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COMPUTER AIDED EVALUATION OF EARLY NEOPLASMS

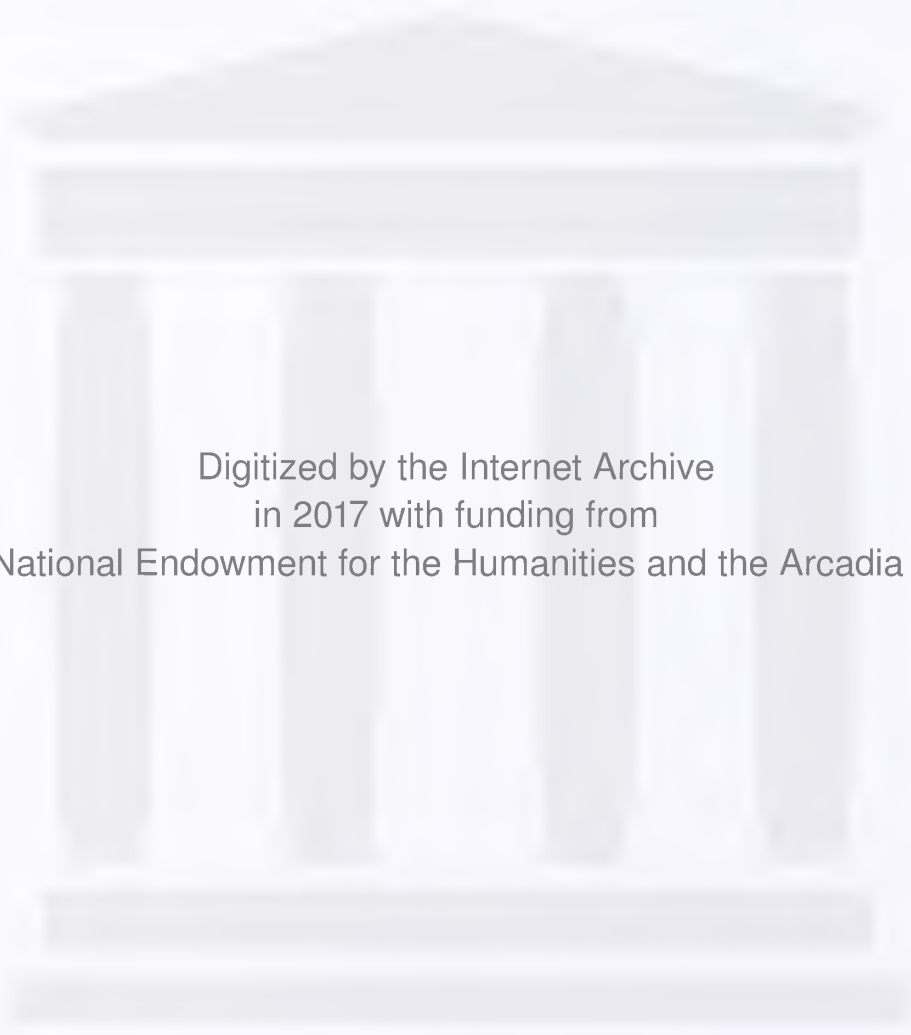
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1987

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Computer Aided Evaluation of Early Neoplasms

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

by

Ian Ainsworth Cook

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ABSTRACT

Computer Aided Evaluation of Early Neoplasms

Ian Ainsworth Cook

1987

This thesis project explores a potential use of microcomputers to encourage the lay public to seek medical care when they first notice clinical evidence suggestive of neoplasms. A model for a clinical decision-making process was constructed: it was hypothesized that a physician's decision to see a patient to rule out a malignancy depends upon a collection of clinical findings which raise his or her "Index of Suspicion" that a neoplastic evaluation is indicated. It was further hypothesized that the degree of suspicion associated with each clinical finding could be quantitatively measured, and that a recommendation about the need to seek medical attention could be formulated from these ratings. To investigate these points, the medical literature was first consulted to formulate a list of clinical findings associated with cancer. Next, data were collected from patients to ascertain how long they delay in seeking care and to determine whether or not they observe the critical findings which signal cancer. Physicians were then surveyed for their impressions of how much each clinical finding contributes to an overall Index of Suspicion, quantitatively measured on a scale of the appropriate urgency of seeing a physician. Finally, a computer program was written to allow a lay person to specify findings which are present and to receive a recommendation, based upon the physicians' data, as to the appropriate course of action. Preliminary testing suggests that use of the computer program can markedly shorten the time-lag between the first appearance of symptoms and efforts to see a physician. The use of this program as a clinical screening test and as a teaching tool are discussed.

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Dedication

to my parents,

Bobette Ringland Cook
1926 - 1984

Charles David Cook

for life, love, and love of life

Computer Aided Evaluation of Early Neoplasms

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Chapter I. Introduction

A. Overview

This research project draws upon the clinical disciplines of oncology, history taking, and clinical decision-making and the basic science disciplines of computer science, clinimetrics, and artificial intelligence to address a clinical problem: how can lay people with cancer enter the health-care system earlier in the course of their disease? The pervasive technology of microcomputers or "personal computers" is brought to bear on this problem by developing a computer program which non-medical people can use as a self-screening tool to evaluate their need to see a professional, based on their own "clinical" observations.

This project comprises four studies which are presented in this paper after a critical review of prior investigations. In Study Phase 1, the clinical literature was culled to create a collection of the physical findings and historical details which might suggest that a patient has a malignancy. Study Phase 2 was conducted to ascertain what factors prompt patients with cancer to see their physicians (the "iatrotropic stimuli") and how long they wait between first appearance of symptoms and seeking care. In Study Phase 3, clinicians were asked to examine 107 possible historical and physical findings and, for each one, to rate how much it raised their "Index of Suspicion" that a patient with that finding might have a neoplasm needing first-hand clinical evaluation. Study Phase 4 applied these clinicians' ratings to the original set of patient data, to

investigate the efficacy of a computer program, based on the Index of Suspicion Ratings (ISRs), in shortening the interval between appearance of symptoms and interaction with a physician. For clarity of presentation, each study is described as a complete unit (methodology, results, and discussion). The implications of this project, both as a teaching tool and as a screening methodology, are discussed in a final, concluding section.

B. Framing the Question

Malignant neoplasms continue to constitute a major health problem in the United States. The American Cancer Society estimates that in 1986, some 930,000 individuals would be newly diagnosed as having a neoplastic disease and that 472,000 people would die from their disease (Silverberg, 1986). It is as Clinical Clerks that medical students are exposed first-hand to this heterogeneous group of diseases. On Ward Rounds, in Conferences, and in the Operating Room, attention is often directed not only to the pathophysiology of a patient's disease, its treatment and prognosis, but also to the clinical presentation of the malignancy. The point is frequently made that, all too often, patients come to medical care when their disease is fairly advanced: large subcutaneous masses, recurring rectal bleeding, persistent hemoptysis, or other signs of systemic or metastatic involvement. While public awareness seems to have reduced the proportion of patients with disease as advanced as what Halsted treated, the lingering impression one retains is that if patients came to attention sooner, their prognoses would be better or, at least, the procedures done could be less disfiguring or disruptive to

their quality of life. This project grew out of such clinical experiences.

The demographic distribution of Americans places a large segment of the population, the "Baby Boomers," into a group which will be at risk for malignant disease over a relatively short span of time (likewise for atherosclerotic coronary artery disease, degenerative joint disease, and other chronic diseases). This segment of the population, now in their 30's and 40's, will begin to have clinical manifestations of malignancies in another decade or so, and thus it could be argued that they should be altered and educated to recognize the earliest signs of neoplastic diseases. Fortunately, the recent "fitness craze" has also taken hold of this cohort, and they may be well primed to discard their parents' traditional notion that "cancer" necessarily equals "death."

Another historical trend has placed this same group in a position to have easy access to an intellectual tool which can potentially aid them in their quest for better health: the personal computer. While at the present time microcomputers serve mainly as engines of commerce, the Baby Boomers have little trepidation about using these tools. (The use of computers by the lay public to help with health issues has been reported with regard to a project in which "Self-Help" groups for smoking cessation were held via "on-line" computer conferences (Schneider & Tooley, 1986).) Although white-collar workers are the main users of PCs today, the notion that computers are the province of upper socio-economic status individuals

is rapidly losing validity as microcomputers are used in public elementary schools and in manufacturing, transporting goods, and other non-white-collar occupations. The importance of these trends is that, by the time they reach their 50's and 60's, the Baby Boomer cohort will be both "computer literate" and "fitness" oriented. This project investigates a way in which the tool of the PC can be harnessed to address the health concerns of an aging population.

C. A Model of Clinical Decision-Making

Iatromathematical enthusiasts could make substantial contributions to clinical medicine if the efforts now being expended on Bayesian and decision-analysis fantasies were directed to the major challenges of algorithmically dissecting clinical judgment, based on the way the judgments are actually performed.

Feinstein, 1977b.

In discussing the clinical diagnosis of diseases using time-honored signs and symptoms, the seasoned clinician often refers to the notion of an "Index of Suspicion," as a degree to which he or she is particularly worried that a given disease may be present in the patient under consideration. In clinically defined syndromes, it is the presence of a cluster of "bedside" findings that determines a diagnosis, without regard to laboratory testing or imaging techniques.

It was the investigator's observation that physicians appear to decide how soon a patient needs a first-hand evaluation on the basis of the clinical or historical findings which the patient reports to the physician. As an example, suppose that a 25 year old man contacts his physician by telephone to report that he has discovered a lump in

his neck. His physician might ask about the lump (is it soft, rubbery, or hard to the touch? painful or not? etc.) and about other important findings (does the young man have active acne on that side of his face?). Upon learning that the mass is accompanied by a recurring fever, drenching sweating at night which requires changing the bedclothes, fatigue, and weight loss, the physician is apt to be suspicious that this individual is manifesting the classic presenting signs of Hodgkin's disease (Wyngaarden, p. 1002). The physician would probably like to see this person in an office visit very soon. On the other hand, if the only findings were a mass and feelings of fatigue, the physician might elect a course of "watchful expectancy" (Feinstein, 1977b) and suggest that the young man call back if these problems persist for more than a few weeks. It appears that the decision of how to pursue a patient's problem is based, at the outset, upon data which the patient provides.

The conjecture was made that if this were the case, then it should be possible to determine formally (at least in part) what the criteria are which clinicians employ in making the judgment of when to see a patient. These criteria were hypothesized to consist of "what findings are worrisome" and "how worrisome are they." The important findings, it was believed, could be ascertained from the medical literature. Determining the degree of suspicion associated with each finding, however, was an exercise in clinimetrics which could best be addressed by directly asking experienced physicians for their impressions, since it is these impressions which were believed to serve as the basis for the clinical decision. It is important to

note that these indices mirror clinical impressions and are not direct reflections of probabilities of the incidence of different neoplasms (a distinction the importance of which will be made clear in the next chapter). Another important point is, as Miller wrote, that "a screening test is not intended to be fully diagnostic. Rather a positive finding will need to be confirmed by special diagnostic procedures" (A.B. Miller, 1982). Thus, the endpoint of such a computer-based screening tool would not be something of the form "you have Hodgkin's disease" but rather "you have the following abnormalities and would be well-advised to see your physician within two weeks." The possibility that a non-neoplastic condition may be the cause of a finding, while critical to programs with diagnostic aspirations, is of much lesser importance to screening tests.

