January 2012

Foretelling The Future Of Prognostication: A Historically Inspired Domain-Based Approach For The Elderly

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FORETELLING THE FUTURE OF PROGNOSTICATION: A HISTORICALLY INSPIRED DOMAIN-BASED APPROACH FOR THE ELDERLY

A Thesis Submitted to the
Yale University School of Medicine
in Partial Fulfillment of the Requirements for the
Degree of Doctor of Medicine

by
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2012

FORETELLING THE FUTURE OF PROGNOSTICATION: A HISTORICALLY INSPIRED DOMAIN-BASED APPROACH FOR THE ELDERLY

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Hypothesis: 1) Physicians' decisions to discuss hospice as an option for terminally ill patients are based on a limited approach to prognostication that excludes many patients who may benefit from discussions. 2) Identifying broader domains of health most important for prognostication, as an alternative to calculating life expectancy or mortality risk, might encourage prognostication and improve physician-patient communication.

Aims: 1) To examine the association between physicians' prognostic assessments and their discussion with patients about hospice. 2) To identify the domains of health-related characteristics of older hospitalized patients and nursing home residents most strongly associated with short-term mortality.

Methods: Following an historical introduction on prognostication, we describe two empiric studies. First, we performed secondary analyses of surveys administered to 215 patients age ≥60 years with advanced cancer, chronic obstructive pulmonary disease, or heart failure that were performed at least every 4 months for up to 2 years, as well as surveys to their respective physicians at least every 6 months. Then we performed a systematic review of prospective studies that evaluated the association between at least one health-related patient characteristic and mortality within one year among patients age ≥65 years. All studies published in English in MEDLINE, Scopus, or Web of Science before August 1, 2010 were eligible. We categorized the characteristics into a series of domains. Using the results of multivariable analyses, we ranked domains within each

study according to strength of association with mortality, then calculated the overall relative strength of each domain as compared to other domains across studies.

Results: Apart from diagnosis of cancer, the factors most strongly associated with hospice discussion in our empiric analysis were physicians' estimate of and certainty about patient life expectancy ($P<0.001$). That said, physicians did not anticipate the deaths of 40% of patients. In the systematic review, we classified characteristics associated with mortality from forty-eight studies into seven domains: cognitive function, disease diagnosis, laboratory values, nutrition, physical function, pressure sores, and shortness of breath. The most important domains for prognostication were nutrition and shortness of breath among general nursing home residents; physical function and shortness of breath among nursing home residents with dementia; disease diagnosis, nutrition, and pressure sores among hospitalized patients for in-hospital mortality; and physical function and nutrition among hospitalized patients for mortality up to one year.

Conclusions: Clinicians' discussion of hospice for patients with advanced illness relies largely on a highly unreliable prognostic approach that involves estimated life expectancy, and many clinicians whose patients might benefit from learning about hospice are not having these discussions. Among a large number of health-related characteristics of older persons shown to be associated with short-term mortality, a few consistently important domains provide broad, easily measurable factors that may promote an approach to prognostication that simply alerts physicians to patients who are at increased risk for mortality, rather than aiming for certainty in life expectancy, thus encouraging physician-patient communication for elderly persons nearing the end of life.

ACKNOWLEDGEMENTS

I thank Dr. Leo Cooney for his invaluable contributions to the systematic review, and Dr. Margaret Drickamer for her review of the final draft of this thesis. I also thank Melissa Grafe for her assistance with historical texts, and Jan Glover and Lei Wang for their assistance with designing the electronic literature search. A portion of this research was supported by the James G. Hirsch, MD Endowed Medical Student Research Fellowship.

“Life is short, the art long,
opportunity fleeting,
experience treacherous,
judgment difficult.”

–Hippocrates, *Aphorisms*

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Historical Introduction

The purpose of this historical exercise, which will be followed by two empiric studies, is not so much to provide a comprehensive account of the thought and practice of prognostication throughout Western medicine, because that would require a great deal more discussion; but rather, to trace the evolution of a word – *prognosis* – and thus support the argument that this venerable and sacred practice of prognostication has lost over time its true appeal and meaning; for the field of medicine, if it truly seeks progress, must look to the past as it looks to the future.

What is the reason for this need to approach medicine, and thus prognostication, with an awareness of historical practice? Does medicine not forge ever onward in its pursuit of knowledge and its ability to heal? The answer lies in the fact that medicine, ever-advancing scientifically, underwent a paradigm shift that directed attention towards individual *diseases* and away from diseased *individuals*, resulting in both tremendous advancements and harmful neglects. In Ancient times and for long after, when the mechanisms of disease had not yet been worked out, an emphasis was placed on the broader manifestations of disease, such as signs and symptoms, for determining prognoses. While this approach may seem oversimplified to the modern reader, it was the best that could be done at the time and served a valuable and cherished purpose when treatments were largely not available. On the other hand, the practice of modern medicine, which understands the histopathological basis for disease, has placed an emphasis on disease diagnosis for determining prognoses. This approach may, too, be oversimplified, especially for elderly patients with comorbid conditions and for whom

treatments often do more harm than good. Although in place for decades, this recent paradigm emphasizing disease diagnosis has become increasingly problematic.

Two Medical Traditions

Although throughout Western history the practice of medicine has varied greatly, appreciating the larger theoretical structures that have informed the practice of medicine over time is essential for understanding the transformation that occurred in prognostication. Indeed, an argument can be made for two largely distinct medical "traditions," separated by a scientific revolution alluded to previously, that have operated under the same name of *medicine* but with decidedly different theoretical bases and emphases.

The first thread of medical "tradition" can be traced from Classical Antiquity until approximately 1800, in which learned physicians fundamentally relied on the writings of their predecessors, recent or distant, in their understanding of health and disease. Scientific knowledge handed down from antiquity went for a long time unquestioned, and even as advances and discoveries were made that sometimes contradicted previous thought, the basic underpinnings of medicine remained the same.[1] A principle example of this is the persistence of the theory of humors, from which the practice of bloodletting was derived.

In the nineteenth century, discoveries were made that forever changed the face of medicine.[2] The acceptance of germ theory brought with it fundamental insights into the mechanisms of disease. Great strides followed, including developments in vaccination and antiseptic practices. A glance at the past exposed glaring errors, and thus the former centuries-old "tradition" of medicine no longer retained its importance or centrality.

While occasional references to the writings of esteemed physicians of the past continued to be made, especially quotes attributed to Hippocrates, such references tended to serve as general "wisdom" in the art of medicine rather than having immediate authority. The rapid advancements of science seemed to cast a shadow over the art of medicine, which, while still present, struggled to adapt to an ever-changing practice as developments exploded into the twentieth century and beyond.

The Decline of Prognosis

An article on prognostication in *Lancet* from 1934 reads: "Of the three great branches of clinical science – diagnosis, prognosis, and treatment – prognosis is admittedly the most difficult. It is also that about which least has been written and of which our knowledge is least systematized." [3] This observation is typical of the second "tradition" of Western medicine, in which a precise understanding of the basis of disease, aided by technological progress, resulted in dramatic advancements in diagnostics and treatment options. The practice of prognosis, on the other hand, did not enjoy the same excited attention. For example, one can see the gradual disappearance of discussions about prognosis from medical textbooks in the twentieth century, whereas during the first "tradition" prognosis was often heralded as something to be cultivated. Although in recent times accurate prognostication has become the target of increased scientific inquiry, attempts to encourage its clinical use have been unsuccessful, especially for elderly persons nearing the end of life. A more thorough discussion of this problem will appear later.

The explanation I would suggest for the decline in status of prognosis is threefold, although essentially a unified concept: first, a transformed understanding of disease

directed attention away from individual patients and towards individual diseases, thus equating prognosis with diagnosis and destroying the tie between prognosis and broader patient characteristics; second, the rise in effective treatments for individual diseases further diminished the need to assess prognosis for individuals with these diseases; and third, prognostication has been perceived as characteristic of the first medical "tradition," which was dismissed by modern science.

Ultimately, in the face of an aging population, physicians would do well to realize that the interplay of comorbid conditions and the often-mixed effects of treatments necessitate the use of signs and symptoms once again, in addition to diagnostics, for the purpose of prognostication. In other words, a careful consideration of both individual *diseases* and diseased *individuals* is required for the restoration of prognosis to the same status as diagnosis and treatment.

In the subsections that follow, prognostication as it has been described in various historical periods will be discussed, with occasional comments about concurrent developments in medicine to provide context.

Classical Antiquity

The body of works attributed to Hippocrates contains several treatises on prognostication, and among these is *On Prognostics*, which contains an excellent overview of the importance of this art in the Ancient practice of medicine: "It appears to me a most excellent thing for the physician to cultivate prognosis; for by foreseeing and foretelling, in the presence of the sick, the present, the past, and the future, and explaining the omissions which patients have been guilty of, he will be the more readily believed to be acquainted with the circumstances of the sick."[4] Notably, the definition of *prognosis*

rendered here is broader than the modern accepted usage. Rather than being limited to predicting the likely course and outcome of illness, it also involves relating to the patient current and prior aspects of that patient's illness. The reason for this becomes clear in his subsequent discussion: that the purpose of prognostication is as much about gaining the trust and confidence of patients as it is about effecting a cure. "Thus a man will be the more esteemed to be a good physician, for he will be the better able to treat those aright who can be saved, from having long anticipated everything; and by seeing and announcing beforehand those who will live and those who will die, he will thus escape censure." The ability to prognosticate, then, was an important means by which physicians could distinguish themselves, demonstrate their worth, and avoid criticism.

To the modern reader, the Hippocratic use of the word *prognosis* might be perceived as heavily contingent upon the concept of *diagnosis*. After all, arriving at the correct diagnosis in modern times generally affords an explanation of the patient's past and present state of health, as well as a prediction for the future. It must be remembered, however, that the understanding of disease in Classical Antiquity was based not on an understanding of "agents of disease" or cellular pathology, but rather on a long-accepted theory of four humors, in which an imbalance of one or more humors would result in a disease state. Thus, prognostication in the time of Hippocrates was rather contingent upon observing the signs and symptoms of illness, and placing them in the context of attributes of the patient, such as age and robustness, to arrive at insights about the past, present, and future course of illness.

Though Hippocrates probably enjoys the greatest renown today among Ancient practitioners of medicine, the central figure in the development of the first medical

"tradition" was probably Galen, who lived nearly five centuries after the time of Hippocrates. Galen's influence was so great that subsequent generations accepted his writings without question. His writings not only documented his own experimental findings, which were considerable in volume, but summarized and synthesized the writing of his predecessors, not the least of which was Hippocrates. Because of the tremendous regard for his work in the centuries that followed, Galen was in effect the "sieve" through which previously known medicine passed onto subsequent generations.[1]

Likewise, with regards to prognostication, his treatise *Of Critical Days* importantly discusses in great detail certain theories that not only indicate some of the practices of the time but would exert a lasting influence.[5] In this treatise, he discusses the concept of crisis, which is the crucial point at which a sick patient either dies or is restored to health. He also describes a method for calculating critical days, or the days in which a crisis is most likely to occur. This method relies entirely upon the principles of astrological medicine, in which the sun and moon were believed to influence the course of illness, for good or bad, in predictable intervals in accordance with their movements with respect to the Earth. Galen's description of astrological technique as a prognostication tool would have influences well into medieval times.

From Medieval to Modern Europe

A great deal of medical texts from Classical Antiquity would have been lost in the centuries that followed, had they not been preserved as part of the Arab-Islamic medical tradition.[1] Indeed, until the late eleventh century, very little changed in the practice of medicine in Europe. It was not until the translation of medical texts from Arabic and

Greek, augmented by the rise of universities, that the tradition begun by Hippocrates and extended by Galen and Arab medicine was introduced into the Latin-speaking world.

One result of this sharing of texts is the *Summary on Crisis and the Critical Days*, a medical work on prognostication written by an anonymous author in the late thirteenth century.[6] It effectively marks the introduction into Medieval Europe of the complex and highly sophisticated astrology described by Galen, as it heavily relies on *Of Critical Days* for its material and frequently cites it. The *Summary on Crisis and the Critical Days* achieved wide popularity among university physicians in the Latin-speaking world over the course of three centuries.

In the sixteenth and seventeenth centuries, a pronounced renewal of interest in Galen and Greek medicine occurred in Europe. Such an interest can be observed in the English text, "Prognostication drawen out of the books of Ipocras, Avicen, and other notable auctours of physycke," printed at least as early as 1550 by Robert Wyer.[7] Noticeably, the use of the word *prognosis* in this text is limited to predicting "whether in peryl of death be in them or not, the pleasure of almyghty God reservyd." An example of its approach to prognostication can be found in the discussion on sweat, here spelled "swete": "Where the swete is, there is the [sickness]. The swete which cometh now and then is nought. Swete with [weakness] of the pulse, is nought. Note swete in the [head], in the continual fever onely is nought. And if it be colde, it betokeneth death." It is unclear for whom this particular publication was intended, but given that in early modern Europe learned medicine was often popularized in the vernacular and used by educated lay people as well as trained physicians (an English statute in the mid-sixteenth century

even legalized the unlearned practice of medicine), it is possible that Wyer published the text for a less discerning population.

Among university-trained physicians, probably the most outstanding work on prognostication in the sixteenth and seventeenth centuries was called *The presages of life and death in diseases: in seven books*, written by Prosper Alpini.[8] This text relies heavily on the Hippocratic and Galenic writings for their descriptions of the methods of prognostication, achieving a comprehensive synthesis. The author claims to have confirmed these methods "not only by the sentiments and opinions of the ancient physicians, but also by a long course of attentive observation and experience." In fact, nearly one hundred pages are devoted to a discussion of critical days and crises, including a description of the astrological origin of the concept of critical days. Alpini's use of the term *prognostication*, unlike that of Wyer, is consistent with the Hippocratic definition found in *On Prognostics*.

