



Unexplained Symptoms: When Diagnostic Uncertainty Becomes a Diagnosis

By Susan Carr, Senior Writer

It is difficult to describe how uncomfortable we physicians feel when we have no idea what is wrong with a patient.¹⁽¹⁶⁰⁾

Brian Hodges, MD

If I had no diagnosis, then my symptoms meant nothing.¹⁽¹⁶²⁾

Chloe G.K. Atkins, PhD

Uncertainty is a given in diagnosis. Sometimes, when the correct diagnosis comes quickly, uncertainty is brief and mild. Other times, uncertainty settles in as a chronic condition, with unfortunate results for both clinician and patient. Between those two extremes, each case travels through a period of dynamic uncertainty as the patient and clinician work their way through history-taking, physical examination, and testing. Hopefully, uncertainty ebbs as more is known, and the mystery is solved.

Traditionally, the goal of diagnosis is to extinguish uncertainty, with both clinicians and patients invested in finding a clear and accurate answer as quickly as possible. For patients, diagnosis is the key that unlocks the door to treatment and financial support. Having a diagnosis allows them to feel they are on the mend, receiving appropriate treatment or therapy. The clinician can feel satisfied that the case is closed, at least for the time being, and move on to the next.

In addition to providing guidance for effective treatment, diagnosis validates the patient's experience: symptoms make sense when understood as derived from a disease, condition, or illness. Without diagnosis, symptoms may be seen as subjective and discounted as psychosomatic.

Medically Unexplained Symptoms

Symptoms that clearly affect the patient physically (are not imagined) and are not understood to be associated with an underlying organic disease for an extended period of time have a diagnosis of their own. Referred to as "[medically unexplained symptoms](#)" or MUS—also known as MUPS (medically unexplained physical symptoms)—this condition is "largely untreated,

common, and costly.”²⁽⁶⁸⁹⁾ It is also difficult to define, sometimes used as a catchall for conditions that resist understanding, including conditions that have both physical and psychosocial elements.

MUS is prone to prejudice and cognitive bias. Some patients diagnosed with MUS feel that when an organic disease cannot be found to explain their symptoms, they morph from being the subject of diagnostic interest to being dismissed as difficult and psychologically suspect.^{1,3,4} And some MUS patients acknowledge that physical and psychological forces coexist and interweave, certainly over time, even if not initially, making it hard for them to perceive and understand their own symptoms.¹

Researchers in the United Kingdom found that physicians were more likely to consider symptoms medically unexplained when they had negative perceptions, associated for example with the patient acting anxious, being unmarried, or receiving public assistance. Physicians were more likely to make a provisional diagnosis that “explains” symptoms for patients who were employed, not receiving alternative therapies, and generally viewed as a positive experience for the physician.⁵

Counting and Classifying MUS

By its nature, medically unexplained symptoms is a condition that is difficult to identify, classify, and manage. It is ill-defined, varied in its presentation, and often unrecognized by patients as a diagnosis in itself. When MUS is recognized and named, the patient may be stigmatized.^{1,4,6,7} Patients with MUS are prone to being overtested and overtreated.²

In 2007, researchers at Michigan State University estimated that 25% to 75% of outpatients exhibit MUS in manifestations across a clinical spectrum, “i.e., on average, approximately one-half or more of all outpatients have little or no physical disease explanation for their symptoms.”²⁽⁶⁸⁵⁾ In 2010, researchers in Germany estimated that MUS represented “two-thirds of all reported symptoms”⁸⁽²⁶³⁾ in primary care. In 2017, researchers in Denmark distinguished between patients seen without a specific diagnosis and patients diagnosed with MUS, finding the first group represented 1 in 3 consultations, and the second, 1 in 6.⁹

Those estimates include patients across the spectrum, from those who have mild symptoms that quickly self-resolve to patients who are debilitated for years by physical symptoms and comorbid psychiatric disorders. Most patients whose symptoms resolve easily without specific treatment are never diagnosed with MUS, although they may have ongoing, recurring episodes that are easily managed, amounting to a normal but “worried well” approach to personal health.² Other patients may develop stress-related symptoms that mimic those of a serious organic disease they have already been diagnosed with, e.g., heart disease.² These, too, can often be managed as episodic and understandable symptoms, different from chronic, truly unexplained problems.