Another point merits comment, especially as it relates to the model employed. Many clinicians are concerned primarily with establishing the correct diagnosis for a given patient (since the choice of the appropriate e.g. pharmacologic therapy follows naturally); many projects to use computers in medicine have paralleled this trend. Surgeons, in general, emphasize not only the importance of the validity of the diagnosis, but also the timing of any needed interventions, be they diagnostic or therapeutic. This focus on the time course of actions is central to the present model and grows naturally out of the clinical interests of surgeons.

A model for this clinical decision-making process was thus constructed. It was postulated that the decision to see a patient (to

rule out a malignancy) depended upon a collection of clinical findings which raise a physician's Index of Suspicion. The degree to which a given finding increases this clinical suspicion could be measured by asking clinicians to apply a quantitative scale to each finding's contribution. This scale would measure "suspicion" in the form of suggestions for the urgency of the need to see a physician. The final recommendation of this model, for any given patient, would reflect the time frame associated with the most worrisome finding. Initially it was believed that not merely the "worst" finding should dictate the recommendation, but that the clustering of several, characteristic findings ought to play a role as well. The model was modified to circumvent this problem by describing some findings with appropriate "pertinent positives and negatives" built into the rating.

The four study phases described in the following chapters detail the process of completing this model with actual clinical data from physicians and applying the model to actual patient cases. Before proceeding to the exposition of these phases, it is worthwhile to review the experiences of other investigators which establish a context for the present work.

Chapter II. Previous Investigations

A. Overview

This project has roots in many, diverse disciplines, and consequently there are many previous investigations which bear some relevancy to the work at hand. The unifying threads which deserve discussion at this point can be grouped into categories of the "uses and abuses" of computers in medicine, the development of automated patient history-taking and screening systems, the uses of computers in clinical decision making, and methods that have been used for screening for cancer.

For many years, the predominant conceptual model associated with computers was that of "number crunchers." Punch cards and reams of green-and-white printouts have done much to further this popular image. In recent times, this notion has been broadened to what might be better described as "symbol manipulation" than as "number crunching." For example, while computed tomography does rely upon many arithmetic operations at the concrete level of photon-count measurements, ultimately it is the radiographic image, with its symbolic levels of white, black, and gray, which is meaningful to a physician. This is a familiar example of how computers can be sensibly used to enhance a physician's activities. The uses of computers in medicine must be examined critically with regard to their sensible use.

B. Uses and Abuses of Computers in Medicine

The incorporation of computers into clinical medicine has not always been smooth. It has been said that "whenever introduced, a new technologic advance has been initially rejected and feared: rejected because of the belief that it could not work, feared because of the suspicion that it might" (Feinstein, 1967). In addition, rejection may occur when the advance is not embraced as "progress" by those for whom it was intended. The history of computers in medicine is an amalgam of positive and negative outcomes, some of which merit recounting here.

In examining past work on using computers in clinical medicine, one should consider that each research project reflects, to some degree, the following hidden assumptions:

- the model of clinical reasoning which those investigators felt was appropriate for the clinical problem at hand (Bayesian, decision-analysis-based, cognitive, etc.; these are described below)
- the desired outcome to the clinical problem (establishing a diagnosis, critiquing a management plan, or guiding therapy)
- the perceptions of how the computer program will help medical care

This last point deserves some special emphasis. Much of the early work on using computers in medicine centered on taking histories and attempting to make diagnoses, and many reports of this work will be discussed below. As Petersdorf has written in another context, at the time of that work (the late 1960's) "... there was an assumption that there was an absolute shortage of physicians; indeed, a decade ago [i.e. 1968] there was general agreement that the country needed at least 50,000 additional physicians by 1980." (Petersdorf,

1978) The "manpower" issue has been addressed both directly (Barnett, 1971) and in passing. Many authors have stated that increasing physician efficiency was an objective of their work, and one may speculate that these early medical computing projects were aimed at alleviating a projected physician shortage. These projects were, in all likelihood, well-intentioned efforts targeted at a widely perceived problem. Nonetheless, critics have found fault with both the aims and procedures of many computer projects. Feinstein observed (1967) that, because clinicians were sub-optimally involved in research involving computers in medicine, "the medical application of computers is now being guided by nonclinical scientists who may understand the machine but not the problems and may produce excellent answers to useless questions." Indeed, this observation raises a crucial policy issue, one which has all too often been left unanswered: what constitutes an appropriate application of computers in medicine? (Cook, 1986) An honest, thoughtful answer must depend upon a close examination of how medical activities are conducted at the present, which things might be done "better" with computer assistance (with careful attention to the definition of "better"), and whether such efforts at computer assistance would be acceptable in terms of enhancing the delivery of care. Computer programs can be of value when they strive to augment the capabilities of physicians to care for patients.

Ten years after Feinstein's commentary, Friedman and Gustafson wrote (1977) that an impediment to widespread use of computers in medicine has been that computer-based medical applications have not

sufficiently augmented physicians' capabilities in acceptable ways:

In mathematics, physics, banking, space exploration, etc., the computer routinely is called upon to perform tasks that all mankind working 24 hr a day from creation could not begin to duplicate, but in medicine our measure of success is diagnostic accuracy approaching a skilled clinician, ECG analysis which is substantially correct, or historical data acquisition which saves the physician 5 min per patient.

Barnett and Greenes have said (1969):

In papers devoted to the problems of hospital information systems, there is often a strong feeling of *deja vu*. For the past decade it has been repeatedly claimed that computers will be of enormous usefulness in patient care and in hospital practice. On innumerable occasions our old men have dreamed dreams and our young men have seen visions. Yet, when we critically examine what is actually implemented in our hospitals, we are most impressed by the number of slow or halting starts, and the number of projects that have been abandoned or in which the objectives have been greatly watered down.

Clearly, some authors have perceived a mis-match between what physicians feel they could use as valued tools, and what research projects have yielded. Indeed, many clinicians find the pursuit of an elusive diagnosis to be rewarding in and of itself, and one must recognize that efforts to deprive them of their "fun" are headed for probable rejection from the outset.

Times have changed, and in Petersdorf's Special Article, he went on to say that the problem, by the late 1970's, was not "... an absolute deficiency of physicians at all, but that they were doing the wrong things in the wrong places. The catchword is 'maldistribution'." Petersdorf asserted that there was an insufficient number of primary-care physicians in the United States. Given the changing needs of physicians in the 1970's and 1980's, there is new value in projects which address the trends that

Petersdorf described by strengthening the conventional channels by which individuals come to see physicians.

C. Automated Patient Histories and Screening

The use of computers to help take a patient's history is an avenue of research which has received much effort in the past several decades, especially in the 1960's. A common goal of the work has often been to increase the efficiency of patient-doctor interactions by minimizing the time spent extracting a detailed history. While the present project has different objectives, several past efforts should be reviewed in this context.

Slack and co-workers at the University of Wisconsin (1966) described a system in which a patient is asked to answer a set of questions (with "yes," "no," "don't know," "don't understand") which are displayed by a computer. Their branching computerized questionnaire was based on the Cornell Medical Index (CMI) health questionnaire (Brodman, 1949) and the Multiphasic Health Checkup of the Permanente Health Group (Collen et al., 1964), and was limited to allergic diseases. A patient's answers could be summarized in a printout which his or her physician could then use. A principal objective was to increase the efficiency of physicians' time (to "... equal the physician history in flexibility and detail while surpassing him in consistency, legibility and economy.")

Brodman and van Woerkom (1966) developed a system to ask detailed questions of patients in order "... to screen patients for

these [100 common] diseases effectively, rapidly, and without strain on the physician's time or facilities." This work at Cornell extended Brodman's earlier development of the CMI and advanced the notion that the significance of each symptom for each of the 100 diseases could be quantitated, based upon statistical measures of the "relative frequency of the symptom in the disease and ... the relative frequency in all patients generally." This program did well in suggesting that particular patients had diseases, by identifying "up to 81% of common diseases and 68% of any diseases diagnosed by highly trained and experience internists in their office practice." They concluded that "... a method like the MDS [Medical Data Screen] can assist the medical profession in obtaining information about the vast reservoir of significant symptoms not spontaneously reported and illnesses undetected to which the medical profession generally does not have access without expending an excessive amount of time. Ostensibly healthy people, as well as those who seek medical care, often harbor such symptoms and illnesses." They note the caution that their screening method

does not rate the clinical importance for the patient of each symptom complex identified, nor does it rate the risk of not recognizing other unidentified disease complexes. Until the storage capacity of a computer approaches that of a human being, and until more is known about the heuristic processes by which a human makes decisions, value judgments like these can be trusted only to a physician. ... [C]linical application of the MDS method can only be as an adjunct to the medical profession in its care of patients.

Mayne, Weksel and Sholtz (1968) commented that "if the time physicians spend in collecting, organizing, recording, and retrieving [clinical] data could be reduced, at least in part, by information technology, more time would be available for actual delivery of

medical care...." They described a system in which a computer-controlled sequence of questions can be administered ("Automated Medical History"); their questions are derived from several questionnaire-based instruments for history-taking. Their branching algorithm was notable because it allowed for follow-up questions (e.g. if abdominal pain were present, the patient would then be asked to select the best description of that discomfort from a list of possibilities). Of 159 patients at the Mayo Clinic who were asked to participate, only three "refused because of an adverse reaction to computer administration." Those who participated expressed an "overwhelmingly favorable" reaction to the program. It is worth noting that this 1960's group had a mean age of 50.1 years and a mean educational level of 11.8 years of schooling completed, hardly a group that would be considered "computer literate" by today's standards.

Slack and Van Cura (1968) also addressed issues of patient acceptance of computers. They studied the reactions of patients to history-taking programs in "allergy, gynecology, and general medicine" at the University of Wisconsin. They found that "patient-machine rapport was quickly established" and that supervising attendants found that "patients were actually enjoying themselves." In their patient sample of 275 individuals, over 90% answered that it was not difficult, boring, or tiring, and that it was interesting. Approximately 80% responded that it was an enjoyable experience. They concluded that there was no correlation between socio-economic background and patient opinion of the system.

Kanner (1969) presented a method for taking a programmed medical history with or without a computer, based upon a pencil-and-paper questionnaire which patients would complete and which might then be typed into a computer for summarization. He wrote "the methods of Slack and of Mayne are excellent, and were it always possible to bring the patient, or informer, and the computer display together, the might be ideal [sic]. Unfortunately, this is not yet economically feasible, nor always practical." His questionnaire at the University of Kentucky was based on Mayne's and those of the Kaiser Permanente group and Lawrence Weed at Cleveland Metropolitan Hospital. Again, the emphasis of the work is on time-efficiency: "Previously, I scheduled 80 minutes of my time for a complete history and physical examination. ... Repeated timing indicates a saving of between 20 and 25 minutes with the PMH [Programmed Medical History]. ... I have been able to perform nearly twice as many complete examinations with no sacrifice in quality of care since development of the PMH."

Mayne's earlier work was followed in 1969 (Mayne et al., 1969, Martin et al., 1969) with a more extensive "Patient Inventory Questionnaire" (PIQ), derived from ten medical history questionnaires. They examined issues of preciseness (i.e. do responses reflect symptoms), reproducibility, completeness, and validity of their pencil-and-paper questionnaire by administering it to 903 patients at the Mayo Clinic. They found that 94% of the patients did submit questionnaires which reflected their symptoms, that on repeated administrations of the questionnaire, patients reported minimally different responses (14.2 average health problems

initially and 13.5 problems on readministration), that patients answered the questionnaires very completely, omitting answers only 5% of the time, and that 94% of the time the questionnaire correctly identified the chief complaint.

