EDITORIALS

Symptoms and Science

The Frontiers of Primary Care Research

I expect that the primary care movement will expand the territory of clinical research. Until now, two areas have occupied clinical investigators: defined diseases, such as cancer, diabetes, arthritis, and coronary artery disease, and risk factors, such as hypertension, hyperlipidemia, and osteoporosis. Risk factors are not really illnesses, but they warrant identification and management in many asymptomatic individuals to prevent complications in a minority of persons, often many years later. Meanwhile, physical symptoms, which account for over half of all outpatient visits,[1] remain a wilderness begging to be explored. Compare the sections in medical textbooks about symptoms with those about specific diseases. The sections on symptoms have exhaustive lists of differential diagnoses but little information on the frequency of specific causes, the natural history of the symptom, or the cost-effectiveness of an evaluation, all because of a paucity of research.

The fuzzy borders of physical complaints may explain this situation. Traditional science prefers a well-marginated problem. For example, funding agencies are organized around end states rather than presenting symptoms. Peptic ulcer, pancreatic cancer, and depression may all present with abdominal pain. While each disease has a federal institute to fund grant proposals, abdominal pain remains an orphan. In addition, the subspecialization of clinical medicine, particularly in academic centers, has fostered disease-based rather than symptom-based research. Chest pain due to angina, gastroesophageal reflux, or panic disorder is likely to be studied with separate protocols in separate clinics. To understand the epidemiology of this symptom, however, would require study of all patients presenting with chest pain in a primary care setting.

The Agency for Health Care Policy and Research (AHCPR) has been the lone source of meaningful federal funding for symptoms research—consider, for example, its funding of research on back pain. Even in its heyday, however, AHCPR had a budget disproportionately small for the task, and politically motivated downsizing of AHCPR has all but gutted its ability to fund symptom-based research. Managed care organizations should be a funding source, particularly if their leadership can be convinced that a more evidence-based approach to evaluating and managing common symptoms might improve outcomes and control costs.

In this issue, Martina and colleagues take a preliminary step toward clarifying the epidemiology of several common complaints.[2] Three findings are particularly salient. First, nonorganic causes of symptoms are common: 59% of abdominal pain and 83% of chest pain in their sample. Previous studies have confirmed that at least one third of symptoms lack a clear-cut physical explanation.[3–6]

Second, history and physical examination are sufficient to establish the diagnosis in most patients, and this finding also is consistent with other reports about selected symptoms,[7–10] and general symptoms.[11,12] These same studies demonstrate that the medical history contributes substantially more diagnostic information than the physical examination, suggesting that the busy practitioner might wisely allocate proportionately more of the limited time typically allowed for outpatient visits to a careful symptom history followed by a brief, targeted physical examination. Clearly, more research is needed to define those aspects of the physical examination that are diagnostically useful for specific symptoms. Meanwhile, the low yield of diagnostic testing has important implications for reducing not only health care costs, but also patient worry and the occasional risk that results from pursuing false-positive or incidental findings.[13,14]

Third, abdominal pain and chest pain considered nonorganic after the initial assessment were seldom harbingers of a serious disorder during long-term follow-up, a finding that also has been demonstrated for several other symptoms.[7,9,15,16] Notably, physicians rated their preliminary diagnosis as "undoubted" in 38% of the cases, and when diagnostic certainty was this high, patient follow-up proved clinical judgment to be almost error-free. Devastating surprises are distinctly uncommon when the initial clinical evaluation is unrevealing, although medical trainees often learn to fear early malignancy, connective tissue disease, multiple sclerosis, or other systemic disease when symptoms are undiagnosed. Medicolegal concerns about unlikely but serious diagnoses drive exhaustive evaluations now, but they may become less compelling as primary care researchers conduct further outcome studies of common complaints.

Martina and colleagues did not specifically assess two other features of symptoms, their prognosis and the hidden agendas that motivate patients to report them. The typical natural history of many symptoms is favorable. In two prospective studies totaling 823 general medicine outpatients presenting with a variety of physical complaints, three fourths improved within 2 weeks of their clinic visit,[6,17] empirically verifying the conventional wisdom that "tincture of time" is a reliable healer. Indeed, the therapeutic value of simple reassurance also has been demonstrated in a clinical trial.[18]

Hidden agendas include treatable mental disorders such as depression or anxiety,[4,5,10,17,19] and symptom-related expectations.[6,17,20] Patient expectations are not mental disorders but rather the natural worries and desires that prompt them to consult a health care provider. Symptoms are ubiquitous in the general population but typically are self-limited or managed outside the formal health care system.[21] A minority of symptomatic persons become patients, and common reasons for seeking care include worry about the cause or prognosis of a symptom and desires for prescription medication, diagnostic testing, or subspecialty referral.

Much of the work cited here is still preliminary because it is limited by small sample sizes, a heterogeneity of symptoms, protocols that do not evaluate both physical and psychological causes, and limited follow-up. For example, in the study by Martina and colleagues, 29% of patients were lost to follow-up, there were few elderly patients, and psychiatric disorders were not evaluated. To address these limitations, future studies of symptoms should include inception cohorts of many primary care patients with a single symptom; determination of the sensitivity and specificity of specific aspects of the history, physical examination, and laboratory testing; etiologic classification of patients using explicit criteria and more than one rater[10]; evaluation protocols to evaluate both physical and psychological disorders; prospective follow-up to determine natural history and the predictors of chronicity; and other relevant outcome measures, such as symptomatic improvement, functional status, the quality of life, health care costs, resource utilization, and the satisfaction of patients and providers, since mortality and even serious morbidity are uncommon.

Primary care investigators embarking on symptom-based research have a lot of forest to clear. However, the prospects for such research are exciting, and the findings are likely to inform a more cost-effective approach to the most common conditions encountered in outpatient medicine. Let's get on with it!—**Kurt Kroenke, MD,** *Regenstrief Institute For Health, Indianapolis, Ind.*

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