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About Premerus

Premerus is the industry's first and only diagnostic management company, representing a new healthcare paradigm: the coordinated focus of resources, expertise and technology to improve the accuracy of diagnosis. Premerus is dedicated to advancing clinical accuracy through diagnostic excellence. Visit www.premerus.com.

**MEDICAL MISDIAGNOSIS in America 2008:
A Persistent Problem with a Promising Solution**

Introduction

Many of us are familiar with the Institute of Medicine's (IOM) 1999 report, *To Err is Human*, which revealed that 44,000- 98,000 Americans die annually as the result of medical errors. However, most of the discussions of medical error have centered on the care received in a hospital setting. Significant medical errors can also occur in other patient care settings such as physician's offices, outpatient surgical centers, imaging centers, nursing homes and retail pharmacies.

The national costs of medical errors resulting in injury are estimated to be between \$17-29 billion annually. The costs to the U.S. health care system represent over 50 percent of these additional expenses.¹ These expenditures burden not only health plans and insurers, but also employers who are already reeling with escalating premiums as well as individuals who must dig deeper to cover co-pays.

The United States healthcare system has lagged behind most other industries regarding the attention paid to ensuring safety. For example, the American aviation industry has focused on producing a safe system since the 1940's, with more public attention centered on improving safety in the aviation industry than on health care -- despite the higher risk of injury or death as a result of medical error versus being involved in an airplane crash. The dramatic media coverage of aviation mishaps has had a significant impact on the public response and concern about airline safety. It is believed that these

media stories were a major factor that encouraged safety improvements within the aviation industry.^{1, 2}

The focus on healthcare quality improvement has been more modest in scale and scope. Changes in operating room protocols have been instituted to reduce surgical errors. Media coverage and litigation regarding wrong-site surgical errors probably played a role in these advances.

With the elevated profile of breast cancer, there have been some good first steps to improve diagnosis. In 1992 congress enacted the *Mammography Quality Standards Act* (MQSA) with the goal of ensuring that all women have access to quality tests for the detection of breast cancer in its earliest stages. The minimum physician requirements outlined by this act are low by subspecialty standards. A physician is required to have 15 hours of continuing medical education every three years and read only 960 mammograms in a two-year period to maintain MQSA certification. This can be accomplished by reading 1-2 mammograms per weekday. It is questionable if a reasonable level of proficiency can be maintained if only these minimum requirements are met.

While the continuing efforts for health care quality improvements are commendable, there is still a great deal of work to be done, especially in the important area of misdiagnosis.

Prevalence of Misdiagnosis in the U.S.

An accurate initial medical diagnosis is the foundation upon which all subsequent healthcare decisions are based. An error in diagnosis can cause a cascade of negative events to occur, affecting the individual patient and their families as well as the healthcare system and our society as a whole.

Medical misdiagnosis has three major categories:

- False positive: misdiagnosis of a disease that is not actually present
- False negative: failure to diagnose a disease that is present
- Equivocal results: inconclusive interpretation without a definite diagnosis

Many research studies have demonstrated the frequency of medical misdiagnoses. There have been multiple autopsy studies that have uncovered frequent clinical errors and misdiagnoses, with some rates as high as 47 percent.³

A study of autopsies published in the *Mayo Clinic Proceedings* comparing clinical diagnoses with postmortem diagnoses, for medical intensive care unit patients, revealed that in 26 percent of cases, a diagnosis was missed clinically. If the true diagnosis were known prior to death, it might have resulted in a change in treatment and prolonged survival in most of these misdiagnosed cases. The study's researchers concluded, "Despite the introduction of more modern diagnostic techniques and of intensive and invasive monitoring, the number of missed major diagnoses has not essentially changed over the past 20 to 30 years".⁴

Medical imaging has become one of the cornerstones of modern medical diagnosis. As a result, radiologists and the imaging interpretations they provide are critical factors in the formation of most medical diagnoses. An error in image interpretation can result in an undesirable series of events leading to medical misadventure.