The population of patients with MUS includes subgroups diagnosed with complex mental and/or physical problems, each with its own special characteristics. Chronic fatigue syndrome, chronic Lyme disease, irritable bowel syndrome, and fibromyalgia are among the diagnoses applied to patients with MUS. Some patients diagnosed with MUS are eventually found to have a rare disease or a rare presentation of a common disease that has confounded diagnosticians in some cases for years. MUS patients may also be found to have “somatoform” disorders, where physical symptoms are caused by a mental disorder, a diagnosis that can be made only after ruling out organic diseases. MUS occurs in children¹⁰ as well as in adults.

Uncertainty, a Constant Companion

MUS is both pervasive and largely invisible. When recognized as commonly occurring, it stands as a reminder that uncertainty “typifies the nature and complexity of clinical knowledge”¹¹⁽²⁴⁴⁾ especially in general practice and could be seen as a constant, not always unwelcome, companion.

Researchers from Scandinavia and New Zealand observe a discord between the “gray-scaled narrative”^{11(244),12} of each patient’s experience and “black-and-white diagnosis.”^{11(244),12} Medical educators in Massachusetts note numerous pitfalls associated with suppressing uncertainty and note that:

*Key elements for survival in the medical profession would seem, intuitively, to be a tolerance for uncertainty and a curiosity about the unknown.*¹²⁽¹⁷¹³⁾

A strong desire for certainty and diagnostic clarity—felt by clinicians as well as patients—can cause trouble, especially when symptoms remain unexplained over a long period of time. Some patients who continue to need care and persist in pursuit of a diagnosis report developing a reputation among providers for being “difficult,” psychologically unsound, and demanding.^{1,13,14} Some patients feel their medical records haunt them “like a criminal record,”¹⁴⁽¹⁹²⁾ prejudicing clinicians against them for the condition that has brought them in for consultation and relief.

In addition to peace of mind, treatment, and insurance coverage, diagnosis provides patients with a recognized label and coherent story—e.g., cancer, heart disease, diabetes—they can use to explain their experience. Louise Stone, a physician, educator, and researcher in Australia, points out that a diagnosis offers meaning that can be structured as a narrative and shared with others. Patients with MUS may become personally invested in a different diagnosis for their unexplained symptoms, replacing uncertainty with a known disease that provides an explanation and story that makes sense to others.

Developing meaning and a coherent story about MUS is challenging but not impossible and may improve outcomes.¹⁴ Stone refers to sociologist Arthur Frank’s metaphor of patients feeling shipwrecked by disease as she encourages clinicians to help patients with MUS develop their narratives:

*Creating an explanatory framework that respects and incorporates the patient's models of illness and a future direction for care involves using storytelling 'as repair work on the wreck.'*¹⁴⁽¹⁹³⁾

Going forward, knowledge of the wide range of situations currently held under the umbrella of MUS and the current approach to diagnosing and treating them will evolve. Science may provide new understanding to inform diagnosis of specific conditions, such as chronic Lyme disease and fibromyalgia. The interplay between physical and mental health is an active topic of debate among clinicians and is central to the experience of many patients with MUS.^{1,9} The role of gender in MUS diagnosis must be investigated, as the majority of MUS patients are female, which seems clearly related to earlier beliefs about the role of “hysteria” in illness.³ Researchers note an association of childhood abuse and trauma with adult MUS, which also needs further investigation.¹⁴

Diagnosis in Context

The nature of diagnosis itself is also an area of learning. In a clinical commentary to a patient-told story about MUS, Brian David Hodges, MD, points out,

*...diagnosis is not a fixed entity—but rather a product of the scientific, social, economic, and cultural milieu in which both the doctor and patient exist: it is a shared creation.*¹⁽¹⁶²⁾

Describing diagnosis as a “creation” that develops in the real world, within a context of complex relationships, Hodges reminds us that diagnosis is often far from cut and dried, offering continual opportunities for refinement and improvement.