Kanner, too, continued his work in the field and reported in 1971 on a "Programmed Physical Examination." In this work, physicians completed a pencil-and-paper questionnaire (1753 questions) with a branching process to limit the number of needed responses (i.e. vital signs and 16 questions for a well individual). The purposes of this project included "efficient use of physician time" and "development of a complete and standardized examination and report" which was easily read.

Grossman, Barnett, and colleagues (1971) evaluated their own system at the Massachusetts General Hospital for collecting patients' histories by computer ("AMH" or Automated Medical History). They found that patients had a favorable attitude toward the system, while physicians' attitudes were mixed. Their program provided for screening patients' symptoms for irregularities which needed follow-up by physicians. They noted that, while a physician may record data from a history in such a way as to "defend his diagnostic hypotheses," and thus uses history-taking "to corroborate a hypothesis," their program's printout was "merely an orderly statement of a patient's perceptions," including all positive findings. They suggested that the mixed reception by physicians was related to the way in which use of their AMH required alteration of

the physician's usual habits.

Hershberg and co-workers (1971) examined the questionnaire used at the Lahey Clinic in terms of sensitivity and specificity measures of validity. They examined 20 "arbitrarily" selected questions and the responses to them. They found that some of their questions ("exertional dyspnea") had lower sensitivity values (37%) than related ones ("one-flight dyspnea" at 59%), and consequently concluded that questions with low yields ought to be rephrased or eliminated.

Slack's group (Bloom et al, 1978), realizing that "dialogue with computers is here to stay," developed a system which would allow non-programmer experts in a field (e.g. physicians) to set-up computer-based systems which would interact with others (e.g. patients). Physicians could use the CONVERSE program to set up a series of "frames," each with text and/or questions and answers, which would appear to the patient in a sequence determined by a logical branching arrangement established by the physician. The methods to summarize the patient's responses could also be specified by the physician. By providing a general-purpose framework, they hoped their work would "enable writers who work with computers to devote less of their time to complicated mechanics [of programming] and more of it to the content and quality of their prose [instructions]."

D. Computers in Clinical Decision Making

Other researchers have concentrated their efforts toward

applying computer-based tools to drawing diagnostic conclusions from patient information rather than simply collecting it. The discipline of artificial intelligence in medicine (AIM) is largely devoted to tasks of modelling the intellectual processes which physicians use in making diagnostic decisions and formulating treatment plans. In contrast to purely statistical or probabilistic computer programs (e.g. Bayesian based programs, discussed below), Clancy and Shortliffe have observed, "medical AI programs are based on symbolic models of disease entities and their relationships to patient factors and clinical manifestations." (Clancy and Shortliffe, 1984, p. 2). A number of past efforts in this field are pertinent to the present project.

In the early 1960s, researchers in AI tended to focus their work along such avenues as game playing (e.g. Chess), image recognition (e.g. robotic vision), and language understanding (e.g. automatic translation). Out of these efforts grew an interest in the underlying ways in which humans organized and used knowledge. The explosive growth of medical knowledge made medical AI a particularly appealing field of endeavor, and many "Computer Consultant" programs were developed. Issues of knowledge representation, acquisition, explanation, and manipulation have been addressed in various ways in each major program. Research efforts may be categorized by the underlying organization of the methods employed.

"Algorithmic methods" are said to be used when the computer program embeds the clinical information used to make decisions

directly into the branching logic of the program. For example, in Bleich's work on electrolyte and acid-base disorders (Bleich, 1972), the information about clinical medicine and how to approach it, was built into the very essence of the program. This method has also been applied to guiding digitalis therapy (Gorry et al., 1978). An algorithmic approach to decision making has been explored for general surgical problems by Norton and Eiseman (1986), although they do not report any use of their algorithms by computer programs. The program described in Phase 4 of this project embeds information about neoplasms in the algorithmic procedures it implements.

"Statistical pattern classification" methods encode information about diseases, symptoms, diagnoses, prognoses, etc., in terms of probabilities of their associations and occurrences. A Bayesian approach (discussed below) was used by the British surgeon de Dombal and his colleagues in a program to diagnose the cause of abdominal pain (de Dombal et al., 1972, Horrocks et al., 1972, Wilson et al., 1975, de Dombal 1979) and by Warner, et al., in evaluating congenital heart disease (1961). Hall provided a general discussion of how Bayes' theorem could be applied clinically (1967). The basic Bayesian method was modified to allow "sequential" application of the method to Warner's heart disease data (Gorry & Barnett, 1968). Gustafson and colleagues developed a statistical approach which used subjectively estimated "patient attribute - disease relationships" to circumvent "the tenuous assumption that input data must be conditionally independent" for conventional application of Bayesian procedures (1973). They applied this to thyroid disorders to classify patients

as hypothyroid, euthyroid, or hyperthyroid based upon subjective estimates of the importance of symptoms, physician signs, and laboratory data, and found that, in comparison with three physicians, the program did not do as well as the best physician or the majority physician opinion, but did better than other computer models.

Many difficulties of a Bayesian approach were detailed in an article appropriately titled, "The haze of Bayes, the aerial palaces of decision analysis, and the computerized Ouija board" (Feinstein, 1977b). Bayesian analysis relies upon knowledge of the probabilities associating a given finding with a given disease, the prevalence of the disease in the population, and the prevalence of the finding in the population. These values, when related by a formula, yield an answer in the form of the conditional probability that a patient with (for example) hemoptysis has lung cancer. The mathematical machinations which yield this sort of a conditional probability are very unlike those used by clinicians. Feinstein pointedly commented:

Anyone who has ever practiced clinical medicine will recognize that the [Bayesian] approach just cited does not resemble even a weird parody of clinical reasoning.

The differences between "natural" clinical reasoning and Bayesian calculations, the different emphasis (a mathematical probability rather than a "diagnostic explanation of clinical evidence"), the different purposes (Bayesian approaches to a diagnosis, rather than to diagnosis and/or treatment and/or watchful expectancy), the need for independency of findings in the Bayesian methods, the pitfalls of estimating the needed probability numbers, and the lack of demonstrable usefulness have all contributed to infrequent adoption

of methods based upon Bayes theorem.

The statistical method known as Decision Analysis was also taken to task (Feinstein, 1977b, Ransohoff & Feinstein, 1967). Schwartz and colleagues developed a decision analysis system for hypertensive patients with possible renal artery stenosis (1973). Pauker and Kassirer have described a decision analysis system which will run satisfactorily on smaller machines, such as personal computers (1981), and more recently summarized the present state of Decision Analysis in medicine (1987). The basic concept in this approach is that, once a clinical algorithm has been formulated, one can be guided to an optimal plan, if one has estimates of the probabilities of each outcome (of the algorithm) and the "utility" of each outcome (or its cost). Difficulties arise in designing a complete algorithm, in establishing probabilities, and in judging utilities.

"Production Rule" methods rely upon the application of "IF ... THEN" rules to encode the knowledge base of the program, be it clinical data for establishing a diagnosis, or antimicrobial agents used for therapy. The MYCIN program was developed at Stanford by Shortliffe as his dissertation project, and refined by an active group thereafter (Shortliffe et al., 1973). Its extensive use of production rules permitted both an explanation of the reasoning process used and expansion of the knowledge base with time. As a simple example, a production rule of

```

PREMISE:  ($AND (SAME (VAL CNTXT GRAM) GRAMPOS)
              (SAME (VAL CNTXT MORPH) COCCUS)
              (SAME (VAL CNTXT CONFORM) CHAINS)
              3)
ACTION:   (CONCLUDE CNTXT IDENT STREPTOCOCCUS TALLY .7)

```


would be a representation of the rule (in English)

IF: The gramstain of the organism is Gram Positive, and
 the morphology of the organism is Coccus, and
 the growth conformation of the organism is chains

THEN: Conclude that the identity of the organism is
 streptococcus (Modifier: the certainty tally for the
 premise times .7)

The MYCIN program was designed to assist physicians not only in identifying organisms, but in selecting appropriate antimicrobial therapy, even when there is uncertainty in the putative organism. Yu et al. (1979) found that, in trials with clinical situations, MYCIN performed well as a consultant, providing courses of action which were deemed acceptable by experts in 14 of 15 cases (with notable differences shown between how Stanford's infectious disease experts manage some infections and how they are managed elsewhere).

The PUFF program for interpreting pulmonary function tests (Aikins et al. 1983) also used the MYCIN-based scheme of production rules, as did a program in the NEUREX project which localized nervous-system lesions (Reggia in Reggia, 1985).

Finally, in a group called "Cognitive Systems," the programs create a complex model both of the clinical information physicians use to think about disease, and of the data concerning a particular patient, and then provide a series of steps linking the two. The INTERNIST program (R.A. Miller et al., 1982) used this method to embrace much of general internal medicine. The PIP program used a cognitive model to evaluate patients with edema, and was developed more to cast light on how clinicians think than to create a usable

tool in the short run (Pauker, Gorry, Kassirer, Schwartz, 1976). But as Miller has remarked, "Feinstein has emphasized the importance of explanation as a part of diagnostic reasoning. INTERNIST-1's greatest failing during the evaluation ... was its inability to attribute findings to their proper causes." (R.A. Miller et al., 1982.)

P.L. Miller has described a different approach to providing useful clinical tools (1984a). His group has developed "Critiquing Systems" which a physician can use to get an opinion on his or her own plan of action. He notes that "this approach casts the computer in the role of the physician's ally, rather than as a potential competitor." Furthermore, "the physician must think through the problem himself ... [and thus] it keeps the physician centrally involved in the decision-making process." Finally, the ATTENDING series of programs provides for incorporating the subjective nature of medical practice (there is seldom a single "right" approach) by providing a critique which encompasses differing approaches ("conflicting advice").

His model accounts for the special role that a consultant plays in "real" clinical medicine:

a specialty consultant is much more than a source of information for a primary physician. A consultant is someone to whom a physician can pass responsibility when confronted by a problem where he feels beyond his depth. In private practice, the consultant frequently takes over that aspect of the patient's care.... A successful computer-advisor is therefore probably best designed to give assistance in a domain where the physician has the basic competence to evaluate the advice given, and is ready to take full responsibility for the patient's care. A computer cardiology advisor, for example, would therefore be designed to assist a cardiologist, or to assist the primary physician only in some aspect of cardiac management where he was expected to be fundamentally competent.

The ATTENDING program has been applied to critiquing and teaching in anesthesiology (P.L. Miller, 1984b), to critiquing the management of essential hypertension (Miller & Black 1984, Miller, Blumenfrucht, & Black 1984), and to critiquing the process of radiological diagnosis (Wetlin et al., 1986, Swett et al., 1986).

Computer aided prognostication was an application which Feinstein and colleagues reported in the early 1970's (Feinstein & Koss, 1971, Koss & Feinstein 1971, Feinstein et al., 1972). Their computer program served as a tool for clinicians to search a database of clinical experience with primary lung cancer patients, in efforts to aid in prognostication and therapy choices. They observed that a physician's prognostic ability normally stems from past experience with other patients who had that disease and their outcomes. They suggested that the size of a physician's own experience often limits his or her ability to find patients whose cases match the present patient's, and that accurate recall of the vast amounts of data from that patient base is taxing if not impossible. Thus their project developed a clinician's tool which would act as a "device for storage, retrieval, quantification, and display of the data needed for [clinical] decisions." A method was developed for storing in a database thorough descriptions of the demographic and clinical qualities of a large group of patients and their subsequent clinical courses. A physician using the program could specify more or fewer critical parameters and their ranges in order to select from the database a group of past patients which the physician believed to be

similar. From these similar case histories, the physician would be able to formulate a better-informed plan. A key feature of this project was the way in which it could expand a physician's experience while fully preserving the clinician's role as interpreter of the data.