Radiology-specific studies have shown significant error rates, with the failure to detect abnormalities in 25-32% of cases where disease was present (false negative) and incorrectly diagnosing diseases in 1.6-2% of cases that were actually normal (false positive).⁵ This has been consistently documented in multiple studies, dating from Garland's classic article in 1949⁶ to a report by Renfrew et al. of the University of Iowa in 1992.⁵ In an article published by *Imaging Economics*, Christopher M. Shively stated, "Despite advances in training and technique, little change in the radiology error rate has occurred over the past 50 years." He added, "The internal error rate by the same radiologist can range as high as 25-30 percent. Eighty percent of errors are perceptual errors, which are present on the film but not seen."⁷

In the pilot test of the RADPEER peer review program conducted in 2002, misinterpretation and difficult-case disagreement rates were higher for more advanced modalities.⁸ One study showed substantial disagreement between radiologists when using MRI for diagnosis in patients suspected of lumbar disk herniations, despite its status as the gold standard. Disagreeing results or non-concordance were present in 30 (51 percent) of 59 patients. In most of the patients, the radiologists disagreed on whether

a bulging disk was present or whether no abnormality was present at all.⁹ This type of disagreement can be clinically relevant, because the decisions regarding when and where to surgically intervene depend greatly upon an accurate MRI diagnosis.

A 1993 study by Harvey et al. at the University of Arizona reviewed the previous mammograms performed on women who developed breast cancer. Seventy-five percent of the most-recent previous mammograms, which were initially interpreted as having normal findings, were found to actually show signs of cancer by at least one of three radiologist-reviewers.¹⁰

The Impact of Medical Misdiagnosis

Quality of Care

Errors in diagnosis have serious impact on patients and the quality of care they receive. Patients who receive a false positive diagnosis may endure unnecessary treatments or even surgery before discovering that they do not have the disease that was diagnosed. When a patient receives a false negative diagnosis, the undetected illness can cause the patient's condition to deteriorate to the point where more extensive intervention becomes necessary with the increased risk of a poor outcome. Equivocal interpretations usually result in additional testing with a delay in definitive treatment or reassurance for the patient.

Patient Anxiety and Distress

In addition to the symptoms of the actual medical condition, patients and their families also suffer increased anxiety and stress from misdiagnosis. They may worry when an illness is not improving, despite treatment, or when a disease has progressed to a serious stage, because necessary care was delayed due to inaccurate test results. Patients and their families are usually also concerned by lost income and mounting costs if their treatment is prolonged, or if they must undergo repeated testing as a result of diagnostic errors or equivocal interpretations.

Sometimes, the occupational consequences can be catastrophic, as in the case of a 34-year-old postal worker with a back injury who underwent an MRI that was interpreted as normal by a general diagnostician. When conservative treatment failed, the patient was

accused of fraudulent injury and lost his job. However, when the same MRI results were interpreted by a subspecialist with greater expertise in spinal imaging, a disc herniation with multiple annular tears was detected. The patient underwent successful surgery and returned to work, but only after a grueling experience.

Aims for Healthcare Improvement

More recently there have been proposed objectives to reduce medical errors. In the report *Crossing the Quality Chasm*,¹¹ the Institute of Medicine identified six aims for improvement in healthcare which directly impact the discussion of misdiagnosis:

1. Safe: avoiding injuries to patients from care that is intended to help them.
2. Effective: providing services based on scientific knowledge to all who could benefit, and refraining from providing services to those unlikely to benefit (avoiding underuse and overuse).
3. Patient-centered: providing care that is respectful of and responsive to individual patient preferences, needs, and values and ensuring that patient values guide clinical decisions.
4. Timely: reducing waits and sometimes harmful delays for both those who receive and give care.
5. Efficient: avoiding waste, such as waste of equipment, supplies, ideas, and energy.
6. Equitable: providing care that does not differ in quality because of personal characteristics such as gender, ethnicity, geographic location, and socioeconomic status.