At the same time that a renewed interest in Classical Antiquity occurred in the sixteenth and seventeenth centuries, which comprised part of the early modern era in Europe, various challenges against conservatism developed and ran alongside it.[1] The problems of plague and syphilis, which seemed to be "contagious," forced flexibility into the Galenic approach that did not allow for "agents" of disease to be communicated from one person to another. New discoveries were made in anatomy and physiology, including quite influentially the concept of circulation of the blood. Finally, the introduction and acceptance of modern philosophy promoted a "new science," which reduced biological processes to mere mechanical events, removing the mysterious, cosmological component allowed for by Aristotelian philosophy. Overall, it was

increasingly acceptable, even fashionable, to reject Galen's teachings. In contrast to Galen, however, the reputation of Hippocrates was relatively unscathed. While Galen was accused of going beyond experience and thus dogmatically espousing erroneous teachings, Hippocrates was seen as guided by experience and personifying great bedside observation.

The resultant transformation of medical ideology that well over a century of "new science" incited may be seen in a treatise by James Harvey written in 1706, called, *Praesagium Medicum, or, the Prognostick Signs of Acute Diseases*.[9] In the text, signs and symptoms are discussed in exquisite detail with respect to their further characterization, likely cause, and the likelihood of recovery. Although descriptions of the mechanisms of disease are often reminiscent of humoral theory, Harvey decidedly discounts the approach of Classical Antiquity in his discussion of crises and critical days, proclaiming the progress of medicine in its improved knowledge of prognostication: "Everybody knows how religiously critical days were observed by the Ancient physicians. But, later ages have wiped off the dust of antiquity, discovered its infirmities, and enriched the art of physick with closer observations and discoveries…" He specifically discounts astrological medicine, stating that crises and critical days were "not fixed to a certain and determinate number, the moon's motion, or that of any other constellation…" His understanding of crises and critical days, rather, was based upon the inner workings of the body without regard for the influence of the cosmos.

Nevertheless, Harvey's use of the word *prognosis* remains consistent with the Hippocratic definition. In addition to stating the likely outcome associated with particular signs and symptoms, he characterizes them in detail and discusses their causes.

In fact, the minority of the discussion is devoted to predicting the future course of illness. Instead, Harvey emphasizes the importance of not being too specific in prognostication: "A prudent and wary physician therefore will be moderate and ambiguous in his promises, and reserved in his prognostics, unless founded upon certain and infallible signs."

It would seem that Harvey's approach to prognostication is the result of a keen awareness of the Hippocratic writings combined with a heightened scrutiny and skepticism towards certain concepts passed down from Classical Antiquity. His reluctance to offer predictions about the future outcome of illness is perhaps a characteristic of the "new science" that rejected the orthodox explanations of crises and critical days and acknowledged an uncertainty about the timing of recovery or death. Nonetheless, he appreciated the scope of prognostication as defined by Hippocrates and discussed fully the aspects of prognostication where he felt the science had advanced. This advancement was limited, however. Despite the accumulation of greater knowledge during the sixteenth and seventeenth centuries, only rarely did effective new treatments develop. Instead, the focus of scientific progress was on anatomy, physiology, and the mechanisms of disease.

Although the eighteenth century still saw no radical transformation in medical therapeutics, the Enlightenment movement strengthened physicians' ambitions to further medical "progress" through scientific findings, with the ultimate aim to gain better control over nature.[1] Certain strategies, including quantification and classification, allowed for greater objectivity and a more systematic approach to understanding health

and disease. The future loomed large as the science of medicine progressed, although major breakthroughs were still lacking.

Characteristics of the eighteenth century approach to medicine can be found in the treatise, *Observations on the prognostic in acute diseases*, written by Charles Le Roy and published in English in 1782.[10] For instance, there is an attempt to achieve greater precision in prognostication: "In a work of this sort, only by much the smaller number of prognostics, can be as certainties: the rest will vary in their degrees of probability. It has, therefore, been my aim, to adapt my expressions to the degree of probability, which seemed to belong to each prognostic." While the treatise is a tribute to Hippocrates, making frequent reference to him, Le Roy emphasizes the need to verify the observations handed down from Antiquity: "I have very seldom spoken of any prognostics, that I have not seen confirmed in my own practice…"

In the organization of the treatise, and in the use of the word *prognosis*, Le Roy takes very much the same approach found in the Hippocratic writings. An important underlying assumption is that particular signs and symptoms, even if they may be caused by a variety of different diseases, still portend the same prognostic significance and can be addressed in the same way regardless of the underlying disease.

The Nineteenth Century

In the aftermath of the political revolutions of the late eighteenth century, Western society was becoming increasingly fluid, with a growing emphasis on the rights of individuals.[2] This was the milieu in which profound change and upheaval occurred in medicine. On the one hand were physicians who looked to the future and saw "tradition" as something to be avoided; on the other hand were physicians who held fast to

"tradition," even all the way back to Hippocrates, and were suspicious of so-called scientific "advancements." Some saw the time-tested method of acquiring knowledge through clinical observation at the bedside as being threatened by the growth of experimental science. This tension makes Pasteur's achievements as a non-physician scientist all the more remarkable, as he helped define a revolution in medicine through his advocacy of germ theory and his developments in the fields of microbiology and immunology. Although new scientific discoveries often met with resistance and only gradually won general acceptance, the underpinnings of health and disease were profoundly changing.

In *The Sequels of Disease,* written in 1896, Dyce Duckworth offers some insights into the dramatic changes occurring in medicine and their impact on the practice of prognostication: "I venture to state that…in spite of the extraordinary advances made in all branches of the sciences…the attention of physicians has been somewhat inadequately directed to the subject of prognosis in diseases."[11] In fact, Duckworth was unaware of any other work in the nineteenth century purely dedicated to the subject of prognosis. He asserted that so much attention in medicine was being devoted to acquiring accurate factual knowledge that few physicians had taken the time to synthesize and reflect upon the information so that broader observations could be made.

In lamenting the endangered status of prognostication, Duckworth observes a key distinction: "It was in connection with a humoral pathology that prognosis made the greatest progress, and achieved its highest triumphs. The doctrines of solidism on the other hand have uniformly proved inimical to the study of prognosis." It is unclear exactly what he means by this, because he does not go on to explain why "solidism," the

doctrine that cells and tissues are the focus of disease, is not conducive to prognostication.

One can observe, however, that *The Sequels of Disease* is organized in its discussion of prognosis according to disease rather than by sign and symptom. Thus, the discussion becomes quite different: there are no assumptions about particular signs and symptoms having the same prognostic significance regardless of disease, as was the case in Le Roy's work and all the works on prognostication prior to it back to the time of Hippocrates. This new approach reflects the revolution that had occurred in the understanding of pathogens as agents of disease. The science of prognostication, then, was to have a different foundation, and the writings on prognostication prior to the revolution, including the Hippocratic works, would seem less relevant than ever.

The Twentieth Century

The tumultuous era that encapsulated the two World Wars was characterized by a steady growth in medicine.[2] Hospitals grew in size, specialization increased, medical technologies such as x-ray machines and electrocardiographs came into widespread use, and penicillin was developed and successfully aided Allied troops in the later years of World War II. After the war, the field of medicine developed at an unprecedented rate, with immense increases in research funding and extensive drug development. The strong awareness of the past that had characterized the practice of medicine throughout the entire "first" tradition had essentially vanished, as physicians no longer looked to the writings of Hippocrates. An ever-increasing body of knowledge and technological capability was seen as affirmation that progress was being achieved. By the 1970s, however, the public increasingly began to question medical authority, as healthcare

expenses kept escalating and occasional mishaps like the thalidomide tragedy occurred. The surge of new treatment options began to slow by 1980, and it became clear that cures for cancer and other diseases like Parkinson's would be slow in development. Infectious disease, once thought to be nearly a thing of the past, began to reassert itself with drug-resistance; the identification of HIV/AIDs in particular extinguished hopes of eliminating infection. Despite increasing treatment capabilities and financial investments in medicine, the ironic phenomenon of "doing better and feeling worse" arose in the developed West.

Evidence for the decline in attention to prognostication over the course of the twentieth century can be seen quite simply in the evolution of medical textbooks. Nicholas Christakis demonstrated this through a content analysis of a series of editions of *The Principles and Practice of Medicine*, a textbook authored originally by William Osler.[12] From 1892 to 1988, the percentage of chapter lengths devoted to prognosis decreased steadily from about 10% to 0%. He observed that as the discussion of treatment on a topic increased, the discussion of prognosis inversely decreased, presumably because as disease became more treatable the likely outcome became more routine. For highly treatable diseases, then, the need for prognostic considerations was diminished.

In the same article, Christakis argued that the status of prognostication also suffered in the context of an evolving concept of disease during the "Oslerian era." Whereas prior to the time of Osler disease was considered to be highly personal and greatly influenced by the "constitution" of the patient, in the "Oslerian era" a shift occurred towards focusing on the agents of disease. In this way, two very dissimilar

patients infected by the same pathogen could be seen as having the "same" illness, with characteristics of the individuals relegated to the background.

Perhaps a third explanation for the decline of the status of prognostication at the turn of the century was its perception as "unscientific." In *The Evolution of Modern Medicine*, for example, Osler discusses medical knowledge and practice as it developed from the time of the Classical Antiquity to the present, and the only mention of prognostication in the entire volume is in the context of the astrological practices of medieval physicians.[13] Although Osler indeed devoted portions of his medical textbook, *The Principles and Practice of Medicine*, to discussions of prognosis, a close inspection of the final edition written solely by him reveals high variability in whether prognosis is discussed for any given disease.[14] To cite a few examples, the discussion of prognosis for lobar pneumonia is extensive, for typhus fever it is limited to an estimated mortality rate, and for Hodgkin's disease it is absent.

Despite the general decline in attention paid to prognostication over the course of the twentieth century, the topic never disappeared entirely from academic discussion, and even some attempts to foster the general practice of prognostication occurred. The start of the twentieth century seems to have been, at least in part, a time for retrospection. An editorial from the *Journal of the American Medical Association* (JAMA) in 1901 assures readers that prognostication "is not entirely a natural gift, or a mysterious power granted to the few, but that it is just as much the result of reading, study, observation at the bedside and in the deadhouse, and of logical reasoning as is a scientific diagnosis or rational therapy."[15] One physician, in 1904, referring to the legacy of Hippocrates, writes, "The older prognosis, far from being negligible, is really of fundamental

importance. It gives the accumulated experience of ages that, untrammeled by detail, carefully noted broad and elementary features of disease."[16]

In the decades that followed, discussions about prognostication seem to have shifted away from historical contextualization towards improving the science. From 1934 to 1936, an entire series of articles dedicated to disease-specific discussions on prognostication were published in *Lancet*.[3] In 1953, a physician describes prognostication as a "stepchild in medical advance," and insists that "we can do better than we have in the past, or are doing now, by approaching the subject more scientifically and seriously."[17]

That same year, the first prognostic index was developed for patients admitted to the hospital with a myocardial infarction.[18] While the original purpose was to develop a way to quantify patient severity of illness for the purpose of comparing the equivalency of the experimental and control arms of an experiment, this "Pathologic Index Rating" was found to be closely related to mortality rate. Following this initial paper, countless other prognostic indices were developed covering a multitude of patient populations, with newer indices sometimes offering advantages over older ones. An editorial in the *New England Journal of Medicine* in 1971, on the calculation of prognosis, states, "Properly derived, a prognostic index can guide the physician in his discussion with the family. It can provide a basis for evaluating the consequences of medical care and for assessing therapeutic innovation."[19]

Clearly, as evidenced by the exponential development of prognostic indices from the 1950's onward, a promising approach had arrived, one that would ensure the advancement of the science of prognostication. Would this development finally restore

prognosis to the same status in medicine as diagnosis and treatment? The likely answer could be found in an in-depth analysis of a landmark study.

The SUPPORT Experiment

The largest-scale attempt to improve prognostication through a research intervention was the Study to Understand Prognoses and Preferences for Outcomes and Risks of Treatment (SUPPORT), conducted in the mid-1990s.[20] The basis for the intervention was the initial observational finding that discussions and decision making between physicians and patients regarding end-of-life care uncommonly happened substantially before death. Only half of physicians knew when their patients preferred not to have cardiopulmonary resuscitation (CPR), and half of do not resuscitate orders were written within 2 days of death. Furthermore, patients were found to commonly receive aggressive treatment near the end of life: half of patients in their final hospitalization spent at least 8 days in the intensive care unit (ICU), on a mechanical ventilator, or in a comatose state. Finally, pain control was largely inadequate, given that half of able-to-communicate patients reported moderate to severe pain most of the time in their final days.

Based upon the largely unfavorable data on the care patients received approaching the end of life, an intervention was designed to address these deficiencies by providing physicians with accurate prognostic information regarding individual patients, including the likelihood of mortality each day up to 6 months and predictions of future functional ability, as well as providing physicians with patient preferences for end-of-life care. A prognostic model was derived from a population of seriously ill patients who had one of the following diseases: acute respiratory failure, multiple system organ failure with

sepsis or malignancy, coma, chronic obstructive pulmonary disease, congestive heart failure, cirrhosis, colon cancer, and lung cancer.[21] The steepness of the prediction curve used for any given patient was based on the class of disease, and the placement of the curve with respect to the x- and y- axes was based on severity of disease, as calculated from 14 variables easily obtained from hospital records. Thus, the model generated a point estimate of the likelihood of surviving to each day shown on the graph, along with error bars to show variability in these estimates. A unique prediction could be made for a given patient on every reporting day. This model was shown to be about as accurate in its estimates as attending physicians were, but combining the estimate of the model with that of the attending resulted in a much improved estimate over either alone.