The National Cancer Institute has recently provided a clinical tool which similarly places a specialized database at the fingertips of clinicians caring for patients. The Physician Data Query (PDQ) system was described by Hubbard, Henney, and DeVita (1987) as an on-line database describing the current state of the art for cancer treatment protocols. Files on active research protocols and on centers which provide treatments, are all updated monthly. The system was reported to be "designed for physicians who may not be familiar with computers, to permit them to search for and display information without learning a specialized search language." As such, it too serves a useful role in augmenting a physician's knowledge about a clinical problem while preserving the role of the clinician in interpreting the data and making appropriate choices.

E. Cancer Screening

The Breslow's have written critically on the historical perspectives of cancer prevention. They stated (1982) that screening for cancer

involves the application of tests routinely to large numbers of people. With private general physicians insisting on keeping such functions in their offices, and with no financial reimbursement to physicians for screening or other preventive services by prevailing health insurance mechanisms, a technology with demonstrated value may be hindered by lack of a delivery system to exploit it.

Further, they cautioned that "the history of cancer control vividly illustrates Sigerist's admonition not to waste effort by opposing powerful social trends. The interplay of social, political, and economic forces -- as well as technology -- determines the nature and extent of any disease control effort. Cancer is no exception." In recounting efforts at cancer screening and prevention in this century, they tell a story of a road as rocky as that of using computers in medicine. They describe in scathing terms the interplay between gynecologists and pathologists concerning the Pap Smear, the relation between industrial forces and the medical community with regard to mammography, and the role of the tobacco industry lobby in determining policy (Breslow & Breslow, 1982). The overall impression they create is that there is no assurance that a screening test, even one with first rate scientifically documented value, will be accepted if it contravenes powerful societal trends.

Shimkin has commented on the detection and prevention possibilities in oncology (1982). He reiterated the distinction between primary and secondary prevention. Primary prevention is accomplished "by avoiding the [disease-causing] stimulus, or the protection of the organism against the stimulus." In contrast, secondary prevention "includes prevention of complications and sequelae of disease, by earlier detection and institution of therapeutic measures." He noted that "for many cancers, screening procedure either are not available or are not practical or

acceptable. In these, dependence must be placed upon the recognition of symptoms, such as the Seven Warning Signals, that might connote the presence of cancer of one type or another. The identification of an individual with symptoms or with signs that might betoken the presence of cancer places the individual into the more usual clinical setting for a differential diagnosis." He urged that "categorical 'cancer prevention clinics' should be broadened to multiphasic approaches that uncover other health-threatening conditions," since non-neoplastic diseases may often be uncovered by cancer screens. He argued for "the participation of the informed public, not as passive recipients of services but as partners in the planning process." Clearly, methods to enhance the public's ability to participate vigilantly in secondary prevention would serve a useful role in cancer prevention.

Engle discussed the role of history forms and questionnaires in relation to cancer detection (1982). He noted that checklists and forms can be filled out by the physician as a result of taking a history in the traditional (face-to-face) way, that a physician's aide may supervise a patient in completing a questionnaire, or that the physician may "send the patient a questionnaire to fill out before being seen." These all presuppose that the preliminary step is that a patient will (for some reason) contact his or her physician, and that the questionnaire (computer-based or not) follows. When this work was published in 1982, personal computers were regarded as expensive oddities with limited capabilities. The changes since that time would lead one to add that today, a computerized "questionnaire"

could be the initial step which would lead to calling a physician, and that this could take place outside of the doctor's office.

Holleb commented on the role of self-examination in asymptomatic people (1982). He noted that routine periodic health examinations are seldom performed on "'well' people" (which he attributed to a lack of time and interest), and in underserved areas of the country the "detection of asymptomatic early cancer [is] a luxury." He went on to state that

The course of a few cancers may be unaffected by early diagnosis; however, there is convincing evidence that early detection and prompt treatment are directly responsible for cure or longer survival in many types of cancer. [e.g. breast, colon, cervix]

He reiterated the "Seven Warning Signals" promoted by the American Cancer Society:

- Change in bowel or bladder habits
- A sore that does not heal
- Unusual bleeding or discharge
- Thickening or lump in breast or elsewhere
- Indigestion or difficulty in swallowing
- Obvious change in wart or mole
- Nagging cough or hoarseness

He discussed the utility of the Breast Self-Examination, occult blood tests for colon cancer, Papanicolaou and irrigation smears for cervical cancer and sputum cytology for lung cancer (which has a more questionable benefit), and noted that "because the American public seems to want to participate in health programs, more and more 'do-it-yourself' techniques have been promoted [occult blood, cervical irrigation]." As a secondary benefit, the present project can serve as an adjunct to these screens by promoting awareness of them in the lay public.

The American Cancer Society has formulated recommendations for screening asymptomatic individuals for cancer, and reported on patterns of physician utilization of these guidelines (American Cancer Society, 1985). These recommendations are reiterated in Figure 2.1.

In summary, computers have been used as clinical tools with mixed results. The fruition of many projects was limited by lack of general acceptance in the medical community for a host of reasons: obscure methods, unclear clinical utility, misjudged expectations for clinical relevancy, esoteric aura, high costs, and unproven benefit, among others. By emphasizing clinical relevance and closely following the existing clinical traditions, one might develop a more acceptable tool, for if a program is intuitively unappealing to clinicians, no amount of statistical demonstration of utility will cause a stampede toward its widespread adoption.

Given that a screening test does not so much aim to arrive at a definitive diagnosis as to raise warning flags, it would appear that a useful and different clinical tool would be a program which closely emulates the clinical approach to screening, provided it actually could increase the speed with which patients receive care.

Chapter III. Study Phase 1: Historical and Physical Findings and Neoplasms

A. Introduction

In the initial phase of this project the clinical literature was culled to determine a set of the physical findings and historical details which might suggest that a patient has a malignancy. Because this set of findings forms the basis for all phases of this research project, its derivation merits a brief description, even though this phase is not experimental in nature.

B. Methodology

Numerous texts on clinical evaluation were consulted to determine if a consistent set of findings could be assembled. DeGowin and DeGowin's Bedside Diagnostic Evaluation, Blacklow's MacBryde's Signs and Symptoms, Wyngaarden and Smith's Cecil Textbook of Medicine, Harrison's Textbook of Medicine by Petersdorf et al., Principles of Surgery by Schwartz, Shires, Spencer and Storer, Sabiston's Textbook of Surgery, and Clinical Oncology for Medical Students and Physicians from the American Cancer Society served as major resources. These tomes were consulted at length and an assemblage of potential findings formulated empirically. A preliminary list of findings was discussed with several clinicians who suggested ways to clarify the prose description of each finding.

C. Outcome

Figure 3.1 enumerates the set of 107 findings which were drawn

from the literature. They are grouped into a set of constitutional findings and 13 more sets by organ system. Nine fundamental constitutional findings are augmented with specific associated circumstances (e.g. "fever" vs. "fever between 101 and 104 degrees, persisting for more than two weeks, and not associated with another illness (cold, sorethroat, etc.)"). Organ system groupings range from two to 18 findings each.

D. Discussion

In the development of this list, concern was expressed by senior clinicians over the completeness of description for several findings as it relates to the specificity of a finding for cancer. For example, a finding of "hoarseness" could have many etiologies, very few of them neoplastic. The common cold, an evening at a black-tie gala with many cigarette smokers, an afternoon at a football game, or speaking at Grand Rounds, could all lead to the presence of hoarseness without the suspicion of a malignancy. To accommodate these important distinguishing features, the carefully-worded descriptions were formulated and incorporated into the final list presented in Figure 3.1.

These findings were chosen to be discernible by individuals who had no special medical training. Prose descriptions were formulated to avoid the obfuscation encountered when precise medical terms are used to communicate with lay people.

In summary, the work of Phase 1 produced a set of 107 clinical findings which appeared to be of use in detecting the presence of a

malignancy. That being accomplished, the research project next turned to investigating the real usefulness of these findings in a clinical setting.

Chapter IV. Study Phase 2: Patients as Observers

A. Introduction

The second phase of the investigation was conducted to determine whether or not patients with neoplasms are able to detect physical or historical findings which would be suggestive of their diseases. If patients are, as a group, insufficiently observant to detect the important findings, then it would be futile to provide the lay public with a computer program which depended upon these observations.

Data from patients was needed to address two additional questions: how long do patients wait between noticing something abnormal (if anything), and seeking medical care? This interval is important because the efficacy of early detection through physical and historical findings depends upon shortening this time period. Finally, the list of findings from Phase 1 needed to be evaluated in the light of real clinical data to see if it formed a sufficiently tight "mesh" to detect a worthwhile fraction of those with cancer.

B. Study Methodology (HIC # 3732)

To examine the issues outlined above, patients with diagnosed neoplasms were invited to participate in this study phase. They were asked to complete a brief written questionnaire while waiting to be seen in an out-patient clinic at Yale-New Haven Hospital. The questionnaire was designed to elicit information regarding what the patient had noticed (clinical signs) which led him or her to seek medical care, what knowledge deficit he or she might have had with

regard to the underlying disease, and how long the individual delayed before seeking care and the factors which contributed to this delay. Additional opportunities were provided for patients to indicate if there were social factors affecting their perceptions of the diseases, and to describe the general degree of involvement the patients had with their health care. A sample questionnaire is shown in Figure 4.1. This is appropriate to note that the questions posed were mainly open-ended, rather than forced choice. Thus, the findings which patients cited were volunteered, rather than being selected from a checklist of what were believed to be useful findings.

These questionnaires and methods for their administration were approved by the Human Investigations Committee for use in an out-patient clinic setting (HIC Protocol #3732). These questionnaires were available in the Comprehensive Cancer Clinic for medical oncology patients and in the Dana Surgical Clinic for patients seen by surgical oncologists. Large, colorful posters in the clinic explained the project to potential participants, inviting them to help others by sharing their experiences anonymously and confidentially. A supply of blank questionnaires, writing implements, and a box for returning completed questionnaires were located adjacent to each poster and were restocked regularly by the investigator. Patients were asked to place their completed questionnaires into the box without providing their names, hospital unit numbers, or other identifying information.

Data were collected for a period of 100 clinic-days, consisting of 59 days in the Comprehensive Cancer Clinic and 41 days in the Dana

Surgical Clinic, all between January 20 and April 16, 1986.

The data from returned questionnaires were entered into a computerized database for tabulation and analysis with the aid of an analysis program (Reflex: the Analyst, Borland Int'l, Scotts Valley CA). Data were stored and analyzed on a microcomputer (IBM-PC. IBM Corp., Armonk NY).

C. Results

During the study period, 77 patients returned questionnaires. The distribution of patients with regard to age, gender, clinic, and diagnosis are presented in Figure 4.2. Of these individuals, 19 were men and 58 were women (1:3). In absolute figures, more patients completed questionnaires in the CCC than in the Dana Clinic (44 vs. 33); this represents a normalized rate of 0.75 questionnaires per day in the CCC and 0.80 in Dana. The most commonly diagnosed neoplasm was breast cancer (33 of 77 patients or 43%), including one male patient.