The Positive Impact of Experience and Case Volume on Patient Outcome

In the past three decades, there has been extensive research demonstrating the relationship between case volume and patient outcome for a variety of medical conditions and procedures. Two large reviews evaluated the results of many of these studies.

One review found that of 128 studies, which examined 40 conditions or procedures, 80 percent revealed a statistically significant relationship between higher case volumes and better clinical outcomes. It was estimated that 26 percent of the deaths among patients

in facilities with low volume could be attributed to their low case volume, when compared to higher volume facilities for the same conditions. None of these published studies reveals worse outcomes with higher volumes.¹²

Another review evaluated 135 studies of 27 conditions or procedures, some of which were included in the review cited above. These authors found that 70 percent of those studies of either institutional or physician case volumes demonstrated a significant relationship between higher volumes and better outcomes. Hospitals with lower volumes had a median difference of up to 13 percent more deaths for the same procedures, such as pancreatic cancer surgery. Lower volume physicians had a median difference of up to 14 percent more deaths than those with higher volumes for the same surgical procedures. Physician volume was found to be a more important determinant for outcome in procedures such as CABG, carotid endarterectomy, surgery for ruptured aortic aneurysm, and surgery for colorectal cancer.¹³

The volume-outcome relationship differences have been demonstrated among physicians, independent of the facilities in which they practice. One study examined the mammographic interpretation sensitivity demonstrated by individual radiologists. In this study, high sensitivity indicates the detection of a high percentage of true positive breast cancer cases. The study was performed using a standardized set of 60 films with known long term follow-up results. Radiologists who read more than 300 mammograms per month detected an average of 78.6 percent of cancers. This was much higher than the 71.5 percent found with radiologists who read 100 or less per month.¹⁴ As a result, the higher volume, more experienced radiologists were more likely to detect a cancer with the mammogram. This increased sensitivity with earlier detection of mammographic abnormalities and subsequent treatment should result in improved breast cancer survival

The physician's specialty may also affect patient outcomes. In an evaluation of 3067 ovarian cancer patients, 33 percent of these patients were treated by a gynecologic oncologist, 45 percent by a general gynecologist, and 22 percent by a general surgeon. The patients treated by the gynecologic oncologists had the best outcomes and lowest mortality rates. At 60 days after the most extensive surgical procedure, the mortality rate for the gynecologic oncologists was 5.4 percent compared to 6.4 percent for the general gynecologists and 12.3 percent for general surgeons. Also, 97 percent of the

gynecologic oncologists provided complete surgical staging, describing the extent of other structural or organ involvement by the cancer, which is essential for further treatment decisions. Only 52 percent of the general gynecologists and 35 percent of the general surgeons completed the staging procedures.

Of all three categories, the gynecologic oncologists provided care that was most closely aligned to the National Institutes of Health (NIH) defined best practices. The research data cited above supported the professional societies' recommendations that it is preferable for ovarian cancer patients to be treated by gynecologic oncology subspecialists when it is possible.¹⁵

Addressing the Need for Access to Subspecialty Radiologists: The Premerus Solution

Currently, most imaging tests are read by general radiologists rather than subspecialists. A typical imaging facility might have a single radiologist on staff to read all of its studies. This individual may be called upon to make precise diagnoses for conditions outside his or her area of expertise or qualification. Although subspecialization can deliver better outcomes, for individual patients to benefit, the most appropriate subspecialist needs to be identified and available.

Scott W. Atlas, M.D., a professor of radiology and chief of neuroradiology at Stanford University Medical School, advocated radiology subspecialization in a recent article. He said, "To continue having non-subspecialty-trained radiologists interpreting sophisticated, complex imaging studies on patients with diseases that are virtually always cared for by subspecialist-referring doctors is unacceptable patient care."