The intervention aspect of SUPPORT utilized this model in an attempt to improve the parameters of patient care described above through the provision of timely and accurate prognostic information to physicians and patients, the elicitation of patient preferences for end-of-life care, and the facilitation of communication and planning by a skilled nurse. Despite all these efforts, the experiment was a failure in that it did not improve any of the target outcomes although the study was sufficiently powered to detect small differences. The authors were at a loss to explain the reasons for this. Many hypotheses were generated about potential limitations of the study design, but the ultimate consensus was that none of these limitations could account for the utter lack of change in any measure. Questions were asked about whether physicians and patients even agreed that these measures of end-of-life care were in need of improvement. Perhaps there was nothing wrong with the design of the trial itself, it was suggested, but rather more systemic changes were required before real changes could occur.

Clearly, the failure of SUPPORT was of such epic proportions that one could reasonably suggest the trial's inability to win the hearts of the physicians involved. The task of relaying the prognostic information itself was not a problem, given that reports were automatically provided to physicians and that nurses were hired to discuss prognosis with patients. However, the provision of this information, even in an environment that encouraged discussions, did nothing to change the approach of physicians.

One is tempted to ask about the attitudes of physicians towards the provision of this meticulously calculated but highly statistical prognostic information. Did it actually change their perceptions about the patient's life expectancy? After all, estimates of the model were only as good as the physician's best guess. The additional consideration of combining estimates of the model with physicians' estimates to result in a more accurate prediction at first seems encouraging, but it offers a mixed message to physicians that makes it unclear whether the model can even be trusted, and if not trusted, exactly how much the prediction should be altered. Given that discussions were suggested to be explicitly based on the calculated prognostic information provided, how would physicians explain to patients such alterations in a way that inspires confidence?

Physicians' reservations about offering prognostic estimates to patients were later characterized in a national survey of internists, in which they described prognostication as being "stressful" and "difficult," and believed that patients expect too much certainty and may lose confidence in them if an incorrect prediction is made.[22] Perhaps most revealingly, 90% of physicians believed they should avoid being too specific in their prognostic estimates, which calls into question the very approach of the SUPPORT trial. Thus, evidence suggests that physicians were probably less than enthusiastic about being

offered calculated prognostic estimates and had misgivings about discussing them with patients.

In addition to questioning the approach of offering calculated prognostic estimates to physicians and patients in SUPPORT, one might also wonder about the lack of improvement in communication between physicians and patients. The proportion of patients reporting a discussion about CPR was no different from that of the control group, even though over 40% of patients for whom CPR was not discussed reported that they wished to discuss it. Nor was the proportion of patients reporting a discussion about prognosis with their physician different from that of the control group, although again over 40% of patients not reporting this discussion said they wished to have it. Granted, physician reporting of these discussions was not obtained, allowing for the possibility that patients forgot about conversations or did not recognize them as such; however, such an influence would be expected to affect both the experimental and control groups equally, thus maintaining whatever differences may have resulted from the intervention. Therefore, it seems that while many patients wanted to have these discussions, their physicians were either unaware of it or unwilling to honor the wishes of their patients. Clearly the problem of lack of communication was rooted in more than simply the lack of readily available prognostic estimates.

The SUPPORT trial is the strongest scientific demonstration available that the meticulous provision of prognostic calculations that are as accurate as can be reasonably achieved does not improve communication between physicians and patients, and has no effect on decisions about the aggressiveness of care at the end of life. Supported by evidence from physician survey, there are strong reasons to assert that such calculations

cannot achieve enough accuracy to make physicians comfortable with these sensitive discussions of prognosis for patients approaching the end of life. The provision of detailed estimates that are no better than physicians' estimates and that could perhaps be improved by physicians' estimates introduces a complex psychological game for having end-of-life discussions that is challenging at best.

The Legacy of Prognostic Models for Seriously Ill Patients

Two years after the publication of the primary results of SUPPORT, Joanne Lynn and others published a paper in a low impact journal with data on the limited ability of prognostic models to identify patients near the end of life.[23] Two different models were analyzed for the relationship between median estimates of survival and actual time to death: the SUPPORT model, whose population is described above, and the APACHE III model, whose population consisted entirely of ICU patients.

In the SUPPORT model, the median predicted chance of survival for 2 months was 0.51 (0.31-0.66) 1 week before death, with substantial variations according to disease diagnosis. The APACHE model was slightly less optimistic for the same parameter (0.45 median predicted chance of survival).

The overall conclusion was that in order to make plans about care and properly support patients and families, discussions need to happen while the patient still has a decent chance of surviving the current episode of illness, and that designations of "terminally ill" for the sake of public policy would be necessarily arbitrary and controversial.

Into the Twenty-First Century: Prognostic Indices for Clinical Practice?

The future of prognostication in both clinical research and clinical practice has been unclear for well over a decade. Overall, it would seem that the lessons from the SUPPORT trial were either ill-acknowledged or quickly forgotten: the failure of SUPPORT was followed by a surge of new prognostic models, many of which attempted to identify patients at risk for mortality within 1 year or less. Typically, the information provided in indices generated from these models was less extensive than the information provided to physicians and patients in SUPPORT, and prognostication based on these indices required calculation on the part of the physician.

An editorial on the use of prognostic indices in clinical practice appeared in JAMA in 2001.[24] The authors observed that while prognostic indices are widely developed in clinical research, their use in clinical practice is surprisingly rare. Various challenges in the development and use of prognostic indices were discussed, including the greater difficulty in generating life expectancy estimates as opposed to mortality risk estimates, the difficulty of memorizing the elements of a risk index and calculating a score, the lack of data comparing model estimates against clinician estimates, the lack of explicit advice for applying estimates to clinical decisions, the "fatalism" implicit when factors included in prognostic indices are unmodifiable, and the difficulty patients sometimes have in comprehending probabilities. Overall, the authors declared that "the strongest argument for prognostic indices is that they facilitate professional communication," although such communication of probabilities among physicians is unlikely to dominate the medical field in the near future.

An evaluation of selected mortality prediction tools, published in 2011,[25] demonstrated that most tools have only modest accuracy, with large variation in

discriminating performance when compared in different clinical studies. Even tools that have found wide clinical use, such as APACHE II and MELD score, had inconsistent accuracy when tested in different studies. It was suggested that existing literature may even be biased toward exaggerating the accuracy of these tools since studies with unimpressive results are less likely to be reported or published. Additionally, most mortality prediction tools lack demonstrated clinical utility.

Prognostication for the Elderly

There has been a recent surge of interest in evaluating prognostic models designed for elderly populations. The concurring opinion is that the use of such models in clinical practice is premature. For instance, one systematic review identified a total of 193 models consisting of participants 50 years and older, and found that only 34% of these models were externally validated, and only 2% were validated in more than two studies.[26] Another systematic review identified 16 prognostic indices generated from patient populations whose average age was 60 years or older and that predicted absolute risk of mortality from 6 months to 5 years.[27] It was found that none of the indices had excellent discrimination (C statistic of $\geq$0.90), and only 2 indices were externally validated by researchers other than those who developed the index. The authors concluded that while prognostic indices are potentially useful for influencing clinical decisions that rely on estimated life expectancy, their use cannot be recommended before further studies demonstrate their accuracy in diverse populations and their ability to modify clinical outcomes.

An editorial accompanying the latter systematic review discussed the importance of prognostication for making fully informed clinical decisions.[28] It argued that elderly

populations, who are more likely to have competing comorbidities and decreased life expectancy, can especially benefit from the use of prognostication. For instance, estimates of life expectancy can be directly applied to clinical guidelines as outlined in the systematic review; some examples of decisions related to considerably diminished life expectancy, in addition to the hospice eligibility guidelines, include discontinuation of statins with life expectancy of ≤6 months, and non-operative management of asymptomatic abdominal aortic aneurysms with life expectancy of <1-2 years. The editorial also discussed a number of problems with current prognostic indices. In addition to being premature for clinical use, most indices are designed to generate mortality risk for a specific time interval rather than estimates of life expectancy; the latter approach would be more clinically applicable. Also, there is the problem of the lack of evidence that prognostic indices can improve patient outcomes. Despite these limitations, the editorial argued that clinicians ought to be trained currently in how to use prognostic tools.

The Future of Prognostication for the Elderly

Despite the greater accumulation of prognostic indices for elderly persons over the past two decades, a substantial amount of evidence calls into serious question whether such methods will ever achieve enough accuracy to have more than limited usefulness in the clinical setting. Even if one or more indices eventually manages to gain acceptance by clinical research standards, based on accuracy in diverse populations and improvement of clinical outcomes in randomized controlled trials, it has yet to be shown that doctors will be willing to use these inherently imperfect tools in prognostication for individual patients. One might expect that if these prognostic indices are ever applied to specific

clinical decisions, the higher the stakes of the decision, the less likely doctors will be to use them. For example, they would be especially problematic for identifying elderly persons nearing the end of life for the purpose of discontinuing curative treatments.

What is the underlying problem with prognostic indices? Do they not at least consider more than individual diseases in generating prognostic estimates? Perhaps the problem lies in the *quantification* itself, which not only may give a false impression of accuracy, but also represents a population-based average rather than truly representing an individual.

The future of prognostication for the elderly lies in realizing that certainty is unachievable, especially for persons with comorbid illness and for whom treatments are often problematic. Instead of aiming for an unachievable goal, clinical researchers might seek to use the substantial amount of available scientific evidence in a way that considers broader manifestations of disease, such as signs and symptoms, in addition to disease diagnosis, while deemphasizing quantitative prognostic estimates. This approach draws upon historical perspectives on prognostication, while simultaneously maintaining the scientific rigor that has long characterized clinical research.

STATEMENT OF PURPOSE

Hypotheses:

1) Physicians' decisions to discuss hospice as an option for terminally ill patients are based on a limited approach to prognostication that excludes many patients who may benefit from discussions.

2) Identifying broader domains of health most important for prognostication, as an alternative to calculating life expectancy or mortality risk, might encourage prognostication and improve physician-patient communication.

Aims:

1) To examine the association between physicians' prognostic assessments and their discussion with patients about hospice.

2) To identify the domains of health-related characteristics of older hospitalized patients and nursing home residents most strongly associated with short-term mortality.

PART I: Prospective Cohort Study

While attention to prognostication in medicine has declined over the past century, so that it no longer enjoys a status alongside diagnosis and treatment as it once did, it has regained some consideration in recent years with the development of an ever-increasing number of prognostic models. That being said, the concept of *prognosis* has narrowed significantly since the first medical "tradition," now referring almost exclusively to quantitative estimates of life expectancy or mortality rate. Perhaps the most classic example of the modern use of prognosis is the Medicare Hospice Benefit requirement of a life expectancy of ≤6 months for hospice enrollment,[29] although notably alterations to the eligibility criteria have been suggested in an attempt to more reliably identify persons who would be appropriate for hospice.[30] Proposed characteristics to identify such persons include functional status, quality of life, and burden of symptoms rather than estimates of life expectancy.

Hospice referral is simply one issue among many that physicians face as they attempt to guide patients who are approaching the end of life. Another issue is informing patients about their potential care options, including hospice services. In fact, one identified barrier to hospice use is physicians' lack of discussion about hospice with the patient and family. [31,32] This observation has been supported by retrospective studies, in which caregivers, recalling their conversations with physicians, often deny any communication about hospice or alternative treatment options.[33-35] Such discussions about treatment options may be vital for guiding patients in their transition from being gravely ill to dying.[36]

Although a few studies have examined determinants of patient referral to

hospice,[37-39] no prospective study has examined determinants of discussions about hospice, regardless of whether the patient ultimately utilizes hospice services. Thus, it is unclear what role prognostication has in physicians' decisions to discuss the option of hospice with seriously ill patients.

The aim of this prospective cohort study[40] was to examine patient-and physician-related factors associated with reported hospice discussions, with a particular emphasis on the relationship between physicians' prognostic estimates and hospice discussions.

METHODS

The data set used for this first component of the study was created by Dr. Fried and detailed elsewhere.[41] A description of participants and data collection contributing to the data set appears below.

Participants

Participants of the study were ≥60 years of age and had a primary diagnosis of cancer, chronic pulmonary obstructive disease (COPD), or heart failure (HF). Persons screened for the study were being cared for as inpatients in a Veterans Affairs hospital, a university teaching hospital, and a community hospital; as outpatients in two Veterans Affairs hospitals; and as outpatients in four oncology, three pulmonology, and six cardiology practices in the greater New Haven area. Each of the participating hospitals' human investigations committees approved the study protocol. All patients gave informed consent.

Sequential medical charts were reviewed for the primary eligibility criterion of advanced illness, as defined by the National Hospice Guidelines[42] or those criteria used in

the SUPPORT trial.[43,44] A second eligibility criterion was the need for assistance with one or more instrumental activities of daily living (IADLs)[45]; this was determined by telephone screening and chosen to improve the identification of persons with advanced illness,[46] Patients were required to be full-time residents of Connecticut and have no cognitive impairment as evaluated by a test of executive functioning[47] and the Short Portable Mental Status Questionnaire.[48] Screening and enrollment were stratified according to diagnosis in order to achieve equal numbers of participants with a diagnosis of cancer, COPD, and HF.