Researchers from the University of California in San Francisco recently proposed a model of four categories for calibrating the relationship between diagnostic certainty and accuracy.¹⁵ Their model encompasses “slam dunk” diagnoses that are clearly accurate and certain, through some that are accurate but uncertain, inaccurate and uncertain, to the inaccurate and certain category they call “diagnostic hubris.”¹⁵⁽¹²³⁾ They offer the model as a tool to help medical educators begin “important conversations [with trainees] about issues that are often left unspoken.”¹⁵⁽¹²³⁾ The awareness and transparency their model provides about degrees of certainty might also help future conversations about MUS and the issues it raises for patients and clinicians alike.

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Diagnosis Education – A Pathway to Improving Diagnosis

There's a breath of fresh air in healthcare education – and it's all about improving diagnosis.

The [oft-quoted wisdom](#) from Paul Batalden that “Every system is perfectly designed to get the results it gets” can be applied to health professions education as well. As summarized in the landmark report from the National Academy of Medicine (NAM), [Improving Diagnosis in Health Care](#), our current education system generates clinicians who get the diagnosis right roughly 90% of the time. It is reasonable to ask, “Can we improve diagnosis by improving education?”

The NAM report concluded that the answer is “yes.” One of its most important recommendations was to improve health professions education, based on the hope that the next generation of clinicians could reach higher levels of diagnostic quality and safety if they received more effective training. The report

and its recommendation to improve education, along with the growing interest in diagnosis and diagnostic error more generally, provide the impetus for renewed attention to what is taught today and how it can be improved.

Goal 2: Enhance health care professional education and training in the diagnostic process

Recommendation 2a: Educators should ensure that curricula and training programs across the career trajectory:

- Address performance in the diagnostic process, including areas such as clinical reasoning, teamwork, communication with patients, their families, and other health care professionals, appropriate use of diagnostic tests and the application of these

Improving Diagnosis in Health Care, pg. 9-10

Problems with educational programs in use today are many and varied, including:

- Training is idiosyncratic; the quality of teachers varies dramatically, and the number and types of cases a trainee may see also vary greatly.
- There is not enough content on how diagnostic errors arise and how they can be avoided, nor how to work in teams, partner with the patient, or work more effectively in one's healthcare system.
- There is little or no exposure to using decision-support resources to improve diagnosis.
- Training doesn't take advantage of [the most up-to-date advice](#) on pedagogy.
- Case studies and simulation are underutilized as ways to standardize training and improve recognition of disease variants.

Special Issue of *Diagnosis* Focuses on Education

The good news is that there is growing consensus that education needs to and can improve. As evidence, the latest [special issue of *Diagnosis*](#) focuses specifically on diagnosis education and on early experience with pilot programs working to improve diagnosis-related training. Andrew Olson, Geeta Singhal, and Gurpreet Dhaliwal—representing the SIDM Education Committee—served as guest editors, highlighting in their opening editorial many recently implemented or ongoing SIDM initiatives:

- [Virtual patient cases](#) illustrating and discussing diagnostic error for senior medical students
- [Education resources for the SIDM website](#), such as the Clinical Reasoning Toolkit and the Assessment of Reasoning Tool
- Monthly #teachdx Twitter chats
- [SIDM's Fellowship in Diagnostic Excellence](#) – New fellows are selected each year for this competitive fellowship and are paired with SIDM mentors

- A [consensus curriculum](#) that identifies 12 key competencies for the education and training of all health professionals

The special issue of *Diagnosis* includes 15 articles that illustrate the breadth of work now in progress relating to “[diagnosis education](#),” the new term that refers to this growing area. Several articles focus on using technology to enhance case-based learning, including simulation, [point-of-care ultrasound](#), and smartphone apps. Articles examine using [simulation to familiarize trainees with heuristics](#) in clinical reasoning is one such application, and remind us that “serious games” have been used successfully to teach “debiasing” skills in decision-making. Another looks at a [new app that facilitates the use of Bayes theorem](#) to help clinical decision-making by taking into account the characteristics of diagnostic tests. Other projects focus specifically on improving diagnostic reasoning. For example, using [checklists](#) at the point of care allows trainees to recognize information that “doesn’t fit” in time to revise incorrect diagnoses.