Dr. Atlas concluded by saying, "Americans have come to expect the most advanced health care in the world, perhaps rightfully so, considering that America leads the way in technology-based medical innovation. For its own sake as a vital field of critical importance, and for the sake of clinical patient care in our advanced, technology-based medical system, radiology must finally step up to the plate and fully subspecialize."¹⁶

There has been a recent launch of the nation's only company dedicated to advancing clinical accuracy through diagnostic excellence. Premerus (www.premerus.com) creates the first

nationwide platform of leading diagnostic subspecialists to improve the accuracy of diagnoses, enhance patient outcomes and reduce healthcare costs. Premerus represents a new healthcare paradigm to address the aims for healthcare improvement outlined by the IOM *Crossing the Quality Chasm* report.

Premerus Demonstrates the Positive Impact of Subspecialty Radiologists

Premerus is currently completing a study comparing the medical imaging interpretations of general radiologists to subspecialty radiologists. These subspecialty radiologists have had additional training and experience in Neuroradiology (brain and spine), Musculoskeletal Imaging (bones and joints), or Body Imaging (neck, chest, abdomen, and pelvis soft tissues). Their practices include a high volume of these subspecialty specific cases.

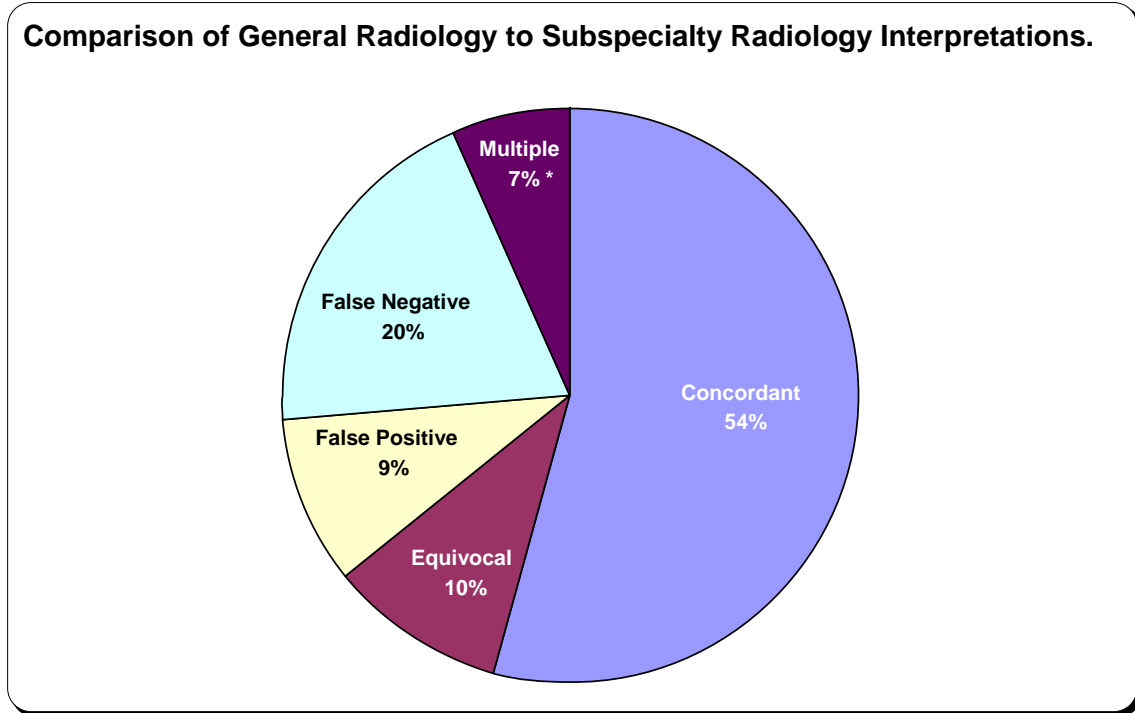
Computed tomography (CT) and magnetic resonance imaging (MRI) procedures for 149 patients of a single health plan in two southwestern states were re-interpreted by subspecialty radiologists. These cases were distributed to the subspecialists according to their area of expertise. The subspecialists were provided with the original clinical history and images for each case, but were not given the original interpretation results.