Of the 548 persons identified by medical chart review, 30 were not contacted because their physicians declined permission, 24 died prior to telephone screening, 19 declined screening, and 6 could not be reached. Of the persons screened by telephone, 108 were excluded because they were independent in all IADLs, 77 because they were cognitively impaired, and 6 because they were residents of a state other than Connecticut. Of the 279 eligible persons, 51 declined participation and 2 died before enrollment. The final sample consisted of a total of 226 persons, with 82% participation of eligible persons. Participants and non-participants did not differ statistically according to gender, age, or Charlson comorbidity index score,[49] with $P<0.05$ as cutoff. Eight percent of eligible persons with HF declined participation, compared to 19% with cancer and 25% with COPD ($P=0.02$). Of the 226 participants, eight (4%) withdrew after the initial interview, 26 (12%) died before a follow-up interview, and three (1%) were not able to complete follow-up interviews. Of the 124 participants still living one year after initiation of the study, 98 (79%) agreed to participate for the second year.

Patient participants identified the physician primarily responsible for the management of their primary diagnosis. Of 105 physicians identified, 96 (91%) consented to participate and completed interviews for a total of 215 patients. Patient participants whose physician participated in the study did not differ from patients whose physician did not participate, when compared according to age, gender, ethnicity, education, and income. None of the physicians of patients with cancer declined to participate, compared to 15% of physicians for patients with HF and 2% of physicians for patients with COPD and ($P<0.001$). The database used for this study included only the 215 patients whose physicians participated.

Data Collection

Patients were interviewed in their homes every four months for up to two years and immediately following any decline in status, defined by the presence of one of the following: need for assistance with an additional activity of daily living,[50] hospitalization for ≥7 days or resulting in discharge to a nursing home or rehabilitation center, or enrollment in a hospice program. Physicians filled out a survey by mail every six months. For this study, we used the last completed physician survey for each respective patient. To ensure correspondence of information, we used the patient interview that most closely preceded the physician survey.

The outcome variable was whether the physician discussed hospice. We determined hospice discussions by physicians' answer to the question of whether they had discussed hospice with the patient and/or family. If physicians reported not discussing hospice, they were asked to choose from a list of reasons why. We determined receipt of hospice services by patient self-report, which was supplemented by

surrogate report if the patient was too ill to participate in an interview or died during the study.

Descriptive and analytic variables extracted from patient interviews included measures of health, sociodemographic, and psychosocial status. We dichotomized ordinal variables at clinically relevant cut points. Health status variables included self-rated health ("excellent," "very good," "good," "fair," or "poor") and an assessment of symptoms, using the Edmonton symptom assessment scale.[51] Sociodemographic variables included gender, age, education, ethnicity, marital status, living arrangement, and sufficiency of monthly income.[52] Psychosocial variables included perceived prognosis (patients were asked, "If you had to take a guess, how long do you think that you might have to live?," with responses of "<1 month," "1-6 months," "7-12 months," "13-23 months," "2-5 years," "6-10 years," or ">10 years"), overall quality of life ("best possible," "good," "fair," "poor," or "worst possible"),[53] willingness to undergo major or minor therapies if they would restore the patient's current state of health (major therapies were described as "being in the intensive care unit, receiving surgery, or having a breathing machine" and requiring hospitalization of "at least a month," while minor therapies were described as "[receiving] intravenous antibiotics and oxygen," and hospitalization of "a few days to a week"), and awareness of alternatives to hospitalization (patients were asked a series of questions: "If your illness should become worse than it is now, what, if anything, has your doctor told you about how you could be treated?," then, "If you were sick enough that you potentially would need the hospital, do you think that you would have any choices other than being hospitalized?," and if so, "What is/are the choices?," followed by, "If you wanted to stay out of the hospital, do

you know of any services that could help you?," and if so, "What are they?"). Each interview contained the health status and psychosocial variables described above.

Physician surveys included the following descriptive and analytic variables: best prediction of the patient's life expectancy (<1 month, 1-6 months, 7-12 months, 13-23 months, 2-5 years, 6-10 years, or more than 10 years), and level of certainty regarding it (≥99%, >90% certain, 50-90%, 10-49%, <10%, or <1% certain); whether they had told the patient that he or she could die as a result of the disease; and whether they had discussed with the patient his or her life expectancy.

Statistical Analysis

Statistical analyses were performed by Mr. O'Leary. Patient-reported and physician-reported variables were described using frequencies and proportions, with the variables expressed in total and stratified according to diagnosis. Bivariate analysis was used to examine the association between these variables and physician report of hospice discussion, by means of the chi-square test or, in the case of small cell sizes, the Fisher exact test. Variables associated in bivariate analysis with hospice discussion ($P<0.15$) were included in a logistic regression model (gender was entered into the model a priori). Given that physicians' estimates of life expectancy and discussions of hospice were strongly associated, we examined the accuracy of physicians' estimates by calculating the frequency of these estimates among the subset of patients who died during the study.

RESULTS

Patient Population

Patient-related characteristics are shown in Table 1. Although 71% of patients reported their health to be fair or poor, only 12% reported their quality of life to be poor. Patients' estimates of their life expectancy were considerably more optimistic than their physicians' estimates. While 10% of patients believed they had ≤1 year to live, 41% of physicians estimated their patients' life expectancy to be ≤1 year. Of the patients whose physicians made this estimate, the largest proportion had a diagnosis of cancer (76%), as compared to COPD (22%) or HF (19%). Only 14% cited hospice as an alternative to hospitalization, and of these patients, 52% had physicians who reported discussing hospice, suggesting that few patients knew about hospice outside of a conversation with their physician.

Table 1. Characteristics of older persons with advanced illness

Characteristic	Total (N=215)	Cancer (n=79)	COPD* (n=79)	HF* (n=57)
Age, %				
60-69	35	42	37	25
70-79	45	46	43	47
80+	20	13	20	28
Education ≤ 12 years, %	68	63	75	67
Female, %	42	43	49	30
White[†], %	91	92	92	86
Lives alone, %	25	16	27	33
Health perception fair to poor[‡], %	71	68	71	75
Quality of life poor to worst possible[§], %	12	13	13	11
Selected moderate to severe symptoms, %				
Pain[‖]	29	38	19	29
Decreased activity level[§]	63	56	73	60
Depression[§]	13	11	15	13
Shortness of breath[‖]	42	20	71	32
Unwilling to undergo therapies for return to current health, %				
Major therapies[‡]	11	9	14	9
Minor therapies[§]	2	3	1	4
Physicians' estimate of patient life expectancy ≤ 1 year, %	41	76	22	19
Physician reported informing patient of life expectancy, %	30	62	10	14
Patients' self-perceived life expectancy ≤ 1 year[¶], %	10	10	13	7

*COPD = Chronic obstructive pulmonary disease; HF = heart failure

[†] N=214; [‡] N=211; [§] N=212; [‖] N=213; [¶] N=210

Hospice Discussion and Associated Factors

Overall, physicians reported discussing hospice with 22% of patients. The reasons most frequently cited for not discussing hospice were "not terminally ill" (50%) and "prognosis too uncertain" (37%). Patient-centered reasons were less frequently cited, such as "would take away patient's hope" (10%) and "patient wants life-sustaining therapies" (9%) (Table 2).

Table 2. Physician reports of hospice discussion and reasons for not discussing hospice

Characteristic	Total (N=215)	Cancer (n=79)	COPD* (n=79)	HF* (n=57)
Physician discussed hospice with patient or family†, %	22	46	10	7
Reasons for not discussing hospice†, %				
Not terminally ill	50	32	66	55
Prognosis too uncertain	37	29	48	34
Patient would not handle this discussion well	5	0	10	4
Patient wants life-sustaining therapies	9	15	6	5
Would take away patient's hope	10	8	19	2
Services would not benefit patient	9	11	5	13

*COPD = Chronic obstructive pulmonary disease; HF = heart failure

† N=214

Selected patient- and physician-related characteristics and their association with hospice discussion are shown in Table 3. Physicians of patients with cancer were more likely to report a discussion (46%) than physicians of patients with COPD (10%) or with HF (7%) ($P < .001$). Among physicians who estimated their patients' life expectancy to be ≤1 year, 49% reported discussing hospice, compared to only 4% when they estimated a longer life expectancy ($P < .001$). Within the subset of physicians who estimated their patients' life expectancy to be ≤1 year, hospice discussion was reported much more frequently by physicians who were >90% certain about their estimate than by physicians who were less certain (93% versus 40%, $P < .001$). Physicians were more likely to report discussing hospice for patients who self-reported poorer quality of life, moderate to severe pain, a perceived life expectancy of ≤1 year, an unwillingness to undergo minor therapies for a return to current health, and that their physician informed them of their life expectancy. However, 40%-69% of physicians whose patients had these characteristics did not report a hospice discussion. There was no association between hospice discussion and patients' self-rated health or unwillingness to undergo major therapies for a return to current health.

Table 3. Association of patient- and physician-related factors with hospice discussion.

Characteristic (N=215)	Discussion of Hospice (n=48)	No Discussion of Hospice (n=167)	*P*-value
Diagnosis, %			
Cancer	46	54	
Chronic Obstructive Pulmonary Disease	10	90	
Heart Failure	7	93	<.001
Pain*, %			
Moderate to severe	31	69	
None to mild	19	81	.057
Activity level reduction†, %			
Moderate to severe	26	74	
None to mild	17	83	.113
Quality of life†, %			
Poor or worst possible	42	58	
Best possible, good, or fair	20	80	.011
Patient unwilling to undergo minor therapies for return to current health†, %			
Yes	60	40	
No	22	78	.043
Patients' self-perceived life expectancy‡, %			
≤1 year	41	59	
>1 year	20	80	.028
Physicians' estimate of patient life expectancy, %			
≤1 year	49	51	
>1 year	4	96	<.001
Physicians' level of certainty about patient life expectancy when estimate is ≤ 1 year, %			
>90%	93	7	
≤90%	40	60	<.001
Physician reported informing patient of life expectancy, %			
Yes	57	43	
No	7	93	<.001

*N=213; †N=212; ‡N=210

In multivariable analysis, physicians' estimate of patient life expectancy ≤1 year was the strongest determinant of hospice discussion (odds ratio (OR) = 13, 95% confidence interval (CI) = 4.3–39) (Table 4). A cancer diagnosis was independently associated with hospice discussion; other factors associated with hospice discussion in bivariate analysis did not retain their significance. One variable, "physician informed patient of life expectancy," was not entered into the model because of its high correlation with "physician-estimated life expectancy ≤1 year" (Pearson correlation coefficient, >0.3). Another variable, "physician certainty about life expectancy," was not entered into the model because it was measured only among the sub-group of physicians who estimated their patients' life expectancy to be ≤1 year.

Table 4. Multivariable model for characteristics associated with hospice discussion

Variable	Odds ratio (95% confidence interval)
Cancer diagnosis	3.4 (1.3-8.9)
Male	1.9 (0.8-4.5)
Moderate to severe pain	1.0 (0.4-2.5)
Moderate to severe reduction in activity level	1.6 (0.7-4.0)
Fair/poor self-rated quality of life	2.1 (0.6-7.6)
Patient self-perceived life expectancy ≤ 1 year	1.7 (0.5-5.8)
Physicians' estimate of patient life expectancy ≤ 1 year	13 (4.3-39)
Patient unwilling to undergo minor therapies for return to current health	5.2 (0.2-131)

Accuracy of Physician Prognosis

A total of 56% of the patients died during the course of the study, including 77% of patients with cancer, 42% of patients with COPD, and 47% of patients with HF. Of patients who died, 40% had physicians who estimated that their life expectancy was >1 year, within six months before patient death. Stratified according to patient diagnosis, physician overestimate of prognosis applied to 11% of patients with cancer and 68% of patients with COPD or HF.

DISCUSSION

In this study consisting of older adults with advanced cancer, COPD, and HF, physicians reported discussing hospice for nearly one-half of patients with cancer but only a small fraction of patients with COPD or HF. Several characteristics suggesting that patients might benefit from hospice were associated with a greater likelihood of discussion, including moderate to severe symptoms, unwillingness to undergo minor medical interventions, and poorer quality of life, but nonetheless, a considerable number of patients with these characteristics did not have the discussion. Other characteristics of a similar nature, such as poorer self-rated health and unwillingness to undergo major medical interventions, were not associated with hospice discussion. The strongest determinant of hospice discussion was physicians' estimate of and level of certainty about patient life expectancy. Nonetheless, physicians were unable to identify as having a poor prognosis a considerable percentage of patients who subsequently died within six months.

These findings are consistent with a prior study in which physicians reported that the difficulty of prognostication was the foremost barrier to the physician offering hospice.[54] However, in contrast to the prior study, physicians in this study did not cite patient readiness to handle the discussion and preferences for treatment as major barriers to discussion. One conceivable explanation for this discrepancy is that in the current study physicians were asked about specific patients at specific times rather than general barriers to discussion. Nonetheless, given evidence from previous research suggesting a substantial lack of communication between physicians and patients about end-of-life preferences,[20] it is possible that most physicians do not assess whether patients are ready to handle these discussions or willing to undergo major or minor therapies. Given the results of this study, it would seem that patients are often not informed about alternatives to standard therapy because physicians' discussion of hospice is determined largely by their assessment of and level of certainty about patient life expectancy.