These early research efforts are interesting and important, both in terms of preventing harm from diagnostic errors and in [promoting high value health care](#). Another study examines how [many training programs have little or no content on diagnostic error](#) or quality assurance more generally. Research at a basic level is needed to understand the different [subtasks that make up the diagnostic process](#) and how to incorporate this knowledge to improve education. Several articles report early experience in this regard, presenting [clinical reasoning curricula for clerkships](#) and [residents](#) and advice on how to understand and communicate [uncertainty in diagnosis](#).

Articles in the special issue also focus on [faculty development](#), one of the key unmet needs for moving diagnosis education forward. [Faculty today aren’t comfortable](#) discussing diagnostic error with trainees and aren’t generally familiar with the common biases that lead to diagnostic errors.

These articles are a starting point for moving diagnosis education from the drawing board to classrooms, clinics, and wards. This work will continue for years to come. It is exciting to see that work has started and interest is growing, especially among trainees, to address diagnostic quality and safety.

Addressing the Disparities Gap in Diagnosis

Patients entering the diagnostic process exhibit several highly visible risk factors—eg, age, race/ethnicity, and sex—that affect efficient and accurate diagnostic decision-making. Yet there have not been focused efforts to understand how these factors impact symptoms, test results, and diagnosis. Consequently, there are no strategies to assure best diagnostic processes and systems supports around cognitive reasoning vulnerabilities or “pitfalls” related to obvious but insufficiently examined patient factors.

When risks related to age, sex or race/ethnicity suggest low likelihood of a particular condition, clinical decision makers may narrow their diagnostic focus too much. This clinical judgment problem is referred to as *overweighting of a visible risk factor*. Limited systematic research is available to determine the scope of this patient-perceived problem and the circumstances under which it might lead to significant problems in diagnosis.

Media reports, medical malpractice lawyer websites, and peer-reviewed literature suggest two related sources of cognitive reasoning pitfalls: a lack of diagnostic knowledge about symptoms experienced by understudied groups and a lack of understanding about tailoring testing to specific populations, given that medical research has historically been primarily conducted on middle-aged white men.

For example, women are less likely to get accurate results from the traditional treadmill stress test to detect heart problems because the scoring system was derived from experiments on middle-aged men. These contributory factors are referred to as *underappreciating knowledge about differences in symptoms or testing*. To the extent that the knowledge is available but not aggregated or formatted for practical use, this is a systems level gap in tools and techniques to support patients and clinicians with needed information at the right moment.

At a Patients Improving Research in Diagnosis (PAIRED) meeting hosted by the Society to Improve Diagnosis in Medicine (SIDM), approximately one-third of the patients shared a story of diagnostic error in which they perceived that being too young, female, or African American contributed to not getting a timely and accurate diagnosis for conditions that can cause the most harm such as stroke, colon cancer, sepsis and heart attack.

In response to this clear gap in the system, SIDM has partnered with Stanford University to conduct a first-of-its-kind study of diagnostic disparities due to age, race/ethnicity, and sex. Funded by Coverys, this study aims to identify specific diagnostic error vulnerabilities for young people, women, and African Americans.

SIDM is also partnering with patient members from the PAIRED community to ensure that the research integrates the real-world perspective of patients and family members who have experienced diagnostic error. “This provides the highest level of patient centeredness in our work and addresses the priorities and outcomes that matter most to patients,” says Sue Sheridan, director of patient engagement at SIDM.

“Our goal is to explore how visible factors relate to clinical decision-making, cognitive pitfalls, and systems vulnerabilities in order to enable innovative solution design work,” says Dr. Kathryn McDonald, principal investigator at Stanford University.