After the subspecialist reading was obtained, these were compared to the original general radiologist's report. Reports that were not in agreement were labeled as non-concordant. Both concordant and non-concordant reports were then examined by clinical specialists in the appropriate fields of medicine (Neurology, Orthopedic Surgery, Family Practice, General and Cardiothoracic Surgery) in order to assess for differences in patient management based on the two reports. As much as possible, the available clinical information regarding the patients' care after the initial imaging was also collected. This included outpatient progress notes, hospital discharge summaries, subsequent imaging reports, operative reports and biopsy results.

The preliminary results of this study have demonstrated that about 45 percent of the reports had disagreements between the original general radiologist's reading and the

subspecialist's interpretation. These non-concordant cases were categorized as false positive, false negative or equivocal as defined above. (See figures one and two below.)

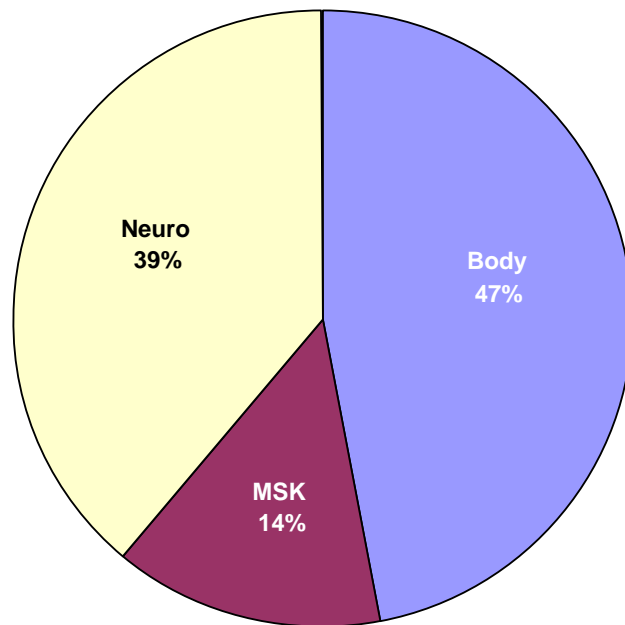
Figure One:



* Multiple: cases with combinations of non-concordant interpretations.

Figure 2:

Subspecialty Specific Non-concordant Interpretations



Neuro: Neuroradiology, brain and spine.

Body: Neck, chest, abdomen, and pelvis soft tissues.

MSK: Musculoskeletal, bones and joints.

A significant number of the false positive and equivocal original interpretations resulted in additional diagnostic procedures being performed. These included additional imaging and laboratory tests, as well as invasive procedures such as endoscopy, needle and surgical biopsies. Overall, the subspecialist reports were more definitive and less likely to recommend follow-up procedures.

The clinical data collection is not yet complete. The preliminary results of this data and the clinician reviews largely support the greater accuracy and efficiency of the subspecialists' interpretations.

An examination of the insurance claims data for these non-concordant cases was performed. Procedures that appeared to be the result of these non-concordant interpretations were identified with their costs to the insurance company. This did not include any other expenses incurred by the patient. This resulted in a demonstration of

potential savings by the health plan of \$5.75 per member per month. There were 565,849 members in the health plans for these two states. The potential annual savings would have been more than \$39M.

With this study, it was difficult to accurately assign monetary cost to the false negative, non-concordant cases. It is generally recognized that most disease processes are more efficiently handled at an earlier stage, before spread to other areas or complications arise. In the 2003 article describing the cost-effectiveness of early lung cancer detection, Juan Wisnivesky, M.D., noted that the cost for stage I treatment was 22-38 percent less than for later stages.¹⁷

The final results of this study will be provided as soon as it is completed.

Premerus harnesses the power of specialization

Premerus delivers access to the subspecialty expertise of some of the nation's leading diagnostic physicians, by using proprietary technology to match individual cases with diagnostic subspecialists and then transmit the clinical data and images to them for near-real time interpretation. Premerus increases diagnostic accuracy by bringing Certified Premerus Experts to the reading of MR, CT, PET and mammography studies. It is based on a simple principle: The more experience a diagnostician has for a specific condition the more likely he or she will deliver an accurate diagnosis.