Critically, of the 77 respondents, 74 stated they had experienced findings which appeared on the extensive list compiled from the literature (96%). No patients reported findings which were not on the list. There were twelve patients whose findings were not detected by themselves but rather found by physicians; of this dozen, nine (75%) provided evidence that they could have been self-detected had they known the "Warning Signals" of cancer. The remaining three patients (of 77 or 4%) were asymptomatic and were detected solely by lab tests. These were a 65 year old woman with chronic lymphocytic

leukemia detected on a "routine blood test," a 42 year old woman with cervical cancer found by an abnormal Pap smear, and a 45 year old woman with breast cancer detected by findings of breast calcifications on a routine mammogram. These data on patient responses are presented in Figure 4.3.

In all, 96% of the patients who participated in the study would have been detected with a screening test based upon historical and clinical findings. 100% of the findings reported by patients were on the extensive list of findings culled from the literature.

With regard to length of delay between appearance of symptoms and seeking care, Figures 4.4 and 4.5 show the distribution reported by patients. Of the 77 patients, only 66 indicated how long they had waited; the interval ranged from "immediately" (presumed to be the same day) to several years. In Figure 4.4, the time-course categories were based upon those used in the Phase 3 study ("less than 2 weeks," "2 weeks to 2 months," and "more than 2 months"). Figure 4.5 shows the data from the 66 patients divided into groups according to the time-divisions used by Hackett, Cassem, and Raker at the Massachusetts General Hospital (1973), plotted alongside the data from the MGH study which they reported in their study on "patient delay in cancer."

D. Discussion

The results of this study phase show that, for this patient group, lay individuals observe and are cognizant of the historical or physical findings which suggest cancer, but that a large fraction of

them do not act promptly to have a medical evaluation in response to their observations. If detection were based solely on chance, one might expect 50% of the population or about 38 individuals to have noted these findings (30 - 47 at 95% intervals), whereas in this group 74 patients (96%) reported they were positive for findings. There are two important implications of this success rate in self-detection: first, if this study population is representative of cancer patients in general, then screening on clinical findings which patients can notice themselves shows promise as a sensitive methodology; and second, the extensive list of findings is an appropriately thorough mesh for screening these individuals. Some observations on the assumptions underlying these assertions must be made.

First of all, is this study population a good estimate of cancer patients in general? Clearly, there are some features which raise this question. A strikingly large portion of those individuals who chose to participate were women, and many of them had breast cancer (58 of 77 or 75% were female, and 33 of 77 or 43% overall had breast Ca). Is it possible that these individuals were more willing to share their experiences so that others might not endure the problems they had experienced (given the "humanitarian" tone of the posters inviting participation), or that they were perhaps more aware of their physical findings? Such conjectures are possible (e.g. a "responsible citizen" effect for the former), and the psychological aspects of coping with a disease as commonly feared as breast cancer might well be hypothesized to serve as motivating factors for

participation in a study such as this.

If the predominance of one subpopulation in the sampled group were skewing the overall impression, then exclusion of that group should yield rather different statistical results. Thus, if one excludes all patients with breast cancer (32 women and one man), this leaves a smaller data set in which 41 of 44 individuals (93%) still would be detected on the basis of the physical and historical findings on the list. In contrast, by chance alone one might expect half of 44 (or with 95% confidence limits, a range of 15 - 29 individuals) to be found. Thus, this major subpopulation in and of itself does not seem to be skewing the overall results in a significant way.

As a further point of comparison, one can examine the data from this phase in light of those reported by Hackett, Cassem, and Raker (1973). They studied all patients in the MGH tumor registry from 1968 to 1970 by means of a questionnaire which included several questions related to the delay between noticing symptoms and seeing a physician. A chi-square statistical test can be performed to determine whether or not their patient population and that of Phase 2 exhibited comparable delay intervals. By using their choice of categories for time-delay and their proportions of the population falling into each group, one can calculate a set of "expected values" for a comparable population of 66 patients (vs their 563) to permit a chi-square calculation. Figure 4.5 shows the data from this Phase 2 study and from Hackett's group. Figure 4.6 shows the numerical data

involved in the chi-square test. With five degrees of freedom (six groups - 1), the chi-square value is 2.15 which is not significant ($p = 0.05$ at 11.07). Thus, the Yale patients from 1986 and the MGH patients from 1968-70 are not statistically different in the time they waited between noticing symptoms and getting help.

From a broader perspective, one may ask what features might distinguish the patients who volunteered to participate in this study from those patients who decided not to complete a questionnaire? Certainly there was more than one eligible patient seen in each of the clinics each day, yet on average less than one person (per clinic day) chose to fill out a questionnaire. There are no substantiated data to suggest what the distinguishing factors may be, but one may make some conjectures. It may be that a person who filled out a questionnaire felt that he or she had "something to say" to the study's investigator, and that a positive observational experience is a necessary prerequisite for one to feel inclined to complete the questionnaire. This self-selection could introduce a bias because, conversely, those who did not return a questionnaire may either not have noticed the (admittedly obvious) posters inviting participation, or had feelings of guilt about not noticing things about their own bodies which might have made a difference, or did not have a great sense of responsibility for matters of their health in general. It is conceivable that these individuals might have noted other findings but, because they did not return questionnaires, there is no evidence to support the need to include other findings on the extensive list. An alternative point of view would suggest that individuals who fit

any of these stereotypes would be unlikely to notice the physical or historical findings and so would have provided an important complementary part of the total population of patients with cancer (observant vs non-observant subpopulations). The potential biases introduced by examinee self-selection have been discussed by Friedman (1982), and the potential distortions introduced by an incomplete assessment of the population must be kept in mind.

Unfortunately, a medical student study lacks the authority to urge hesitant patients to complete questionnaires as a part of a study from which they will receive no direct, tangible benefit. Had the questionnaires been given to patients by their own physicians, with a personal request to complete and return the forms, then perhaps this other segment of the total spectrum of cancer patients would be better represented in these statistics. Alternatively, had there been some remuneration offered, these patients might have agreed to participate. Neither of these methodological avenues were available. The question of whether or not the participating patients are a good estimate of cancer patients in general, vis a vis their observational abilities, must remain incompletely answered at this time.

In summary, data from this phase suggest that patients can be appropriate observers of ominous findings, but that they often do not seek medical care quickly. Additionally, the system of 107 historical and physical findings was shown to detect all of the findings which patients actually reported. Consequently, this list was deemed sufficient to serve as a basis for the next study phase, in which

clinicians were asked to rate their concern over the presence of each finding.

Chapter V. Study Phase 3: Quantifying an Index of Suspicion

A. Introduction

The aim of this phase of the study was to understand the relative degree to which physicians are suspicious of signs, symptoms, and historical findings which may represent an underlying malignancy. This clinician's "hunch" or "Index of Suspicion" was hypothesized to rely on judgments made on a set of non-laboratory-derived data (i.e. physical findings or historical information) such that the presence of some findings would make a physician increasingly concerned that a neoplastic disease might be present and ought to be evaluated.

In Phase 1 of this project, a set of such historical and clinical findings were constructed by examining the medical literature. In Phase 2, these findings were found to constitute a set which would have detected all of the clinically-detectable neoplasms in the patients who responded to a questionnaire (i.e. all but the 3 of 77 patients whose diagnoses were made on a laboratory or radiological test result). In the present section, Phase 3, Attending Physicians at Yale were asked to serve as clinical research subjects whose expertise in rating the importance of the findings could be translated into a numerical, graded scale (the "Index of Suspicion Ratings" or ISRs).

B. Study Methodology (HIC Protocol # 3856)

The study utilized a written questionnaire which was distributed

to full-time Attending Physicians affiliated with the Yale University School of Medicine and Yale-New Haven Hospital or the West Haven Veterans Administration Hospital. The lists of professors associated with the Departments of Internal Medicine, Obstetrics and Gynecology, Pediatrics, and Surgery were drawn from the most recent Bulletin of the School of Medicine (1985-86 issue). These departments were selected because these physicians were more likely to act as primary care providers who might initiate a diagnostic evaluation for a suspected neoplasm, without being limited to a heavily pre-screened patient population. (For example, therapeutic radiologists see many patients with cancer, but they see comparatively fewer patients with other diseases, and thus might be anticipated to have a higher expectation that a given finding signifies cancer than a physician seeing a more balanced population.) The study population was limited to physicians who were accessible by Campus Mail either at Yale-New Haven Medical Center or the West Haven V.A. Medical Center.

After the questionnaires and procedures for their administration were approved by the Human Investigations Committee (HIC Protocol #3856), the Professors were sent a mailing containing a covering letter which explained the project and asked for their participation by completing a questionnaire, copies of the two questionnaire forms used, and envelopes for return to the principal investigator via Campus Mail. Figures 5.1 and 5.2 illustrate the questionnaires used. A copy of the covering letter can be found as an appendix. The Brief and Extended versions of the questionnaire were initially distributed because it was unclear a priori whether physicians would prefer

a quickly completed questionnaire or one which might take more time but which had more specific (or less ambiguous) findings.

Findings were organized in a way that could be translated directly into a form usable by a lay-person screening program. Thus, a set of constitutional findings were followed by organ-system based groupings (HEENT, Chest, Breast, Gastrointestinal, "Kidneys, Bladder, Reproductive Tract," "Spine and Extremities," Skin, and "Hematologic"). In all, 107 findings were enumerated. Physicians were also instructed that questions would be posed to patients about pertinent demographics (age, gender, race, pertinent family history) and habits (use of tobacco, marijuana, snuff, and alcohol).

A uniform clinimetric scale was developed to allow physicians to convey their degree of suspicion with an established convention. The numerical scale ranged from the most worrisome level, "4+," which was defined as meaning that the physician thought an individual with this finding "should be admitted this week," to "1+," meaning "the individual should follow the usual screening exam recommendations," and a level of "0+," which was provided to indicate "this finding isn't useful for detecting Cancer." This scale is presented in Figure 5.3. These points were intended to serve as benchmarks on a continuum of how vigorously one should pursue a work-up (e.g. there are possibilities between a patient being "admitted this week," being seen "by a physician within 2 weeks," and being "followed-up in the next 2 months if findings persist"). A continuous black line was drawn as a scale for each finding on which physicians were asked to mark an "X" to indicate their answers on a "visual analog scale"

(Feinstein, 1985b, p. 74).

Physicians were requested to place their completed questionnaires inside envelopes in the following way to protect their confidentiality. A larger, outer envelope was addressed for return to the principal investigator via Campus Mail. This envelope bore the physician's unique identifying number and a box which he or she could check to indicate a desire to receive a copy of the study results. Each physician was asked to place a completed questionnaire in the smaller (unmarked) envelope and then put it into the larger envelope for return. Once received, the smaller envelopes were placed, unopened, into boxes (by departments) when separated from the larger envelopes with the identifying numbers. This was done to obviate the possibility of linking responses to individual physicians.

Physicians were presented with the option of declining to participate but responding courteously by returning an empty inner envelope. Here again, procedures for confidentiality were designed to prevent anyone from ascertaining which physicians had returned questionnaires and which had returned empty envelopes; it was possible to assess from the total set of outer, numbered envelopes, which physicians had responded and did not need further follow-up. Physicians who did not return any envelope after the first mailing were contacted with a second letter and provided with another set of the cover letter, the questionnaire, and the envelopes, so that they could again decide to participate or not.

As an incentive to participate in the study, all physicians who

returned an envelope could check the appropriate box (on the outer envelope) to indicate their desire to receive a tabulation of the findings of the study. They might thus learn how they and their colleagues collectively ranked their suspicion of the various clinical and historical findings.