The disparities project has four specific aims:

1. To gather stories in the words of patients and their representatives about how they perceived that one or more of the three visible factors (being female, young adult, or African American) contributed to a diagnostic error where a final accurate diagnosis is known.
2. To develop a clinical view through literature sources, medical malpractice data, and clinician input as to whether there is a plausible sequence of diagnostic reasoning for each final diagnosis that would include using one more of the visible factors as relevant diagnostic information, and if so, how.

3. To produce detailed diagnostic scenarios where the visible factors could plausibly contribute through either or both of the posited mechanisms (overweighting and underappreciating) to a cognitive reasoning pitfall.

4. To co-design with SIDM leadership, researchers, patients, and clinicians a set of solutions that could address the overweighting and/or underappreciating problem described in the diagnostic scenarios, and that could feasibly be implemented in clinical practice settings or incorporated into educational modules for clinicians or patients.

The findings of the two-year study will help healthcare providers improve clinical judgement and help their institutions support prompt and accurate diagnosis by characterizing specific diagnostic error disparities related to clinical reasoning pitfalls. Patient engagement and close partnership throughout the project will help make sure that the results are significant for the ultimate beneficiaries – the patients.

“It is essential that we engage patients and family members with lived experience of diagnostic error to ensure that the research reflects the priorities and outcomes that matter most to patients,” says Sheridan.

Similarly, engaging other stakeholders through SIDM’s leadership on this project will guarantee that project results catalyze further partnerships to understand and reduce diagnostic error disparities.

Learn more about SIDM and Stanford’s [study on disparities in diagnosis](#).

PAIRED Patient Discusses Diagnostic Error on Maternal Sepsis Day

On May 15, 2019, the Sepsis Alliance launched [Maternal Sepsis Day](#) “to raise awareness of the unique signs and symptoms of maternal sepsis.” To help others understand the importance of a timely and accurate sepsis diagnosis, Sarah Kiehl shared her story on the Sepsis Alliance website, which receives about 300,000 unique visitors a month. Sarah is a patient partner in the Society to Improve Diagnosis in Medicine (SIDM)’s [Patient Improving Research in Diagnosis \(PAIRED\)](#) project.

Surviving Sepsis Leads to Advocacy

On Thanksgiving Day 2015, Sarah delivered twins via C-section. Having suffered for many years from endometriosis, she had a routine laparoscopic hysterectomy 11 weeks later. Two weeks following the hysterectomy, she noticed abnormal vaginal discharge and immediately consulted her doctor. He assured her that her symptom was just part of the healing process.

Two days later, she became violently ill and went to the emergency room with nausea, vomiting, elevated temperature and severe pain. Following a CT scan and some confusion between her surgeon and radiologist, it was determined that she had some type of infection. She remained in the hospital overnight for antibiotics. She was ultimately diagnosed with sepsis due to low blood pressure, high temperature and rapid heart rate; she received medication and underwent emergency surgery.

“After months of healing, I am forever changed by this experience, and have decided to become a sepsis advocate in search of healing,” says Sarah. Read more about her story in the SIDM [Story Bank](#).

As a sepsis survivor, Sarah was invited to join SIDM’s PAIRED project, which trained patients how to engage, as equal partners, in the design, conduct and dissemination of diagnostic research to improve diagnostic quality and safety. She and the other PAIRED graduates learned about the diagnostic process and how to identify possible research topics and questions, as well as the nuances of diagnostic research.

As a result of the training, Sarah is now actively engaged as a member of the Patient Advisory Board of the Disparities Project, a newly funded research project that addresses disparities in diagnosis. The Disparities Project is conducting a study to identify specific diagnostic error vulnerabilities for young people, women, and African Americans. Sarah will be focusing on the areas surrounding sepsis, with the goal to initiate protective strategies to reduce error.

Sarah is now a happy, healthy mother of three daughters. She feels that her experience with sepsis has given her a second chance. “I am honored to advocate for young women and mothers about the signs and symptoms of sepsis, and, ultimately, survival,” she says. “I will continue to fight to help save lives.”



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