For example, some radiologists may be qualified to read breast images for cancer while others may be qualified to evaluate injuries of the bones and joints. Depending upon the clinical question posed, Premerus identifies a Certified Premerus Expert, whose area of demonstrated competency relates to the patient's clinical needs. By matching physicians with expert diagnostic skills to individual cases based on the clinical needs of each patient, Premerus expects to deliver the most accurate diagnosis possible. The Premerus Platform gives any patient, anywhere, direct access to these expert diagnostic physicians.

Certified Premerus Experts™

Premerus quality is built around the Certified Premerus Expert™ process. Premerus experts must show documented experience, board certification, advanced training, and

peer recognition in an imaging subspecialty. They also must pass a rigorous testing and credentialing program. What's more, Premerus analyzes the results of their interpretations that include evaluation of image quality, a rigorous peer review process and monitoring of patient health care outcomes compared to the imaging interpretations and diagnoses. Premerus uses sophisticated data analysis which assures the diagnostic subspecialists have maintained their clinical expertise for specific body parts and medical conditions.

Here's how Premerus increases accuracy:

- **SELECTION** – Expert selection is based on rigorously documented and tested clinical expertise for a specific subspecialty area.
- **EXPERTS** – Certified Premerus Experts oversee the imaging protocols and interpret all diagnostic studies.
- **TECHNOLOGY** – Premerus uses proprietary technology to match the diagnostic tests with the most appropriate subspecialist and generate an accurate diagnosis.
- **REPORTING** – Premerus uses a structured diagnostic format and uniform lexicon for definitive diagnostic reports.

Here's how Premerus works:

- The patient can go to a local imaging center or hospital facility in the Premerus Platform, and the diagnostic imaging would be performed in the usual manner.
- Using telemedicine, the imaging study will be digitally transmitted to a Premerus subspecialist.
 - Premerus uses proprietary technology to match the specific patient needs with a Certified Premerus Expert who specializes in the relevant body part or organ system.
 - Because Certified Premerus Experts can be based anywhere in the United States, the Premerus technology can eliminate geographic barriers to accessing highly specialized doctors.
- Written reports and findings are then sent to the patient's ordering physician.

Premerus improves diagnostic quality while reducing costs:

- *Improved Outcomes* – The goal of the Premerus approach is to provide an accurate diagnosis the first time. This subspecialty expertise improves the

effectiveness and accuracy of the patient's diagnosis. As a result, ordering physicians can provide appropriate treatment more efficiently.

- *Reduced Costs* – Premerus mitigates the high medical costs associated with misdiagnosis by eliminating the cascade of expenditures and possible medical complications generated by repeated, unnecessary, additional testing and other procedures.
- *Participant Satisfaction* – Members and associates experience reduced anxiety from false positives and equivocal results. Patients will understand the implications of their condition in a more timely fashion. They will also avoid the physical and emotional stress related to unnecessary testing, biopsies and surgeries.

Support for the Premerus concept emanates from prestigious sources nationwide, including Edward Coleman, M.D., professor and vice chairman of the department of radiology, Duke University Medical Center:

“Premerus is founded upon the fundamental fact that for specific medical problems, experienced specialists provide more accurate diagnoses and better outcomes than do generalists. In the past three decades, there has been a great deal of research demonstrating the relationship between volume and patient outcome for a variety of medical conditions and procedures.”

He concludes that an accurate diagnosis mitigates downstream expenditures and minimizes emotional distress for patients that result from an inaccurate diagnosis, adding, "An early, accurate diagnosis provides the best prognosis for the patient."

READY TO LEARN MORE?

Contact Dr. Scarborough and colleagues at 866-600-3016 or visit www.Premerus.com to learn how Premerus can increase diagnostic accuracy, improve patient outcomes and reduce your healthcare costs.

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