Two databases were constructed for this phase: first, a listing of all professors, their departments, and their addresses, and second, a matrix of the 107 rankings (ISRs) and the several prose comments from each of the returned questionnaires. These databases were also maintained on a microcomputer (IBM-PC) with the Reflex database manager (described in Chapter IV).

C. Results

The initial mailing was sent to 226 Professors. Of these, 105 were in the Department of Internal Medicine, 19 in Obstetrics and Gynecology, 51 in Pediatrics, and 51 in Surgery. Among these Professors, 16 indicated that they were ineligible to participate (e.g. sabbatical leave, a Ph.D. or non-clinician professor), which left 210 Professors who were eligible.

Of these 210 Professors, a total of 145 returned envelopes (69%) which yielded a total of 84 Extended Questionnaires and 13 Brief forms. Yields ranged from a low of 38% participation (Ob-Gyn) to a high of 52% (Surgery). In all, 40% of the eligible physicians returned an Extended Questionnaire and 6% returned a brief form. Figure 5.4 shows a tabulation of the return rates.

The composite results of all physician answers are presented in the columns of Figure 5.5 For each finding, data are tabulated to show the number of physicians who answered that question, and the appropriate mean and standard deviation values for the Index of Suspicion ratings.

For the composite data pool, mean rankings ranged from a high of 3.70 (sigma 0.43, N = 71) for the finding of jaundice without pain in the right upper quadrant, to a low value of 1.12 (sigma 0.64, N = 63) associated with the use of oral contraceptive agents. Figure 5.6 shows the "Top Dozen" findings for the composite pool and for each department.

The largest variability in ranking was associated with the finding of fainting, which had a mean rating of 2.50 with a standard deviation of 1.06 (N = 69), in contrast with the finding of weight loss which had a mean ISR of 3.00 and a standard deviation of 0.40 (N = 81). Figure 5.7 shows these data.

D. Discussion

Of the 107 findings, 36 had ISRs between 3.0 and 3.7, i.e. 34% of the findings merited a very prompt work-up for cancer but were not life-threatening enough to merit an initial admission. Only nine findings were rated below 2.0 (minimum 1.1). This would suggest that the bulk of the findings (which were rated between 2.0 and 3.0) would be best managed with a moderate period (2 weeks to 2 months) of watchful expectancy and an evaluation to take place after that time

if the finding persists. For these recommendations to make a difference to patients, the duration of these waiting periods would need to be shorter than the time which the patients actually did wait. This question is addressed in Phase 3 (Chapter 6).

In summary, a substantial number (40%) of physicians completed questionnaires on which they rated their Index of Suspicion for a set of findings. Their answers were preferentially distributed in the mid-to-high range of the scale. These data form the basis for the next phase of the project, in which the clinical efficacy of this approach is tested.

Chapter 6. Phase 4: Efficacy of Computer-Aided Evaluation

A. Introduction

In Phase 3, a set of Index of Suspicion Ratings (ISRs) was measured from a diversified group of clinicians. Ultimately, it is the application of these data to clinical situations which will elucidate what impact this approach may have to the treatment of patients with cancer. The present phase of experimentation was conducted to examine this issue of efficacy by applying the data to a patient population and determining, preliminarily, the effect such a screening tool would have on the speed with which patients seek medical care.

B. Methodology and Description of the Computer Program

The data collected from clinicians in Phase 3 of this project were applied to the patient data from Phase 2 using a computer program developed for this purpose. Data were supplied to the computer as they would have been by the actual patients themselves, as far as could be determined from the patient responses to questions on the questionnaires. For example, if a patient indicated that finding a "lump in breast" had been the iatrotropic stimulus, then that information was entered directly; if a patient with breast cancer merely circled the word "lump" on the questionnaire, it was inferred that this was a breast mass and entered accordingly.

The computer program implemented the following algorithm:

1. for each finding, determine if it is present or absent (or unknown) in this individual

2. for each finding that is present, look up the appropriate Index of Suspicion Rating (ISR) from the physicians' data
3. summarize all this information by providing
 - for each finding that is present, a brief statement of possible etiology (e.g. bloody sputum could be spuriously caused by a bleeding cut in the mouth, or may represent a cancer in the lung)
 - a "bottom-line" recommendation as to how quickly the individual should see a physician; this recommendation is the maximum of the ISR values, translated into actual days (i.e. specifying the most brief period of watchful expectancy).

While most programs used in medicine ask for information by presenting a sequence of questions (and thus conveniently provide a transcript of the interaction), the program developed in this project presents an individual with a screen showing a number of choices (a "menu"). As an example, for the "Stomach and Intestines" section, the menu includes 17 findings (re-phrased for lay people):

nausea	borborygmi
vomiting	bloody stool
[-> follow-up with postprandial vomiting]	melena
[-> follow-up with hematemesis]	painful stooling
[-> follow-up with coffee grounds]	increased constipation
dysphagia	back/abdominal pain
persistent hiccups	tenesmus
jaundice	pencil-thin stools
ascites	fecal incontinence

The person using the program responds by moving the cursor (a flashing spot on the screen) to a particular finding and then entering "Y" or "N" to specify presence or absence. Questions left unanswered are assigned a value of "unknown."

Also displayed is a "choices" line, indicating the options open to the individual. The choices include

Back-up	to the previous organ system selections
Go-on	to the next organ system
Arrows Up and Down	arrows to move the cursor to a finding
Y, N	specify Yes and No answers
Help	display a screen of instructions
Finish-up	and make the recommendations
Quit	and leave the program

While the running of the program does not leave a transcript, the program's findings and discussion can be printed out. This explanation consists of summarizing what the findings were, what was abnormal about them, and finally, how quickly (if at all) the patient should be seen by a physician.

C. Results

Of the 76 questionnaires returned by patients, only 66 indicated how long they waited between the appearance of symptoms and seeking medical care. The algorithm, as described above, was applied to these 66. The results of this exercise are shown in Figure 6.1. Examples of the "printout" which this program can generate for the user are included as Appendix II. This appendix shows what the program would have reported to several of the patients who participated in the Phase 2 study.

All 66 patients would have received recommendations to see a physician. 53 patients (80%) would have been urged to see a physician sooner than they reported that they actually did; the other 13 patients (20%) sought help as soon as or sooner than would have been recommended. These 13 patients all reported seeking evaluation in two weeks or less. The group of 53 patients would have experienced

accelerations in seeking care of between one week and several years. Figure 6.2 shows the distribution of this interval. Ten of these patients would have come to medical attention only a month sooner than they actually reported (19%). Of note, however, 29 patients of the 53 (55%) would have been seen between one and seven months sooner, had they responded to the recommendations made by the program. In all, 43 of 53 (81%) would have experienced accelerations of more than one month.

The statistical differences between the actual patient actions of Phase 2 and the actions that would be recommended by the computer program were tested using a chi-square test. Figure 6.3 shows the numerical process involved. The screened and unscreened populations are statistically different in the time-lag between appearance of symptoms and seeking care ($p \ll 0.001$).

D. Discussion

This phase of the project was undertaken to determine the validity of the recommendations derived from this model of clinical decision making: in short, would the recommendations have made a difference in how fast patients sought help? While diagnostic tests are normally judged by sensitivity and specificity values (Ransohoff & Feinstein, 1978), the objectives of a screening test are to minimize the false negative rate (i.e. the missed cases causing "chagrin," as per Feinstein, 1985) while being less concerned about the false positive rate (i.e. tolerating less specificity).

For 53 of 66 patients (80%), the answer to the question of would this screening test make a difference, is made in the affirmative. Indeed, in only ten patients was the difference less than a month faster; the rest would have experienced accelerations ranging from a month to several years. By applying a chi-square test to the data, it can be shown that the differences in seeking professional help are statistically significant ($p \ll 0.001$). If one believes that early intervention makes a difference in the therapy's outcome, then these gains in time are promising. Depending upon the aggressiveness of any particular patient's neoplasm, the time difference could represent several doubling times of tumor growth, or whether or not microscopic metastases could establish footholds. Charlson and Feinstein have written on the heterogeneous growth rates grouped together as the "same" neoplasm (1974, 1982, 1983, 1984), and determinations would need to be made for each individual patient based upon clinical or laboratory determinations (Feinstein, 1966). The deeper question of whether or not early intervention makes a difference, is discussed in the concluding chapter.

A question which should be raised is whether or not an individual will follow through on the recommendation supplied by the program. There are as yet no data to answer this question directly either way. The prose used in presenting the recommendations to the individual was intended to be calm, rational, and matter of fact in tone; the aim was to inform the individual of what findings were abnormal in such a way as to help that person see that it would be in his or her own best interest to have the matter evaluated first-hand.

The possibility that a given finding does not represent cancer is presented as well, so that the lay person can make a better-informed choice about seeing a physician. The important psychological factors related to compliance with recommendations are discussed in the following chapter. In all, clinical experience with real patients would be needed to yield useful insight into this issue.

In these days of concern over escalating health care costs, this discussion would be incomplete without mention of cost effectiveness. What are the costs associated with the use of this screening tool? A version of the program developed in this project will be made available, free to the general public, for anyone to use on a suitable computer. For individuals who do not own their own PC, many will have access to one in the workplace. Additionally, health centers and hospitals could put a low-cost machine (< \$1000) in a lobby or waiting room to make the service available to the public. (Low cost computers have already been used as a decision aid system for rural health workers in Chad, as reported by Auvert et al., 1986.) The costs incurred beyond this stem primarily from increased contact which the individuals may have with their primary care physician, which might increase (Berg & LoGerfo, 1979). Many of these contacts would likely be brief telephone conversations, and would serve to minimize the "false positive" results of the computer-based screening. By providing the screened individual with a printout of the findings, he or she can specify to the physician what the abnormalities were; the physician can then get a head start on evaluating the problem. The principal benefit of the program is that

people will be seen earlier in the course of their disease. The usefulness of this benefit is discussed in the concluding chapter.

Chapter VII. Comprehensive Discussion and Conclusions

Several points are best discussed in the context of the project as a whole, rather than with any one research phase.

As illustrated in Chapter 2, individuals applying computers to clinical problems have often been criticized for straying too far from "real-world" clinical situations. Models have often been simplified to the point of rendering them elegant intellectual exercises which lack any real utility for a doctor who sees patients. Constraints have often been imposed so that problems may be "solvable" but probably not solved any better than could be done by a moderately skilled clinician (let alone by an expert). This project has attempted to avoid these pitfalls by sticking closely to patients and physicians with frequent validation points or "reality checks." Rather than creating a speculative model (cognitive, statistical, or otherwise) to account for different cancer etiologies, for alternative causes of symptoms, and the like, this program uses a straightforward algorithm designed to follow a simple model of one particular clinical decision.

This project represents a departure from past projects, not only in the model of decision-making which was developed, but also in that the users of the program will be members of the public at large, rather than only medical specialists, and so addresses a neglected avenue of computer applications in medicine.

