Costs	40,635	37,800	35,163	32,710	30,428					
Lifetime Costs Avoided		24,235	22,544	20,971	19,508	18,147	16,881	15,703	14,608	13,589

	0.0	1.0	2.0	3.0	4.0	5.0	6.0	7.0	8.0	9.0
Present value analysis:										
Year conversion factor	0.0	1.0	2.0	3.0	4.0	5.0	6.0	7.0	8.0	9.0
Discount factor	7.5%	1.000	0.930	0.865	0.805	0.749	0.697	0.648	0.603	0.561
Discounted operating cash flow		8,385	32,035	29,800	27,721	25,787	18,147	16,881	15,703	14,608
Mortality Adjustment	1.00	0.88	0.84	0.79	0.75	0.70	0.66	0.61	0.57	0.52
Net Impact		\$8,385	\$28,191	\$24,883	\$21,900	\$19,211	\$12,703	\$11,057	\$9,579	\$8,253

NET COST SAVINGS = \$151,230

Discussion: Avoided fracture costs pertain to years 1 through 5 wherein \$35,765 is spread through this period and discounted. Lifetime costs are taken into account for the next ten years, avoided because the fracture had not occurred thereby precluding ensuing long-term patient management.

This opportunity, however, assumes that the patients receiving treatment adhere with medical advice and therapy completely and persist with taking prescribed medication. Long-term adherence and persistence with therapy is typically poor. Less than 50% of patients take their medication and stick with their prescribed therapy throughout its prescribed course. As a result, the prospective costs savings of \$151,230 may more realistically be about \$75,615 assuming a 50% patient adherence rate under normal circumstances. To improve the effectiveness of prescribed treatment, patient monitoring must be implemented to increase and sustain patient adherence.

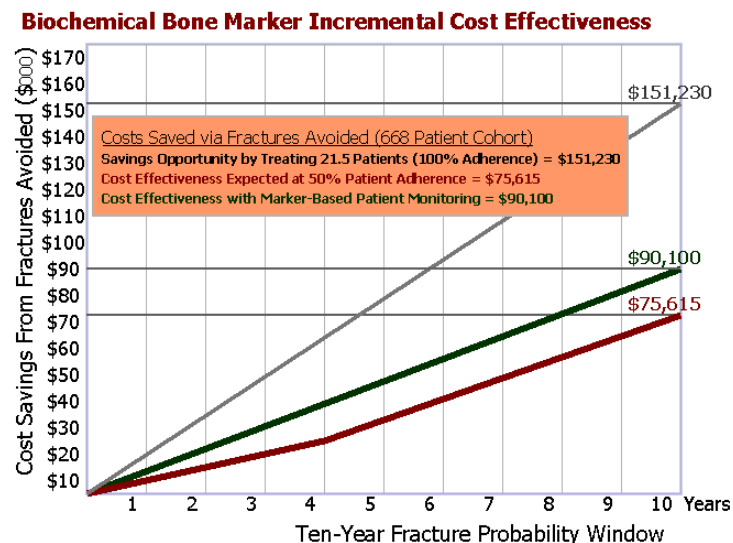
The Economic Value of Markers for Therapy Monitoring & Patient Management

Clinical trials comparing patient therapy with oral bisphosphonates (a first line of treatment for managing osteoporosis in postmenopausal women) and a placebo confirmed that long term treatment is necessary for the achievement of optimal and sustained therapeutic benefits.³⁰ Nevertheless there is documented evidence that a large number of patients are not able to adhere adequately on a long-term basis to treatment regimen.³¹ An open-label, observational, clinic based study investigating patient persistence in taking the medication determined that the probability of persistence dropped to 65% within three months, 60% within six months, down to 49% at twelve months and 30% in 24 months. These findings were supported by other studies. As a result sub-optimal adherence (persistence and compliance) and the means to improve it has been investigated for effect on therapeutic outcomes.³²

Patient adherence is defined as the extent of compliance with medical advice and dosing regimen. Measures of compliance include the percentage of prescribed medication actually taken. Persistence is described as the length of time that patients continue to take their medication and defined as the time from treatment initiation to treatment completion or discontinuation.³³ To maintain adherence at high levels, the efficacy of patient monitoring has been studied whereby healthcare professionals with the support of a functional or biological test pay close attention to treatment results and patient behavior. This protocol has been shown to be effective. Jaime Caro et al. indicate that patient adherence to therapy produces a fracture rate reduction within their study cohort of about 16%.³⁴ Clowes et al. determined that patient monitoring increased adherence to therapy by 57% compared with no monitoring.³⁵ Their study examined whether patient monitoring by nursing staff enhanced adherence and persistence with therapy. They further examined whether the effects of presenting patients with information on their response to therapy provided additional benefit. Treatment efficacy was calculated relative to the impact of monitoring versus no monitoring undertaken at all. Seventy -five postmenopausal women with osteopenia were randomly placed into three groups for comparison: (1) No Monitoring, (2) Nurse-Monitoring, and (3) Marker Monitoring. The nurse monitored group received periodic reviews via a predetermined protocol. The marker-monitored group was presented a graph that displayed their response to therapy using a urinary bone resorption marker.