The close relationship shown in this study between level of prognostic certainty and hospice discussion appears to imply that more accurate prognostication would enhance physician-patient communication at the end of life. However, substantial research evidence indicates the limited value of a quantitative approach to prognostication for patients approaching the end of life. First, clinical prediction criteria based on National Hospice Organization guidelines for patients with COPD and HF have been demonstrated ineffective in recognizing patients with a life expectancy of six months or less.[55] Second, as previously discussed, providing state-of-the-art prognostic information to physicians in the SUPPORT study did not improve physician-patient communication.[20]

Although communication and care at the end of life will be unlikely to improve with greater prognostic accuracy, nonetheless, the results of this study confirm that they may be improved by adequately addressing the problem of prognostication. Given the relatively narrow approach to prognosis taken in the past century, the practice of prognostication is unlikely to improve significantly without a dramatically new approach that is based on sound science but less statistically oriented. One example of this, as stated above, is the suggestion for altering the Medicare Hospice Benefit requirements to include criteria such as functional status, symptom burden, and quality of life.[30] This alternative approach would potentially include the many patients in this study whose state of health or preferences suggest that they may have benefited from hospice services, but who did not benefit from discussions with their physicians about hospice. However, more research is needed to further support this approach, which may not gain easy acceptance among researchers or policymakers who have primarily focused for decades on a quantitative approach.

One of the limitations of this study is that descriptions of the nature of discussions about hospice were not obtained, including whether physicians simply provided information about services or also made a recommendation; nonetheless, given the large proportion of patients in this study who utilized hospice following the discussion, it would seem that discussions were mainly characterized by the latter. A second limitation is that information was obtained by self-report, with no confirmation as to whether the discussions reported by physicians took place. Physicians, who completed surveys at six-month intervals, may have been asked to recall discussions that took place months prior.

Additionally, desirability bias may have influenced the responses. It is also possible that physicians were more likely to have discussions as a result of participating in the study.

In this study, physicians' decisions to discuss hospice for older persons with advanced illness were influenced mainly by an approach to prognostication that focuses on estimates of life expectancy and the predictability of disease course. It is important for physicians to have such discussions with terminally ill patients so that patients can understand their options and make informed decisions about their care at the end of life. Since prognostication for patients with non-cancer diagnoses has particular limitations, hospice discussions occur primarily for patients with cancer near the end of life. Many persons who might benefit from hospice, as suggested by their health status and treatment preferences, are not having these discussions with their physicians. Based on prior evidence, more accurate prognostication tools are unlikely to improve communication between physicians and patients at the end of life, thus necessitating a different approach to prognostication that is less numerical and more conceptual in orientation.

The next section will further explore the possibilities for a more conceptual approach to prognostication for elderly persons nearing the end of life, by means of a thorough literature review and subsequent synthesis of data.

PART II: Systematic Review

Despite a recent increased interest in prognostication, the practice of it remains rare because of a limited conceptual understanding and approach. As a primary example, prognostic models, which are popular in clinical research but not clinical practice, erroneously strive to achieve a level of certainty about life expectancy that can be applied to individuals. The technical problems with prognostic models are numerous: their overall accuracy is only modest,[25,55], they have not been externally validated in most cases,[26] and they contain varying combinations of specific factors that may not be readily measured in all clinical settings. Furthermore, physicians have reported that they prefer to avoid specific estimates when discussing prognosis with patients,[56,57] which is consistent with evidence from the SUPPORT trial, in which the availability of more accurate prognostic information did not improve communication between physicians and patients.[20] Finally, although physicians generally agree that discussions about end-of-life issues occur too late,[40,58] there is no consensus about what clinical markers might prompt discussions[58,59] and prognostic models of mortality do not provide this information.

Alternatively, a broader understanding of the domains of health most strongly associated with mortality might allow for assessments aimed simply at identifying patients with increased mortality risk, so that a deficit in one of the most important domains would prompt re-evaluation of the approach to care. This alternative may be more acceptable to physicians than calculations of absolute mortality risk, and may be more readily used in time-limited clinical settings. It also serves to broaden the approach to prognostication, which has been severely restricted in recent decades to a quantitative estimate of life expectancy.

A systematic review has the potential to take a comprehensive compilation of all known factors associated with mortality and to identify larger patterns of association across studies. This information may then be used to identify broader categories of health-related characteristics associated with mortality. No such review now exists in the literature, the closest being one review[60] that examined factors associated with a number of outcomes in older hospitalized patients, but their goal was to provide a system for measuring hospital case mix. They evaluated length of stay, discharge destination, and readmission rates in addition to mortality, and they combined in-hospital mortality and mortality up to 2 years following admission as outcomes in their analyses.

The goals of this systematic review were as follows: 1) to identify health-related characteristics of older hospitalized patients and nursing home residents associated with short-term mortality (1 year or less), 2) to classify these characteristics into domains of health, and 3) to determine the relative strength of association of these domains of health with mortality.

METHODS

Data Sources and Searches

Mr. Thomas performed an electronic literature search of all English articles published in MEDLINE (1948-), Scopus (1960-), or Web of Science (1899-) before August 1, 2010 to identify prospective cohort studies on factors associated with short-term mortality in elderly hospitalized patients and nursing home residents. The MEDLINE search used a combination of "filters," consisting of MeSH terms, subheadings, text words, and multi-purpose terms, designed to maximize sensitivity and specificity for this topic. The following filters were used: prognosis studies, mortality, predictors, age, hospitalized patients, and nursing home residents. Modified forms of the same filters were used for the Scopus and Web of Science searches (Table 5).

Table 5. Literature search strategies for MEDLINE, Scopus, and Web of Science

MEDLINE Search Strategy

Prognosis studies filter
1. incidence/
2. exp mortality/
3. Follow-Up Studies/
4. mortality.fs.
5. prognos:.tw.
6. predict:.tw.
7. course.tw.
8. outcome:.tw.
9. 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8

Predictors filter
1. risk:.mp.
2. assess:.mp.
3. predict:.mp.
4. factor:.mp.
5. screen:.mp.
6. probability:.mp.
7. exp risk/
8. 1 or 2 or 3 or 4 or 5 or 6 or 7

Mortality filter
1. exp mortality/
2. exp death/
3. exp survival analysis/
4. Life Expectancy/
5. mortality.fs.
6. death.mp.
7. survival.mp.
8. mortality.mp.
9. die:.mp.
10. 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9

Age filter
1. exp aged/

Prognosis study filter and **Mortality filter** and **Predictors filter** and **Age filter = Combo filter**
Combo filter was then combined with the hospitalized patients filter and with the nursing home residents filter in separate searches.

Hospitalized patients filter
1. hospital:.ti. and (elder: or old: or geriatric:).mp
2. (elder: adj2 hospitali#ed).mp
3. (old: adj2 hospitali#ed).mp
4. (geriatric: adj2 ward:).mp.
5. (geriatric: adj2 unit:).mp.
6. intensive care.ti. and (elder: or old: or geriatric:).mp.
7. inpatient:.ti. and (elder: or old: or geriatric:).mp.
8. geriatric: hospital:).mp.
9. ICU.ti. and (elder: or old: or geriatric:).mp.
10. intermediate care.ti. and (elder: or old: or geriatric:).mp.
11. (ward or wards).ti. and (elder: or old: or geriatric:).mp.
12. ((acute: adj2 hospital:) and (elder: or old: or geriatric:)).mp.
13. 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12

Table 5 (continued). Literature search strategies for MEDLINE, Scopus, and Web of Science

Nursing home residents filter

1. exp Residential Facilities/
2. Long-Term Care/
3. Institutionalization/
4. nursing home:.ti.
5. long-term care.ti.
6. extended care.ti.
7. 1 or 2 or 3 or 4 or 5 or 6

Scopus and Web of Science Search Strategy

Prognosis studies filter
mortality OR "follow up" OR outcome OR outcomes OR prognosis OR prognoses
OR predict OR predicts OR predictor OR predictors

Mortality filter
mortality OR death OR "life expectancy"

OR survival OR "survival analysis" OR "survival analyses" OR die*

Predictors filter
risk OR risks OR screen* OR factor OR factors OR predict OR predicts OR predictor OR predictors

Age filter
elder OR elders OR elderly OR old OR older OR geriatric OR geriatrics

Prognosis study filter and **Mortality filter** and **Predictors filter** and **Age filter = Combo filter**
Combo filter was then combined with the hospitalized patients filter and with the nursing home residents filter in separate searches.

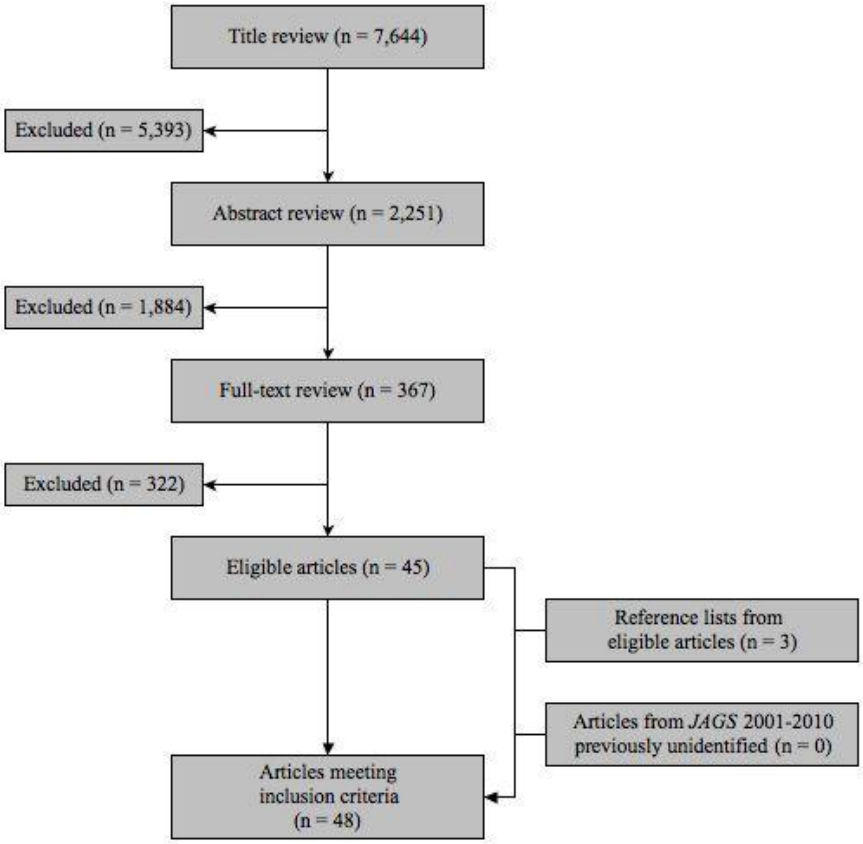
Nursing home residents filter
"Nursing home" OR "nursing homes" OR "long term care" OR "extended care" OR "assisted living" OR Institutionali*

Hospitalized patients filter
Title (hospital* OR ward OR wards OR "intensive care" OR ICU)

Study Selection

A total of 7,644 articles were identified. Of these, 5,393 were excluded by Mr. Thomas through title review, and the remaining 2,251 were reviewed in abstract form by Mr. Thomas and Dr. Cooney independently. The 367 articles appearing to meet inclusion criteria, as presented below, based on review of the abstract alone were then retrieved and examined in full text. Mr. Thomas and Dr. Fried reviewed the articles to determine whether they met inclusion criteria, and consensus was achieved, resulting in a total of 45 articles included in this study. To ensure completeness, the reference lists of the 45 included articles were also reviewed by Mr. Thomas (by title at least, and if necessary, by abstract and full text), resulting in three additional articles. In the same way, all articles published in *Journal of the American Geriatrics Society* from 2001 to 2010 were reviewed by Mr. Thomas, but no additional articles fulfilling inclusion criteria were identified (Figure 1).

Figure 1. Summary of literature search and selection.



The final inclusion list contained 48 articles. These articles were separated into the following categories based on patient population and follow-up period: general nursing home residents, nursing home residents with advanced dementia, hospitalized patients with in-hospital mortality, and hospitalized patients with mortality up to one year following admission.

Inclusion Criteria

Studies were included if their participants were hospitalized patients, long-stay nursing home residents, or nursing home residents with advanced dementia only, regardless of length of stay. Long-stay was defined as residing in the nursing home for at least 3 months, and was specified to avoid cohorts containing patients receiving short-term rehabilitation or other forms of subacute care. We only included studies of persons age 65 years or older, or, if age range was not provided, studies with a population average age of ≥80 years. We only included studies with a prospective cohort design, including studies that use chart or record review in a prospective fashion; studies that examine at least one health-related characteristic, meaning a characteristic inherent to the patient and not involving elements of health care treatment, medical devices, or living location; studies that measure mortality within a follow-up period of one year or less; and studies that contain at least bivariate analysis. The criterion of a follow-up period of one year or less was chosen based on a cursory review of the literature in which a considerable number of studies on mortality specified a follow-up period of one year.

We did not include studies that excluded patients possessing characteristics potentially associated with mortality. Specifically, we did not include studies of nursing home residents that excluded terminally ill persons, those receiving palliative care, or

those with specific illnesses, medications, or nutritional requirements; and we did not include studies of hospitalized patients that excluded nursing home residents, the terminally ill, patients receiving palliative care, those with specific illnesses or abnormalities, those who died in the hospital, or those living outside a prescribed geographical area.

Data Extraction and Quality Assessment

We first sought to identify all markers for short-term mortality, regardless of whether they have independent association with mortality, because of their potential clinical usefulness even if they are subject to confounding. Thus, from all studies fulfilling inclusion criteria, Mr. Thomas generated a list of health-related characteristics associated with short-term mortality in bivariate analysis ($p<0.05$) and organized them according to the categories of patient populations described above.