The ultimate test of any clinical tool has to be a question of does it (be it a lab test, procedure, or drug) make a difference for

real patients? The preliminary results suggest that, for the patient data available, the computerized process developed here can indeed help patients come to medical attention earlier in the course of their disease. While Phase 4 showed that the computer recommendations would have significantly abbreviated the delay in seeking care ($p < 0.001$), the utility of those recommendations hinges upon patient acceptance: can a recommendation from a computer serve as a motivating factor in helping patients see their physicians? The data from Phase 2 show that patients tarry, and the role of denial in delaying is a common clinical observation: patients hope the lump will go away, they are "too busy" doing other things to take care of themselves, they are afraid of the bad news the physician may tell them, etc. Cancer is such a widely feared disease that psychological factors are very important for people who think they may have a malignancy. Hackett, Cassem, and Raker (1973) wrote about factors contributing to patient delay at the Massachusetts General Hospital. They found that delay times had changed little when compared with earlier studies conducted 30 and 50 years earlier. They commented that "delay in seeking medical help appeared to be a conscious and deliberate act rather than a failure to perceive the neoplasm or to comprehend its consequences." The role which the program's recommendations could play in altering this tendency is not well explored. While Slack and Van Cura (1968) and Grossman and Barnett (1971) have written about the positive nature of interactions of patients with interviewing programs, there is no comparable experience with lay people's reaction to computer generated advice

(e.g. what action will someone take if the program plainly states that "you should try to see your physician in between 1 and 2 weeks," a recommendation which is hard to misconstrue?). This issue could best be addressed by actual clinical usage of the program in a study setting; the overall usefulness of this program cannot be fully judged without this information.

But another issue must be addressed as well: granted that patients might seek help earlier because of the program, would this make a difference? Based upon notions of cell kinetics, one would expect that a treatment which can leave less tumor burden after excision or debulking, for example, would present a more favorable situation for subsequent chemotherapy or radiotherapy (given most models of "cell kill"). While many clinicians would argue that early detection is thus worthwhile, work has been published which suggests that therapy (in a lung cancer group), be it early or late, does not contribute to increasing patient survival (Feinstein et al. 1985). The "Will Rogers Phenomenon," as it has been termed, involves the migration (or re-categorization) of patients from one staging category to another, depending upon the data which were used to stage them, and consequently, the erroneous conclusions which may be drawn by trying to compare what are actually incomparable patient groups.

If the Will Rogers Phenomenon holds for cancer patients other than the lung cancer patients studied, and similar results are obtained (i.e. survival statistics are indistinguishable between groups), then one may appropriately ask what value early detection has, since it merely lengthens the time that a patient lives with the

knowledge of a diagnosis of cancer and not the actual length of life (or indeed, one could ask what is the value of any therapeutic maneuver)? The point may be addressed by clarifying the notion of "value." The lung cancer patients studied were examined with regard to survival (or conversely, death) as the measured outcome. Once corrected for categorization biases, no differences could be found between survival of patient groups. While surely death is a suitable experimental endpoint in some contexts, the role of medicine in alleviating suffering, or conversely optimizing quality of life, is insufficiently gauged by this outcome.

Measures of "quality of life" are difficult to agree upon (Wellisch 1984, Barofsky 1984), but experientially speaking, anyone who has taken care of patients can appreciate the benefits which derive from the treatment options which are available only "early" in a malignancy. A radical, Halsted-style mastectomy is much more disfiguring than a simple lumpectomy followed with radiotherapy (Veronesi et al., 1981); the presence of an abdominal colostomy is more disruptive to a patient's life than the construction of an ileal reservoir with an intact anal sphincter (Parks et al., 1980); a larynx-sparing treatment would be preferable to a laryngectomy and tracheostomy, even if metastatic disease would lead inexorably to death. A.B. Miller has noted (1982) that

the major benefit from screening may follow not from the reduction of mortality, but from the reduction of morbidity consequent upon the diagnosis of cancer in a more treatable phase in its natural history. This could mean that the extent of treatment required and the possibility that treatment may be debilitating or mutilating would be much less. Such advantages may be difficult to quantify in other than economic terms;

however, as they may be considerable in psychological terms to individuals, and to communities in the lowering of requirements for extensive rehabilitation services, they should not be overlooked.

Clinical decisions are made with the realization that there are subtleties which are missed by survival statistics.

In reporting their early work in prognostication with computers, Feinstein and Koss commented (1971)

Our purpose in the research reported here was to develop procedures by which clinicians can begin to approach these goals. The procedures we shall report are neither complete nor perfect; they represent a beginning - an early stage of growth from which considerable change can be expected as further development occurs.

Similar remarks are appropriate for the present project, and avenues for further related work should be discussed for completeness.

Further testing with a larger patient base would allow determination to be made for actual "sensitivity" and "specificity" measures. By applying the program to patients who may or may not have cancer and following their course with time, true and false negative and positive values could be ascertained for the recommendations generated by this model. For example, retrospective data could be collected for all patients seen in the Yale-New Haven Primary Care Center over a three month period five years ago; the program could be applied to all these patients (answering the questions based upon the patients' charts); the current health status of these individuals could be determined (again from their charts), and the recommendations made by the program could be viewed in the light of what actually happened (who developed a neoplasm and who did not). Alternatively, a prospective study could be conducted in which two

groups of patients would be selected: one group would receive "normal" standards of care, and the other would additionally have access to the computer program. These groups would be followed for several years, during which time the program-using group would periodically use the screening test, and the groups could be compared at the end of the period both for numbers of malignancies found and for their stages at detection.

If value is found in this approach to evaluating malignancies, the clinicians' database might be strengthened in two ways. First, increasing the number of clinicians who contribute data would incorporate even more collective experience and judgment. Second, because the scale employed had a concentration of answers in the mid-to-high range, a modification could be employed to provide more "benchmarks" between admitting a patient this week and seeing the person in two months (e.g. a ten-point, discontinuous scale with levels added between the 4+ and 2+ levels of the current scale).

Even without further refinement, the approach developed in this project has implications for teaching medical students. The process of learning clinical judgment begins in medical school and is honed during residency training and afterward. To a large extent, medical students learn to make clinical judgments by emulating their attending physicians and residents. Through discussion and rounding on patients, the medical students learn how to decide upon appropriate diagnostic and therapeutic interventions.

The availability of the list of ISRs for the clinical findings

(as presented in Chapter 5) could provide a useful supplement to this learning process, by exposing the medical student to the collective wisdom of many physicians, without regard to the limitations of the patient population with which the student may be involved. Efforts to use the knowledge base supporting INTERNIST-1 as a teaching tool have been reported (First, et al., 1985). de Dombal's group (Wilson et al., 1975) showed that the diagnostic accuracy of physicians-in-training improved when a computer program was available to provide "feedback," and that this accuracy declined when the feedback was withdrawn but increased again when re-introduced. (He suggested that the computer program stimulated young physicians to think more critically (de Dombal, 1979).) Given the possibility of increasing movement of diagnostic evaluations away from teaching hospital in-patient wards, the exposure of students to a variety of situations may depend upon the creative use of teaching instruments such as this tabulation.

In conclusion, this research project accomplished its goal of producing a computer-based screening method for cancer which may have a role in augmenting the ability of physicians to take care of cancer patients. Free distribution of the software will reduce the "cost" in evaluating its cost effectiveness. Further refinements and clinical trials have been outlined as future extensions of this research, but the method in its present state is usable both as a screening tool and as an educational method for teaching medical students how to approach the evaluation of neoplasms.

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	E. normal control

Screen	Gender	Age	Frequency
sigmoidoscopy	M & F	> 50	after 2 negative exams, 1 yr apart, every 3-5 years
stool guiac	M & F	> 50	every year
digital rectal exam	M & F	> 40	every year
Pap smear	F	20-65; < 20 if sexually active	after 2 negative exams, 1 yr apart, at least every 3 years
Pelvic exam	F	20-40 > 40	every 3 years every year
Endometrial Tissue Sample	F	at menopause if high-risk *	at menopause
Breast Self-Exam	F	> 20	every month
Breast Physical Exam	F	20-40 > 40	every 3 years every year
Mammography	F	35-40 40-49 > 50	obtain baseline every 1-2 years every year
Chest Film (CXR)			not recommended
Sputum cytology			not recommended
Health Counseling and Cancer Check-up**	M & F M & F	> 20 > 40	every 3 years every year

* High risk denotes a history of infertility, obesity, failure to ovulate, abnormal uterine bleeding or estrogen therapy

** Cancer Check-up includes examination for cancer of the thyroid, testicles, prostate, ovaries, lymph nodes, oral region, and skin.

Figure 2.1

Screening Recommendations of the American Cancer Society
(based upon their report in Ca 35(4):197-213, 1985)

Figure 2.1

Screening Recommendations

CONSTITUTIONAL Findings:

unintentional weight loss, of more than 10% ideal body weight,
in less than four months
weight gain of more than 10% body weight in less than four months
fever, non-specific
fever, between 101 and 104 degrees, persisting for more than two
weeks, and not associated with another illness
recurrent chills, not associated with another illness
recurrent night sweats which soak one's pajamas, and are not
associated with another illness
fatigue (non-specific)
fatigue, which affects performance at work or ability to maintain
lifestyle, and not attributable to altered sleep patterns
depression, not related to some upheaval in life, and which
affects ability at work or relationships with friends/family
loss of appetite, not related to another illness and not
associated with anorexia nervosa
feeling too cold, compared to others in the same place
feeling too warm, compared to others in the same place

Findings from HEENT:

HEAD headaches of increasing frequency and duration, and not
associated with other illness or trauma
lumps on head, not associated with recent trauma
fainting, not associated with stress, excessive heat or exercise

EYES difficulty moving eyes (any defect), not associated with trauma
changes in ability to see (familiar objects do not look right)
new blind spots
double vision
drooping eyelid(s), not associated with fatigue or staying up late

EARS ringing in ears, not associated with noise exposure, not chronic
poor balance, not associated with intoxication, and not chronic
feelings of dizziness, not from intoxication, and not chronic
ulcer sores on ear
bleeding from ear canal

NOSE bloody discharge (not a brisk bleeding like a nosebleed)
inability to breath through both nostrils equally, not associated
with a cold, sinusitis, or deviated septum
constant "boring" pain in nose, not associated with trauma

MOUTH bumps on roof of mouth, not associated with trauma or injury
pain in mouth on swallowing, not associated with "sore throat"
lip sore that doesn't heal and may bleed
lump in tongue, lasting more than 1 week
tongue pain, not associated with injury to tongue
hoarseness, not attributable to shouting or exposure to smoke
recent voice changes, not related to puberty
new onset of persistent or frequent drooling

Figure 3.1

List of Findings suggestive of Malignancy

NECK pain in throat or neck on swallowing, not attributed to sore throat
swelling in neck or jaw, not associated with trauma
goiter
paralysis in neck or face

CHEST Findings:

coughing up blood on more than two occasions
changes in amount or kind of sputum
bloody streaks or tinges in sputum
pain on breathing deeply on more than two occasions
shortness of breath, not associated with heart disease or asthma
pain in neck or shoulder which is persistent and not from strain
palpitations, not associated with heart disease or medications

BREAST Findings:

pain, not associated with menses or injury
changing breast lumps, either new ones or enlarging ones
change in breast size, not associated with puberty
bloody discharge from nipple
milky discharge from nipple, not associated with nursing
swelling in armpit(s)

GASTROINTESTINAL TRACT Findings:

nausea, persisting for over two weeks, not associated with any particular foods or another illness
vomiting, recurring for over two weeks, not associated with any particular foods or other illness
vomiting as above, but within two hours after eating a meal
pain on eating which feels like the food is "sticking"
recurrent hiccups, persisting for more than two weeks
jaundice, not associated with pain in the right upper quadrant
bulging abdomen which has enlarged rapidly (less than one month) without increased eating
unusually loud rumbling sounds in belly
vomiting blood repeatedly, without excessive alcohol intake
vomiting material which looks like coffee grounds
stool with blood, repeatedly
stools are dark or tarry, repeatedly
bowel movements are painful, not associated with diet changes or trauma
recent onset (or increase) of constipation, without diet changes
back or abdominal pain, repeatedly over a month, not associated with other illness
frequent feeling of needing to move bowels, not associated with another illness, and lasting more than two weeks
"pencil-thin" bowel movements for more than a week
new or increasing problems with incontinence