The use of bone resorption marker versus BMD for therapy monitoring is relevant because BMD evaluations occur at two years due to their “static” measurement of bone density at a moment of time. Bone markers may alternatively be deployed for monitoring within three months of treatment inception. Common sense suggests that this variance in timing may have a positive cost impact when

Figure 8: Prospective Bone Marker Economic Efficacy



ineffective therapy or poor patient adherence with therapy is identified early resulting in measures influencing a behavior change. With markers clinicians are able to monitor within three months to six months their patient's response to medication and thus gain feedback regarding its benefits.

Clowes et al. determined that patient adherence within the nurse-monitored group and the marker-monitored group was statistically equivalent. There was however evidence of greater cumulative adherence (57%) to therapy within these two groups compared to the group not monitored. Their finding of no statistical difference between the nurse-monitored group and the marker-monitored group was not an indictment of marker (or another biological test) irrelevance, however. The value derived was the combination tool of the marker for generation of therapy response information and the nurse for patient communication to influence behavior.

The anticipated clinical effect of monitoring (citing the findings of the referenced Caro study) is a 16% reduction in fracture risk among the 57% who remain adhered to their prescribed treatment. This leads to an estimated prospective 2 fewer fractures in addition to the 11 already avoided (equaling 13 avoided fractures). The potential economic impact of patient monitoring using marker generated information and a healthcare professional for communication and patient management is an increase of cost savings effectiveness in the Delmas and Garnero 668 patient cohort from \$75,615 to an estimated \$90,100 (Figure 8), reflecting a reduction of 13 fractures from the 54 sustained by women not identified as high fracture risk by BMD measurements (thus an overall prospective avoidance of fractures in the cohort to 102 from the 115 reported).

Conclusion

The above findings reflect bone marker technology cost effectiveness for a small population of patients. A cohort of 668 healthy postmenopausal women had sustained 115 incident fractures over a nine-year study period wherein 54 (47%) of the fractures had occurred in women identified as being non-osteoporotic. BMD alone had not picked these women as high risk. A test combination of bone marker, clinical history and BMD was determined to increase sensitivity to fracture risk by 70% - 100%. We therefore examined the prospective economic value of identifying these women for preventive therapy. Antiresorption agent therapy for the prevention and treatment of osteoporosis decreases turnover, increases bone density and reduces fracture risk by as much as 50% thereby developing the possibility that 13 of the 54 women may avoid having a fracture. The economic value of 11 avoided fractures was determined to be \$151,230 given conditions of 100% patient adherence to prescribed treatment. Patient adherence to medication has been shown to be about 50% throughout a period of twelve months therein reducing the savings potential added by bone markers to an estimated \$75,615. To maintain adherence at higher levels, the efficacy of patient monitoring with the support of a bone marker test has been shown to be effective. In reducing the rate of fracture occurrence by 16% thus increasing avoided costs to \$90,100 for the patient cohort (13 fractures avoided from the original 54 "non-osteoporotic" women). We accepted the value of bone marker testing for patient adherence monitoring and management even though the Clowes study had determined that patient adherence within a nurse-monitored group and a marker-monitored group was statistically equivalent. Common sense (at least ours) suggested

that the information provided by timely bone marker resorption data guided health professional communication with patients to effectively influence their adherence behavior. Nurse monitoring does not provide any information whether a patient is either adherent or responding to treatment whereas bone markers do.

The results are substantial enough to infer potentially large implications for healthcare systems and regional communities. For example, the application of these avoided costs results to the average annual occurrence of osteoporotic fractures in the United States results in a roughly estimated potential savings of \$225 million to \$300 million from the current \$15 - \$19 billion annually spent for direct healthcare expenses on osteoporosis (a 1% - 2.5% potential reduction in aggregate costs).

In light of quality of care and reimbursement initiatives being conducted by governments, corporations and healthcare consumer coalitions worldwide, hospital executives are compelled to understand the prospective blended economic impact and clinical outcomes of new technology. They envision pay-for performance compensation strategies currently under development worldwide as potentially being in conflict with federal and payer reimbursement programs that are founded on resource utilization. The relationships between quality and cost are generally accepted as inherently logical, but specific templates to assess and manage them are tough to come by. There are few published findings on the impact of cost control programs on changes in quality of care and clinical outcomes.

About This Study

This is not a scientifically based study. Our analysis was based upon the published findings of various clinical studies rather than a single patient sample population. Cost effectiveness analysis was based upon estimates derived from a several reports published between 1997 and 2005. We did conduct research of patient-based cost records from regional hospital systems located in southern California on a limited basis. The records were not statistically derived, but we do believe, however, that the findings are reasonable.

Much more work on evidenced based cost effectiveness, work that is based upon specified patient populations with concomitant cost records, in compliance with rigorous randomized controlled trials protocol, is needed to accomplish economics research on the diagnosis and treatment of diseases having a huge cost of care impact on society. Our technology economics model is a management tool "works in progress" effort to develop a workable means for hospital executives and clinicians to evaluate and manage on an ongoing basis the blended cost and clinical efficacy of new technology upon the economic value of their healthcare system.

It is our assertion that while new medical technology bears a large responsibility for our ongoing rise in health care costs, hospitals do not possess sufficient knowledge about their relative impacts from a cost effectiveness perspective. Until hospitals secure evidence on costs as they pertain to measured quality of care and clinical outcomes, it will be difficult for them to achieve their clinical goals while sustaining optimal economic efficacy. This article strives to help further the research required in the area of evidenced based economics.

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