For the purpose of quality assessment, we modeled a set of six criteria after recommendations specific to prognosis studies in systematic reviews[61] and applied them to the 48 articles meeting the inclusion criteria. Twenty-four articles were determined to be of high quality, in that they fulfill all our criteria (Table 6).

Table 6. Criteria used for assessing quality of articles that met inclusion criteria.

Study population: For patients who could not be interviewed, we required that the self-reported data be sought from proxies.

Attrition: We required that loss to follow-up be no greater than 20%.

Prognostic factors: The reliability of data collection was considered for the following variables: dementia, delirium, malnutrition or malnourishment, and depression. For these variables, clinical assessment rather than medical chart review was required.

Confounders: Because a determination of independent association was not required for this review, we did not include criteria related to confounders.

Statistical analysis: We required that the number of outcomes be at least ten times the number of variables in the model.

Study design: For studies that utilized secondary analysis of previously collected data, we assessed whether the original study was an observational cohort study or a randomized controlled trial. Because randomized controlled trials may not include representative populations,[62] we considered only studies derived from observational cohort studies to fulfill the quality criterion.

Data Synthesis and Analysis

In order to organize the health-related characteristics associated with mortality and allow for broader, more meaningful comparisons, all three investigators (Mr. Thomas, Dr. Fried, and Dr. Cooney) reached consensus in grouping these characteristics into larger aspects of patient health, or domains. Demographic information was not placed in a domain or included in subsequent analyses because the purpose of the review was to focus on health-related factors.

The heterogeneity of study populations, independent variables measured, and statistical methods precluded combining results in a meta-analysis. Therefore, Mr. Thomas and Dr. Fried developed methods of summarizing the strength of association of the different characteristics and domains with mortality across studies, based on the following: 1) the frequency, across individual studies, with which particular health-related characteristics and domains were associated with mortality in bivariate and multivariable analysis; and 2) the relative ranking, within individual studies, of the strength of association with mortality for each domain of health-related characteristics.

Some single studies contained more than one cohort, and some pairs of studies contained identical cohorts. For the data extraction step (performed by Mr. Thomas), we included such instances of repetition to ensure completeness in identifying all characteristics associated with mortality. In the analysis steps (performed by Mr. Thomas), we excluded repetitive data as follows: when studies consisted of both development and validation cohorts, data from the validation cohort was preferentially used, unless analyses were available only for the development cohort; and when studies were found to contain identical or overlapping populations, a single study was chosen

from among them on a case-by-case basis (Table 8).

Individual characteristics were included in the first step of analysis if they were measured in more than one article category or in more than one study within a given category. For every article that evaluated a given characteristic, we noted whether an association was found in bivariate analysis, and if assessed, in multivariable analysis. Then we calculated frequencies by dividing the number of times a characteristic was associated with mortality by the total number of times assessed for both bivariate and multivariable analysis. Finally, we combined the frequencies for all characteristics within each domain to produce an overall calculation of the frequency with which a domain was associated with mortality out of the total number of times assessed in bivariate and multivariable analysis.

In order to accomplish the second step, which summarized across studies the relative strength of association of a given domain compared to the other domains, we developed and executed a method of calculation based on multivariable analysis data. To achieve this comparison, articles containing multivariable analysis were selected, and hazard ratios or odds ratios from these multivariable models were used to rank statistically significant ($p<0.05$) health-related characteristics from highest to lowest association within each study. Health-related characteristics were then linked with their respective domains, and a ranking of the relative importance of domains for each article was generated. If more than one factor was associated with a single domain, the domain was assigned to the strongest factor. Finally, domains that were investigated but did not attain significance in multivariable analysis were placed at the bottom of the ranking list and set equal to each other.

The ranking of domains within each study was then compared across studies to generate an overall ranking of the relative importance of each domain. Specifically, the number of instances a given domain outranked any other domain was divided by the total number of instances in which that domain was ranked against any other domain; this frequency was then multiplied by 100% to achieve a head-to-head ranking percentage (see Table 7 for an example). These percentages, which we will refer to as measures of "relative strength," were then compared to assign importance to domains. This analysis was also performed for the subset of articles assessed to be of high quality.

Table 7. Example of head-to-head domain analysis to determine the relative strength of association with mortality for each domain compared to other domains.

Nursing home residents (all articles regardless of quality)

	cognitive function	disease diagnosis	physical function	nutrition	pressure sores	shortness of breath	**head-to-head totals**
cognitive function		0:3	0:3	0:2	0:0	0:2	0/10 = 0%
disease diagnosis	3:0		2:1	0:2	2:0	0:2	7/12 = 58%
physical function	3:0	1:2		1:1	2:0	1:1	8/12 = 75%
nutrition	2:0	2:0	1:1		2:0	1:1	8/10 = 80%
pressure sores	0:0	0:2	0:2	0:2		0:2	0/8 = 0%
shortness of breath	2:0	2:0	1:1	1:1	2:0		8/10 = 80%

Each ratio in the white boxes above indicates a head-to-head comparison between two domains. To achieve an overall head-to-head ranking percentage for each domain, the number of instances a given domain outranked any other domain was divided by the total number of instances in which that domain was ranked against any other domain; this frequency was then multiplied by 100%.

Since not all domains were examined in all articles containing multivariable analysis, there was greater evidence supporting the "relative strength" of some domains as compared to others. To our knowledge, no criteria exist for evaluating this variation in the amount of evidence for domains. Hence, Mr. Thomas and Dr. Fried devised criteria that consider both quality and quantity of evidence, and made note of each domain that did not fulfill at least one of the following in its respective article category: examined in at least 2 high quality articles, examined in at least 1 high quality article with a participant population of 10,000 or more, or examined in at least 4 articles regardless of quality.

RESULTS

Our literature search identified 48 articles[63-110] published before August 2010 that met the inclusion criteria (Table 8). Nine studies involved general nursing home residents, two studies involved nursing home residents with advanced dementia, 24 studies involved hospitalized patients with in-hospital mortality, and 17 studies involved hospitalized patients with mortality up to one year.

Table 8. Studies on health-related characteristics associated with short-term mortality in the elderly

General nursing home residents

Reference	*Year*	*Country*	*Sample size*	*Follow-up*	*Quality*	*Domains*
Barca et al.[63]	2010	Norway	902	1 year	+	3
Flacker et al.[64]*	1998	USA	780	1 year		5
Flacker et al.[65]†	2003	USA	15,068	1 year	+	5
Grabowski et al.[66]	2005	USA	2,782	1 year	+	1
Kiely et al.[67]*	2000	USA	778	1 year		5
Kiely et al.[68]†	2002	USA	33,188	1 year	+	5
Mooradian et al.[69]	1991	USA	129	4 months	+	1
Perls et al.[70]	1993	USA	1,951	6 months	+	2
Tsai et al.[71]	2008	Taiwan	308	1 year	+	1

*†These pairs of studies used the same population for their respective analyses; the Kiely articles separated analyses by gender and were chosen for exclusion from analysis in this review.

Nursing home residents with advanced dementia

Reference	*Year*	*Country*	*Sample size*	*Follow-up*	*Quality*	*Domains*
Mitchell et al.[72]	2004	USA	4,631	6 months	+	4
Mitchell et al.[73]	2010	USA	222,405	1 year	+	5

Table 8 (continued). Studies on health-related characteristics associated with short-term mortality in the elderly

Hospitalized patients: in-hospital mortality

Reference	*Year*	*Country*	*Sample size*	*Follow-up*	*Quality*	*Domains*
Abizanda et al.[91]	2007	Spain	356	in-hospital	+	1
Agarwal et al.[92]	1988	USA	80	in-hospital		3
Alarcon et al.[74]	1999	Spain	353	in-hospital		2
Bienia et al.[93]	1982	USA	59	in-hospital	+	1
Covinsky et al.[77]	1997	USA	823	in-hospital		2
Eeles et al.[80]	2010	UK	278	in-hospital		1
Gazzotti et al.[94]	2000	Belgium	175	in-hospital	+	5
Incalzi et al.[95]	1992	Italy	308	in-hospital	+	4
Incalzi et al.[96]*	1996	Italy	302	in-hospital		4
Incalzi et al.[97]*	1997	Italy	370	in-hospital		5
Iwata et al.[98]	2006	Japan	1638	in-hospital	+	2
Jonsson et al.[99]	2008	Iceland	749	in-hospital		3
Marengoni et al.[100]†	2003	Italy	923	in-hospital		5
Marengoni et al.[101]†	2008	Italy	596	in-hospital		5
Narain et al.[85]	1988	USA	396	in-hospital	+	2
O'Keeffe et al.[102]	1997	Ireland	225	in-hospital	+	1
Pompei et al.[103]	1994	USA	323	in-hospital		1
Ponzetto et al.[104]	2003	Italy	987	in-hospital		5
Sampson et al.[105]	2009	UK	617	in-hospital	+	3
Sonnenblick et al.[106]	2007	Israel	779	in-hospital	+	4
Stratton et al.[107]	2006	UK	150	in-hospital	+	1
Terzian et al.[108]	1994	USA	4,123	in-hospital	+	2
Zafrir et al.[109]	2010	Israel	333	in-hospital	+	6
Zekry et al.[110]	2010	Switzerland	444	in-hospital		1

*†These pairs of studies appear to have used the same study population for their respective analyses; Incalzi et al. 1997 was chosen for analysis because it evaluated a greater number of domains, and Marengoni et al. 2003 was chosen because it more thoroughly evaluated physical functional measures.

Table 8 (continued). Studies on health-related characteristics associated with short-term mortality in the elderly

Hospitalized patients: mortality up to one year

Reference	*Year*	*Country*	*Sample size*	*Follow-up*	*Quality*	*Domains*
Alarcon et al.[74]	1999	Spain	353	6 months		3
Boyd et al.[75]*	2008	USA	2,279	1 year		1
Buurman et al.[76]	2008	Netherlands	463	3 months	+	5
Covinsky et al.[77]	1997	USA	823	1 year		2
Desai et al.[78]†	2002	USA	524	1 year		4
Drame et al.[79]	2008	France	1,306	6 weeks	+	5
Eeles et al.[80]	2010	UK	278	1 year	+	1
Flodin et al.[81]	2000	Sweden	552	1 year		3
Gonzalez et al.[82]	2009	Chile	542	3 months		3
Inouye et al.[83]	2003	USA	1,246	1 year		5
Laurila et al.[84]‡	2004	Finland	425	1 year		1
Narain et al.[85]	1988	USA	396	6 months	+	4
Persson et al.[86]	2002	Sweden	83	1 year		1
Pilotto et al.[87]	2008	Italy	857	1 year		5
Pitkala et al.[88]‡	2005	Finland	425	1 year		1
Van Doorn et al.[89]†	2001	USA	524	1 year		1
Walter et al.[90]*	2001	USA	1495	1 year		5

*†‡Duplicate study populations were used for these pairs of studies in their respective analyses; Walter et al. and Desai et al. were selected for analysis because they evaluated a greater number of domains, and Pitkala et al. was selected because it included multivariable analysis.

All health-related characteristics associated with short-term mortality in one or more studies are listed in Table 9. We classified the characteristics into seven domains: cognitive function, disease diagnosis, physical function, laboratory values, nutrition, pressure sores, and shortness of breath. Characteristics with ambiguous classification were placed into domains on a case-by-case basis (e.g., albumin was placed under nutrition, and delirium under cognitive function). Since laboratory values were available in studies involving hospitalized patients but not in those involving nursing home residents, and reports of shortness of breath were only available in the latter, each article category contained six domains rather than seven.

Table 9. Patient health-related characteristics associated with short-term mortality in at least one study

General nursing home residents

Cognitive function
Ability to understand or be understood
Change in cognitive status
CPS
Decision-making ability
Decline in cognitive function
Delirium/delirium symptoms
Dementia
Long-term memory impairment
Short-term memory impairment

Disease diagnosis
Acute episode
Anemia
Asthma/emphysema/COPD
Cancer
Congestive heart failure
Cardiovascular diseases
Depression
Detectable TNF levels
Diabetes mellitus
Fever
Physical health rating
Peripheral vascular disease
Renal disease/failure
Stroke
Unstable condition
Urinary tract infection

Physical function
ADL score
Balance problem
Bed rail use
Bedfast all or most of time
Bowel incontinence
Decline in ADLs
Hearing problem
Not awake most of day
Recent fall
Vision problem

Nutrition
>25% of food uneaten
BMI
Chewing problem
Mechanically altered diet
MNA
Refuses fluids
Swallowing problems
Weight loss

Pressure sores

Shortness of breath

Nursing home residents with advanced dementia

Cognitive function
Absence of Alzheimer's disease
Cognitive deterioration
CPS
Hallucinations or delusions
Rarely understood

Disease diagnosis
Anemia
Asthma/emphysema/COPD
Cancer
Cardiac Dysrhythmia
Congestive heart failure
Diabetes mellitus
Edema
Fever
Heart disease
Hip fracture
Hypertension
Infection
No seizure disorder
Non-hip fracture
Oxygen therapy
Parkinson's disease
Peripheral vascular disease
Pneumonia or RTI
Renal failure
Septicemia
Stroke
Unstable medical condition
Urinary tract infection

Physical function
ADL score
Aspirations
Bedfast
Bowel incontinence
Functional deterioration
Not awake most of day

Nutrition
<25% of food eaten
BMI
Chewing or swallowing problem
Insufficient fluid intake
Weight loss

Pressure sores

Shortness of breath

ADLs=Activities of Daily Living; BMI=Body Mass Index; COPD=Chronic Obstructive Pulmonary Disease; CPS=Cognitive Performance Scale; MNA=Mini-Nutritional Assessment; RTI=Respiratory Tract Infection.

Table 9 (continued). Patient health-related characteristics associated with short-term mortality in at least one study

Hospitalized patients with in-hospital mortality

Cognitive function
Cognitive function score
CPS
Delirium (DSM-IV, unspecified)
Dementia (DSM-IV, Carmel Hospital scale)
Level of confusion/ consciousness
MSQ
MMSE
Moderate to Severe Dementia
Short Portable MSQ

Disease diagnosis
4 or more diagnoses
APS
Admission for new problem & exacerbated old problem
Age-comorbidity index
APACHE II score
APACHE score
Atrial fibrillation
Cancer
CCI
Cerebrovascular disease
CIRS co-morbidity

Disease diagnosis (cont'd)
Gastrohepatic disease
GDS
Heart diseases
Index of Coexisting Disease
Index of comorbidity
Infectious disease
Inotropic therapy
Kaplan score
Mechanical ventilation
No operation
Number of additional diagnoses
One or more procedures
Pseudomembranous colitis
Sepsis

Physical function
ADL dependency
ADLs on admission
Barthel index on admission
Instrumental ADLs
Katz scores
Preadmission ADL impairment
Red Cross Hospital FDS
Upper extremity function

Lab values
Cholesterol
Creatinine
Elevated CRP
Fibrinogen
HDL cholesterol
Hemoglobin
Hyponatremia
Leukocyte count
Neutrophil count
Total lymphocyte count
Transferrin
Urea

Nutrition
Albumin <3.5, <3, and <2.8
BMI
Prognostic nutritional index
MUST

Pressure sores

Other
Diastolic blood pressure
Heart rate
Systolic blood pressure

Table 9 (continued). Patient health-related characteristics associated with short-term mortality in at least one study

Hospitalized patients with mortality up to one year

Cognitive function
Delirium (DSM-IV, ICD-10) or duration of delirium
Dementia
MSQ
Short Portable MSQ

Disease diagnosis
Acute or chronic renal failure
APS
Bone marrow failure
Cerebrovascular disease
CCI
CIRS co-morbidity
Congestive heart failure
COPD
Depression
History of myocardial infarction
High risk diagnosis group
Lymphoma/leukemia

Disease diagnosis (cont'd)
Malignancy
Metastatic cancer
Moderate/severe renal disease
Pneumonia
Respiratory failure
Severe PVD
Solitary cancer

Physical function
ADLs on admission, during stay, or at discharge
Barthel index on admission or during stay
Instrumental ADLs
Katz scores
New self-care ADL disability
Pfeffer functional score
Urinary incontinence
Walking impairment

Lab values
BUN
Creatinine
Hematocrit

Nutrition
Albumin <3.5 and <4
BMI
Malnutrition
MNA
MNA Short Form
SGA

Pressure sores
Presence of pressure sores
Pressure sore risk (Norton scale, Exton-Smith scale)

Other
MP

ADLs=Activities of Daily Living; APS=Acute Physiology Score; BMI=Body Mass Index; BUN=Blood Urea Nitrogen; CCI=Charlson Comorbidity Index; CIRS=Cumulative Illness Rating Scale ; CPS=Cognitive Performance Scale; CRP=C-Reactive Protein; FDS=Functional Disability Scale; GDS=Geriatric Depression Scale; MMSE=Mini-Mental State Examination; MNA=Mini Nutritional Assessment; MPI=Multidimensional Prognostic Index; MSQ=Mental Status Questionnaire; MUST=Malnutrition Universal Screening Tool; PVD=Peripheral vascular disease; SGA=Subjective Global Assessment.

Frequency of association of characteristics with mortality across studies in bivariate and multivariable analyses

The 48 studies that met inclusion criteria reported on data from 41 unique populations, so seven studies were excluded from the analysis steps (Table 8). Health-related characteristics selected according to the criteria described in the methods section, and their association with mortality in bivariate and multivariable analysis, are shown in Table 10. Many characteristics that were associated with mortality in bivariate analysis failed to retain significance in multivariable analysis.

General nursing home residents

Poorer physical function, poorer nutrition, and shortness of breath were significant in 100% of bivariate and multivariable analyses. Poorer cognitive function and the presence of pressure sores were associated with mortality in 100% of bivariate analyses but were not significant in any multivariable analyses. Disease diagnosis was associated with mortality in 89% of bivariate analyses and in 56% of multivariable analyses.

Nursing home residents with advanced dementia

All health-related characteristics were associated with mortality in all bivariate analyses. Shortness of breath was significantly associated with mortality in both multivariable analyses. Poorer physical function, pressure sores, and poorer nutrition were significantly associated with mortality in 64%, 50%, and 44% of multivariable analyses, respectively. Disease diagnosis was significantly associated with mortality in only 15% of multivariable analyses.

Hospitalized patients: in-hospital mortality

Pressure sores were significantly associated with mortality in the only study that examined it in both bivariate and multivariable analysis. Poorer cognitive function, poorer physical function, and poorer nutrition were significantly associated with mortality in 100%, 88%, and 88% of bivariate analyses, respectively, and in 64%, 57%, and 45% of multivariable analyses, respectively. Disease diagnosis and poorer laboratory values were significantly associated with mortality in 74% and 75% of bivariate analyses, respectively, and in 36% and 21% of multivariable analyses, respectively.

Hospitalized patients: mortality up to one year following admission

Poorer nutrition and the presence of pressure sores were significantly associated with mortality in 100% of bivariate analyses and in 86% and 50% of multivariable analyses, respectively. Poorer physical function was significantly associated with mortality in 87% of bivariate analyses and 67% of multivariable analyses. Poorer cognitive function, disease diagnosis, and poorer laboratory values were significantly associated with mortality in 69%, 73%, and 50% of bivariate analyses, respectively, and in 54%, 35%, and 50% of multivariable analyses, respectively.

Table 10. Selected health-related patient characteristics and their frequency of association with mortality across studies in bivariate and multivariable analyses

General nursing home residents

	Bivariate Analyses	Multi-variable Analyses
Cognitive function		
All cognitive measures	9/9 (100%)	0/9 (0%)
CPS	1/1 (100%)	0/1 (0%)
Delirium/delirium symptoms	1/1 (100%)	0/1 (0%)
Dementia diagnosis	3/3 (100%)	0/3 (0%)
Short-term memory problem	1/1 (100%)	0/1 (0%)
Disease diagnosis		
All disease diagnoses	17/19 (89%)	9/16 (56%)
Anemia	2/2 (100%)	0/2 (0%)
Cancer	2/3 (67%)	1/3 (33%)
Congestive heart failure	2/2 (100%)	2/2 (100%)
Diabetes	2/2 (100%)	1/2 (50%)
Renal failure	0/0 (0%)	0/0 (0%)
Unstable condition	2/2 (100%)	1/2 (50%)
Physical function		
ADLs	3/3 (100%)	3/3 (100%)
Nutrition		
All nutritional measures	8/8 (100%)	6/6 (100%)
>25% food uneaten	1/1 (100%)	1/1 (100%)
BMI	3/3 (100%)	2/2 (100%)
Swallowing problem	1/1 (100%)	1/1 (100%)
Weight loss	2/2 (100%)	2/2 (100%)
Pressure sores	2/2 (100%)	0/2 (0%)
Shortness of breath	2/2 (100%)	2/2 (100%)

ADLs=Activities of Daily Living; BMI=Body Mass Index; CPS=Cognitive Performance Scale

Table 10 (continued). Selected health-related patient characteristics and their frequency of association with mortality across studies in bivariate and multivariable analyses

Nursing home residents with advanced dementia

	Bivariate Analyses	Multi-variable Analyses
Cognitive function		
All cognitive measures	5/5 (100%)	0/5 (0%)
Absence of Alzheimer's	1/1 (100%)	0/1 (0%)
CPS	1/1 (100%)	0/1 (0%)
Decline in cognitive function	1/1 (100%)	0/1 (0%)
Disease diagnosis		
All disease diagnoses	33/33 (100%)	5/33 (15%)
Anemia	1/1 (100%)	0/1 (0%)
Cancer	2/2 (100%)	1/2 (50%)
Congestive heart failure	2/2 (100%)	2/2 (100%)
Dehydration	1/1 (100%)	0/1 (0%)
Diabetes	2/2 (100%)	0/2 (0%)
Renal failure	1/1 (100%)	0/1 (0%)
Unstable condition	1/1 (100%)	1/1 (100%)
Physical function		
All functional measures	11/11 (100%)	7/11 (64%)
ADLs	2/2 (100%)	2/2 (100%)
ADL decline	1/1 (100%)	0/1 (0%)
Aspirations	2/2 (100%)	0/2 (0%)
Bowel incontinence	2/2 (100%)	2/2 (100%)
Bedfast	2/2 (100%)	2/2 (100%)
Not awake most of day	2/2 (100%)	1/2 (50%)
Nutrition		
All nutritional measures	9/9 (100%)	4/9 (44%)
<25% food eaten	1/1 (100%)	1/1 (100%)
BMI	2/2 (100%)	1/2 (50%)
Swallowing problem	2/2 (100%)	0/2 (0%)
Weight loss	2/2 (100%)	1/2 (50%)
Pressure sores	2/2 (100%)	1/2 (50%)
Shortness of breath	2/2 (100%)	2/2 (100%)

ADLs=Activities of Daily Living; BMI=Body Mass Index; CPS=Cognitive Performance Scale

Table 10 (continued). Selected health-related patient characteristics and their frequency of association with mortality across studies in bivariate and multivariable analyses

Hospitalized patients: in-hospital mortality

	Bivariate Analyses	Multi-Variable Analyses
Cognitive function		
All cognitive measures	15/15 (100%)	7/11 (64%)
CPS	0/0 (0%)	1/1 (100%)
Delirium	3/3 (100%)	2/3 (67%)
Dementia diagnosis	1/1 (100%)	1/1 (100%)
MMSE	4/4 (100%)	3/4 (75%)
MSQ	1/1 (100%)	0/1 (0%)
Disease diagnosis		
All disease diagnoses	35/47 (74%)	17/47 (36%)
Cancer	2/3 (67%)	2/3 (67%)
CCI	4/4 (100%)	0/4 (0%)
GIC	2/2 (100%)	2/2 (100%)
Physical function		
All functional measures	14/16 (88%)	8/14 (57%)
ADLs	6/6 (100%)	4/5 (80%)
Barthel index	2/2 (100%)	1/2 (50%)
Upper extremity function	1/1 (100%)	1/1 (100%)
Laboratory values		
All laboratory values	15/20 (75%)	4/19 (21%)
BUN	1/1 (100%)	0/1 (0%)
Creatinine	2/2 (100%)	1/2 (50%)
Hematocrit	0/0 (0%)	0/0 (0%)
Hemoglobin	1/2 (50%)	0/2 (0%)
Lymphocyte count	2/3 (67%)	1/3 (33%)
Sodium	2/2 (100%)	1/2 (50%)
Nutrition		
All nutritional measures	15/17 (88%)	5/11 (45%)
Albumin	7/7 (100%)	4/6 (67%)
BMI	1/2 (50%)	0/1 (0%)
MNA	1/1 (100%)	0/0 (0%)
Pressure sores	1/1 (100%)	1/1 (100%)

ADLs=Activities of Daily Living; BMI=Body Mass Index; BUN=Blood urea nitrogen; CCI=Charlson Comorbidity Index; CPS=Cognitive Performance Scale; GIC=Geriatrics Index of Comorbidity; MMSE=Mini-Mental State Examination; MNA=Mini-Nutritional Assessment; MSQ=Mental Status Questionnaire

Table 10 (continued). Selected health-related patient characteristics and their frequency of association with mortality across studies in bivariate and multivariable analyses

Hospitalized patients: mortality up to one year

	Bivariate Analyses	Multi-Variable Analyses
Cognitive function		
All cognitive measures	9/13 (69%)	7/13 (54%)
CPS	0/0 (0%)	0/0 (0%)
Delirium	4/6 (67%)	4/6 (67%)
Dementia diagnosis	3/4 (75%	1/4 (25%)
MMSE	0/0 (0%)	0/0 (0%)
MSQ	1/1 (100%)	1/1 (100%)
Disease diagnosis		
All disease diagnoses	29/40 (73%)	14/40 (35%)
Cancer	3/3 (100%)	3/3 (100%)
CCI	3/3 (100%)	2/3 (67%)
Congestive heart failure	2/2 (100%)	2/2 (100%)
GIC	0/0 (0%)	0/0 (0%)
Physical function		
All functional measures	13/15 (87%)	10/15 (67%)
ADLs	4/4 (100%)	4/4 (100%)
Barthel index	3/3 (100%)	2/3 (67%)
Katz score	2/2 (100%)	2/2 (100%)
Upper extremity function	0/0 (0%)	0/0 (0%)
Laboratory values		
All laboratory values	4/8 (50%)	4/8 (50%)
BUN	1/1 (100%)	1/1 (100%)
Creatinine	2/3 (67%)	2/3 (67%)
Hematocrit	1/1 (100%)	1/1 (100%)
Hemoglobin	0/1 (0%)	0/1 (0%)
Lymphocyte count	0/0 (0%)	0/0 (0%)
Sodium	0/1 (0%)	0/1 (0%)
Nutrition		
All nutritional measures	10/10 (100%)	6/7 (86%)
Albumin	2/2 (100%)	2/2 (100%)
BMI	1/1 (100%)	1/1 (100%)
MNA or Short MNA	4/4 (100%)	2/2 (100%)
Pressure sores	2/2 (100%)	1/2 (50%)

ADLs=Activities of Daily Living; BMI=Body Mass Index; BUN=Blood urea nitrogen; CCI=Charlson Comorbidity Index; CPS=Cognitive Performance Scale; GIC=Geriatrics Index of Comorbidity; MMSE=Mini-Mental State Examination; MNA=Mini-Nutritional Assessment; MSQ=Mental Status Questionnaire

Relative strength of association of domains with mortality across individual studies in multivariable analysis

The relative strength of association of each domain with mortality is summarized in Table 11. For each article category, domains that had ≥50% relative strength (Panel A) and ≥75% relative strength (Panel B) were identified, as were those achieving the same in high quality articles alone ("relative strength" defined as the number of instances a given domain outranked any other domain divided by the total number of instances in which the given domain was ranked against other domains, multiplied by 100%).

General nursing home residents

Among all articles regardless of quality, measures of physical function, nutrition, and shortness of breath had ≥75% relative strength, while disease diagnosis had ≥50% relative strength. Among high quality articles only, nutritional measures and shortness of breath had ≥75% relative strength, while disease diagnosis had ≥50% relative strength.

Nursing home residents with advanced dementia

In both the analysis of all articles and the analysis high quality articles only, physical function and shortness of breath had ≥ 75% relative strength, and no other domain had even as much as ≥50% relative strength.

Hospitalized patients: in-hospital mortality

Among all articles regardless of quality, nutrition and pressure sores were the only domains to have ≥75% relative strength, whereas disease diagnosis had ≥50% relative strength. Among high quality articles only, pressure sores solely had ≥75% relative strength, while measures of disease diagnosis had ≥50% relative strength.

Hospitalized patients: mortality up to one year

Disease diagnosis, physical function, and nutrition all had ≥75% relative strength among all articles regardless of quality. Among high quality articles only, physical function and nutrition had ≥75% relative strength.

Table 11. Domains most strongly associated with short-term mortality in multivariable analysis as assessed by calculations of relative strength

Panel A

	cognitive function*	disease diagnosis	physical function	laboratory values	nutrition	pressure sores	shortness of breath
nursing home							
nursing home: with advanced							
hospital: inpatient mortality						†	
hospital: mortality up to one year				†		†	

*All shaded boxes represent ≥50% relative strength (i.e., domains that outranked the other domains in ≥50% of instances that they were compared in multivariable analysis); darker shadings represent that this value was maintained in a separate analysis involving high quality articles only.
†These domains were less commonly examined in articles containing multivariable analysis, so their respective measures of relative strength may be more subject to chance (see methods).

Panel B

	cognitive function‡	disease diagnosis	physical function	laboratory values	nutrition	pressure sores	shortness of breath
nursing home							
nursing home: with advanced							
hospital: inpatient mortality						†	
hospital: mortality up to one year				†	§	†	

‡All shaded boxes represent ≥75% relative strength in head-to-head comparisons with other domains; darker shadings represent that this value was maintained in a separate analysis involving high quality articles only.
†These domains were less commonly examined in articles containing multivariable analysis, so their respective measures of relative strength may be more subject to chance (see methods).
§Nutrition had ≥75% relative strength for high quality articles only, but not for all articles regardless of quality.

DISCUSSION

This systematic review of the literature identified numerous health-related characteristics of hospitalized patients and nursing home residents significantly associated with short-term mortality. Despite the large number of individual characteristics, we were able to group them into a smaller number of clinically meaningful domains: cognitive function, disease diagnosis, physical function, laboratory values, nutrition, pressure sores, and shortness of breath. When we synthesized the results by calculating the relative strengths of domains across studies, based on performance compared to other domains in multivariable analysis within each study, the emerging patterns identified the domains of health that appear to be most important for prognostication. Among general nursing home residents, measures of nutrition and shortness of breath were the most important, while disease diagnosis and physical function were important to a lesser degree. Among nursing home residents with advanced dementia, physical function and shortness of breath were the most important. In the hospitalized elderly, disease diagnosis, nutrition, and pressure sores were the most important for in-hospital mortality; on the other hand, for mortality up to one year following admission, physical function and nutrition were the most important domains, while disease diagnosis had a lesser importance.

A Domain-Based Approach to Prognostication

Although the literature describes a large number of individual health-related characteristics associated with short-term mortality in the elderly, our review identifies a few domains of patient health that are most strongly and consistently associated with mortality across populations of hospitalized patients and nursing home residents. One

possible explanation for this consistency is that characteristics within the most important domains may be summary measures of a patient's health that cut across individual disease diagnoses and other domains as well. It has been suggested that a person's functional status may incorporate aspects of disease burden, cognitive status, and nutritional status.[111-113] Nutritional deficits have been thought to both influence and be influenced by disease burden and functional status.[114,115] Dyspnea, commonly a marker of cardiac and respiratory disorders, may also induce a high degree of disability.[116,117] In this way, it would seem that these domains are interrelated and broadly reflect a patient's state of health. As risk factors for mortality, they may reflect physiologic reserve in the face of disease burden and other deficits. In the context of medical decisions for elderly patients approaching the end of life, our findings are in keeping with prior arguments that an emphasis on disease to the exclusion of other aspects of patient health may result in inaccurate assessments, overtreatments, and mistreatments.[118]

The domains identified in this review as most important can be easily evaluated in any clinical setting and do not necessarily involve calculations or specific laboratory measurements (nutritional measures include not only albumin, but also BMI, swallowing problems, and weight loss). Although a typical geriatric assessment would provide information about these domains,[119] the substantial lack of physicians' evaluation of functional and nutritional status has been shown in studies involving elderly patients in both the primary care setting[120] and hospital setting.[121] Our findings argue for the utility of incorporating these aspects of assessment into the routine clinical evaluation of the elderly patient.

Rather than aiming for precise prognostic estimates, physicians could use these measurements to easily recognize patients for whom an increased risk for mortality might warrant a re-evaluation of the approach to care. Those patients at increased risk would be defined by the presence of impairments in one or more of the most important domains of health, which effectively serve as markers of vulnerability. The recognition of increased risk for a particular patient may, for example, prompt physicians to engage in advance care planning, to discuss hospice as a potential future option in end-of-life care, to evaluate their willingness to undergo major or minor therapies, or simply to exercise more caution in recommending burdensome treatments or marginally beneficial health screening. Other potential topics for discussion include aspects of life choices, such as financial planning and housing arrangements.[59] Notably, this altered approach on the part of the physician would not necessarily require frank discussions about prognosis with patients.

As an additional possibility, physicians might use knowledge of the most important domains of health to frame discussions about prognosis with patients and families. A discussion framed around domains of health may enable patients and families to appreciate the patient's health in a broader context rather than focusing on a specific diagnosis with a potentially uncertain prognostic course. Changes in these domains may also be readily apparent to patients and families, whereas disease progression may not be apparent without laboratory testing or imaging. Such discussions might aid patients in their transition from being seriously ill to dying.[36]

This proposed alternative approach to prognostication addresses concerns physicians have expressed that they are insufficiently prepared to prognosticate or find it

difficult, and that patients expect too much certainty in prognostication and might judge them adversely if the prognosis is inaccurate.[56] A domain-based method of identifying persons at increased mortality risk would be simple for physicians to use because it avoids complex risk calculations composed of various specific measurements that physicians are unlikely to utilize, and it applies to elderly individuals regardless of primary disease diagnosis. Additionally, its inability to generate specific time estimates avoids both the problem of the inaccuracy of mortality risk calculators and the potential for patients to overestimate the accuracy of prognostic calculations. Finally, it parallels recent research suggesting an altered approach to hospice eligibility criteria that involves broader patient characteristics, such as decline in functional status, quality of life, and burden of symptoms.[30] In order for such an approach to be applied to something so specific as hospice eligibility, guidelines involving broader patient characteristics would need to be made, and significantly more research would most likely need to be performed to build a foundation for it.

Considering the Potential Reversibility of Domain Deficits

Identifying abnormalities in the domains of health most strongly associated with mortality introduces the inherent challenge of deciding whether or not intervention is likely to benefit the patient, although admittedly our review does not demonstrate a causal relationship between any domain and mortality. On the one hand, if a patient has an accumulating burden of these factors, interventions would seem less likely to affect the prognosis and may have considerable adverse consequences. Nonetheless, studies have shown that some of these factors can be individually addressed with success, suggesting that for certain persons, these factors could be reasonable targets for

intervention. Several randomized control trials have shown that interventions can prevent physical functional decline in elderly persons both in the hospital and community.[122-124] Pressure sores can be effectively treated, and early prevention measures are important in reducing their occurrence.[125,126] A Cochrane review indicates that protein and energy supplementation may reduce mortality and the risk of complications.[127]

The challenge for future research, then, is to determine for individual patients whether interventions might improve their prognosis. Greater insight into the interplay among the domains associated with mortality would likely aid in this endeavor. Mapping, which seeks to identify the various routes through which elements can precede or contribute to other elements, is a potential way of achieving this. Another possibility is to examine a large cohort of elderly patients and assign to each domain a percent contribution to mortality.[128] Some of the interventional studies previously mentioned that sought to improve patient outcomes could be used to conjecture about the likelihood of any individual intervention having a positive effect on mortality for a patient. Ultimately, the most definitive way to identify patients who would benefit from a multi-component intervention is to design a randomized controlled trial and differentiate elderly sub-populations according to various outcome measures.

Limitations

One limitation to our systematic review is the heterogeneity of study cohorts. While this issue precluded a meta-analysis, we were still able to synthesize the data in a meaningful way by defining strict inclusion criteria regarding study populations. Specifically, we did not include studies whose exclusion criteria eliminated patients with characteristics potentially associated with mortality. Additionally, while our newly

developed method of calculating relative strength of association of domains with short-term mortality is a helpful way of synthesizing cohort study data, there is a risk of oversimplification in categorizing different characteristics under the heading of one domain. Although conclusions about the usefulness of specific health-related characteristics cannot be made based on these calculations, conclusions about the relative importance of domains are more in keeping with this limitation. Furthermore, our first method of analysis involving the frequency with which individual factors were associated with mortality in bivariate and multivariable analyses provides some data comparing characteristics within domains.

Notably, a few seminal studies on mortality risk for hospitalized patients and nursing home residents were not appropriate for the systematic review either because the study population included non-elderly persons or because the follow-up period was longer than our specified limit of 1 year. The SUPPORT prognostic model was developed in a population of adults 18 years or older with severe illness,[43,129] and to our knowledge, the model was never tested in a cohort of elderly patients. While the HELP prognostic model was developed in a cohort of persons 80 years or older, the follow-up period was 2 years.[130] The Charlson comorbidity index, while developed and validated in non-elderly populations,[49] was assessed in several cohort studies included in this review.[77,104,105,110] Finally, the MDS-CHESS scale for nursing home residents had a 3-year follow-up and included non-elderly persons.[131]

Conclusion

This review identifies several domains of particular importance in their association with short-term mortality (defined as mortality within one year or less) in the elderly. These domains, including physical function, nutrition, and shortness of breath, were important when compared to other domains in results of multivariable analysis across studies. Our findings argue for the inclusion of these domains in the general assessment of the elderly patient, despite evidence in the literature that physicians often do not include them in evaluations. They may be especially of value in easily identifying elderly persons whose increased risk for short-term mortality might prompt a re-evaluation of the approach to care. The challenge for future research is to identify patients for whom interventions might improve prognosis by the reversal of domain deficits.

OVERALL CONCLUSION

This thesis approaches the problem of prognostication in medicine with two empiric studies that follow a historical introduction. The introduction traces the shift that occurred in medicine from the first medical "tradition" to the second, the resulting transformation of the concept of *prognosis,* and its decline in status in the practice of medicine. Then a prospective cohort study illustrates the substantial limitations of the currently accepted approach to prognostication with the specific example of physicians' decisions to discuss hospice with seriously ill elderly patients. Finally, a systematic review identifies the domains of patient health most strongly and consistently associated with short-term mortality in the elderly, in an attempt to suggest an approach to prognostication that does not seek estimates of life expectancy.

As historical writings convincingly attest, prognostication has suffered from a tremendous lack of attention and appreciation for more than a century, in the aftermath of a scientific revolution that dramatically advanced diagnostics and treatment options but shifted attention from diseased *individuals* to individual *diseases*. After a long period of virtually no discussion, a movement to improve the science of prognostication through quantification has grown, but it has offered disappointing results in terms of limited accuracy and lack of influence on physician-patient communication. The Medicare Hospice Benefit requirement serves to reinforce this fallacious approach to prognostication. Because prognostication is now largely limited to quantitative estimates of life expectancy, physicians' inherent uncertainty about prognosis is a barrier to communication with patients as they approach the end of life. Prognostication, long proclaimed an essential component in the practice of medicine, now must acknowledge

that certainty about life expectancy is not achievable and alter its focus to assess for broad elements of health that indicate increased mortality risk. This is particularly important for elderly patients, many of whom have comorbid conditions and may be significantly harmed by available treatments, thus making irrelevant the "diagnose-and-treat" approach to medicine that had originally diminished the need for prognostic skills.

The future of prognostication is exciting, but requires a major shift in both clinical research and clinical practice. Unfortunately, the current pursuit of the "perfect" prognostic model has great appeal and heavy momentum behind it despite the disappointing objective evidence. Nonetheless, in the era of an aging population with ever-increasing complexity, it is hopeful that physicians' desire to optimally care for their patients will eventually restore prognostication to its proper and historical place alongside diagnosis and treatment.

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