Figure 3.1, continued

List of Findings suggestive of Malignancy

KIDNEYS, BLADDER, REPRODUCTIVE TRACT: (with gender-appropriate questions)
frequent urination (more than 3 liters per day total for one week)
painful urination, not associated with known venereal disease,
and lasting more than two weeks
new trouble starting urination
discharge from urethra, not associated with known venereal disease
blood in urine for more than four consecutive days
penile ulcer, not associated with known VD, and persisting more
than two weeks
vaginal or vulvar ulcers, not associated with known VD, and
persisting more than two weeks
testicular mass or tenderness for more than one week
swelling of scrotum for more than two weeks
lumps in groin creases which persist more than two weeks
vaginal bleeding between periods, not associated with using
oral contraceptive pills
post-menopausal bleeding
increasing abdominal girth which has enlarged in less than one
month, and not associated with changes in diet
stool found in vagina on more than two occasions
(i.e. through a fistula)
use of Contraceptive Pills
new, persistent impotence, with no erectile ability at all
new onset of urinary incontinence, persisting more than two weeks

SPINE & EXTREMITIES

new back pain (non-specific)
new and persistent numbness in arms or legs
bone pain which is worse at night
fractures of bones with only minimal impact
swollen joint, without injury or pain
progressive loss of height
black discoloration under fingernails or toenails, not from trauma
painful red or violet spot under nail, not from trauma
new persistent weakness in an arm or leg
problems walking, such as foot drop, or one-sided weakness

SKIN:

history of sunburning easily
flushing of skin, not from blushing or a burn
changes in skin color (new dark or light spots)
itching, without obvious exposure to poison ivy, bee stings, etc
lumps under the skin, which have enlarged or are new
moles which bleed or have changed in size or color

HEMATOLOGIC:

swollen lymph nodes, not associated with other illness, and
lasting more than two weeks
new onset of easy bruising
new onset of easy bleeding

Figure 3.1, concluded

List of Findings suggestive of Malignancy

Questionnaire for Patients at YNHH and WEVAMC

Purpose: The information collected below is for use in a project to help diagnose cancers early, when the prognosis is better. Most of the questions ask you about the time just before your diagnosis was made. Please try to remember as well as you can.

Instructions:

- Please do NOT write your name on this form.
- Please answer these questions as completely as you can. Write down as many details as you can; you can write on the back of this page if you need more space.
- Many of the questions have some answers suggested as examples. They are to help you understand the way to answer the question (there are many other possible answers), and you should write whatever is true for you.

1. General Information:

Your age now 27 circle one: woman man
 Type of cancer: Malignant melanoma

Have you ever had cancer before? Yes No

(If yes, please use the back of this page to answer the questions for that cancer as well)

Has anyone else in your family had cancer? Yes No

(what relation and what kind of cancer)

Have any of your friends had cancer? Yes No

Circle all of these that you have had:

Surgery Chemotherapy Radiation Therapy

2. Date when your doctors first diagnosed that you had cancer: ~ 1/6/86

3. What were the things (symptoms) that led you to see a doctor at that time? (for example: weight loss or gain, pains, bumps or bleeding somewhere, headache, shortness of breath)
Please list as many as you can remember:

thought a mole had grown larger than it used to be

5. What (if anything) did you think was causing your symptoms before you saw the doctor?

I thought I was just imaging it

6. How often did you usually see physicians before your cancer was diagnosed? (example: annual company exam, each 5 years, not for 20 years, or 'I avoided all doctors')

annually

7. Do you have a regular doctor? Yes No

8. Did you see other healers before? (e.g. nurse practitioner, chiropractor, herbalist, faith healer, massage therapist). Please list which types, if any

Yes No

9. How much were you concerned with your health before your diagnosis?

(examples: "I think about my health a lot," "When I was sick I would take care of the problem; otherwise I don't think about health matters much," "I knew I should have changed my habits but I was too busy")

I care a lot about my health & try to live a healthy life, but I'm not sick often & don't worry about it

10. Did you have any other medical problems before this? (e.g. diabetes, high blood pressure, allergies)

Please state which ones

11. Had you ever been hospitalized before your cancer diagnosis? Yes No
If yes, what sort of experience did you have at that time?

12. Is there anything that you know now which you wish you had known before your cancer was diagnosed?

PLEASE RETURN THIS SHEET TO THE BOX MARKED "EARLY SYMPTOMS QUESTIONNAIRE"

Thank you very much for taking the time to help.

4. How long had those problems existed before you saw the doctor?

~ 3 mos.

FIGURE 4.1

SAMPLE PATIENT QUESTIONNAIRE

Age Distribution (regardless of dx)

yrs	#	
20-24	1	F
25-29	4	F F F M
30-34	6	F F F F M
35-39	11	F F F F M M M M M
40-44	11	F F F F F F F F M M
45-49	10	F F F F F F F F M
50-54	10	F F F F F F F F M
55-59	11	F F F F F F F F M M
60-64	3	F F M
65-69	5	F F F M M
70-74	4	F M M M
75-79	0	
80-84	0	
85-89	0	
90-94	1	F

Gender Distribution:

Males	19
Females	58

Clinic Distribution:

CCC	44 individuals
Dana	33 individuals

Findings Present*:

Yes	74
No	3

Self Detected:

Yes	65
No	12

Diagnoses (as described by the patients):

Breast	33	Squamous Cell	1
Melanoma	16	Basal Cell	1
Lymphoma	6	Small Cell	1
Hodgkins	2	Mycosis Fungoides	1
Non-Hodgkins	1	Thyroid	1
Leukemia	1	Adenocystic	1
Colon	4	Cervix	1
Bladder	2	Angiosarcoma	1
Skin	1	Unspecified	3

* i.e. would have been picked up on the list of historical and clinical screening features developed in Phase 1.

Figure 4.2

Characteristics of the patient population completing questionnaires

CN	Patient	Diagnosis	Time-lag	Findings (how many)	Y/N
1001	28 y.o. F	Melanoma	6 mo		y 3
1002	43 y.o. F	Breast mets	as soon as found		y 1
1003	49 y.o. F	Breast	4 wks		y 3
1004	36 y.o. M	Melanoma	6 mo		y 1
1005	48 y.o. F	Breast	7 yrs		y 1
1006	58 y.o. F	unknown	2 wks		y 1
1007	41 y.o. M	Adenocystic Car	2 mo		y 1
1008	52 y.o. F	Breast	3 mo		y 1
1009	49 y.o. F	Melanoma	2-3 mo		y 1
1010	25 y.o. M	Melanoma	days		y 1
1011	65 y.o. M	Bladder	1.5 yrs		y 1
1012	49 y.o. F	Breast	several months		y 1
1013	51 y.o. F	Breast	3 wks		y 3
1014	48 y.o. F	Melanoma	1 mo		y 1
1015	65 y.o. F	Breast	uncertain		y 1
1016	36 y.o. M	Hodgkins	1 mo		y 2
1017	67 y.o. M	Small Cell			y 1
1018	53 y.o. F	Thyroid	1 wk		y 1
1019	44 y.o. F	Breast mets	2 wks at dx		y 2
1020	71 y.o. M	Breast	2 yrs		y 1
1021	55 y.o. M	Melanoma	found at P.E.		y 1
1022	48 y.o. F	Melanoma	5 mo		y 1
1023	62 y.o. F	Lymphoma	2 mo		y 2
1024	50 y.o. M	Melanoma	7 mo		y 1
1025	65 y.o. F	Leukemia	CLL by lab tests		n 0
1026	38 y.o. F	Lymphoma	1 yr		y 1
1027	38 y.o. F	Colon	2 wks +/-		y 6
1028	37 y.o. M	Melanoma	3 mo		y 1
1029	31 y.o. F	Breast	3 mo		y 2
1030	21 y.o. F	Hodgkins	month		y 3
1031	62 y.o. F	Breast	4-5 d		y 1
1032	40 y.o. F	Breast	found at P.E.		y 1
1033	52 y.o. F	Lymphoma	2-3 months		y 2
1034	38 y.o. F	Lymphoma	1 wk		y 2
1035	57 y.o. F	Breast	3 wks		y 1
1036	70 y.o. F	Lymphoma	several months		y 1
1037	41 y.o. F	Melanoma	found at P.E.		y 1
1038	70 y.o. M	Lymphoma	6 mo		y 4
1039	39 y.o. F	Breast	1 day		y 2
1040	44 y.o. M	Mycosis fungoid	3 yrs		y 1
1041	56 y.o. F	Melanoma	6 mo		y 2
1042	59 y.o. M	Melanoma	5 mo		y 1
1043	50 y.o. F	Melanoma	8 yrs		y 2
1044	34 y.o. M	NonHodgkins	6 mo (under MD)		y 6
2001	35 y.o. M	Colon	2 yrs		y 3
2002	32 y.o. M	Melanoma	1 yr		y 1
2003	45 y.o. F	Colon	6 mo		y 1
2004	43 y.o. F	Breast	found at P.E.		y 1
2005	54 y.o. F	unknown	2 mo		y 1
2006	32 y.o. F	Skin	long time		y 1
2007	30 y.o. F	Breast	2 months		y 2
2008	39 y.o. M	unknown	6 mo		y 3

Figure 4.3

Patient responses to the questionnaire regarding the delay between appearance of symptoms and seeking care

CN	Patient	Diagnosis	Time-lag	Findings
2009	42 y.o. F	Cervix	abnormal Pap	n 0
2010	27 y.o. F	Melanoma	3 mo	y 1
2011	59 y.o. F	Breast (Pagets)	immediate	y 2
2012	39 y.o. F	Breast	6 mo	y 1
2013	43 y.o. F	Breast	months	y 1
2014	93 y.o. F	Bladder	immediately	y 1
2015	61 y.o. M	Basal Cell	Skin a few months	y 3
2016	54 y.o. F	Basal Cell	1 wk	y 1
2017	67 y.o. F	Breast	year	y 1
2018	56 y.o. F	Breast	2-3 mo	y 1
2019	43 y.o. F	Breast	few months	y 4
2020	71 y.o. M	Angiosarcoma	2-3 yrs	y 1
2021	45 y.o. F	Breast	1ng time (month)	y 1
2022	34 y.o. F	Squamous Cell	2 wks	y 1
2023	56 y.o. F	Breast	5 mo	y 1
2024	45 y.o. F	Breast	mammography	n 0
2025	26 y.o. F	Melanoma	1 yr	y 1
2026	46 y.o. F	Breast	2 wks	y 1
2027	54 y.o. F	Breast	few wks	y 1
2028	37 y.o. F	Breast	week	y 1
2029	58 y.o. F	Colon	2 yrs	y 2
2030	59 y.o. F	Breast	30 yrs	y 1
2031	40 y.o. F	Breast	6-12 mo	y 3
2032	52 y.o. F	Breast	1 yr	y 1
2033	57 y.o. F	Breast	unaware	y 1

Of 76 patients who returned the questionnaire, 3 would not have been detected on clinical grounds (picked up by mammography, blood test, pap smear).

Time between Symptoms and Evaluation

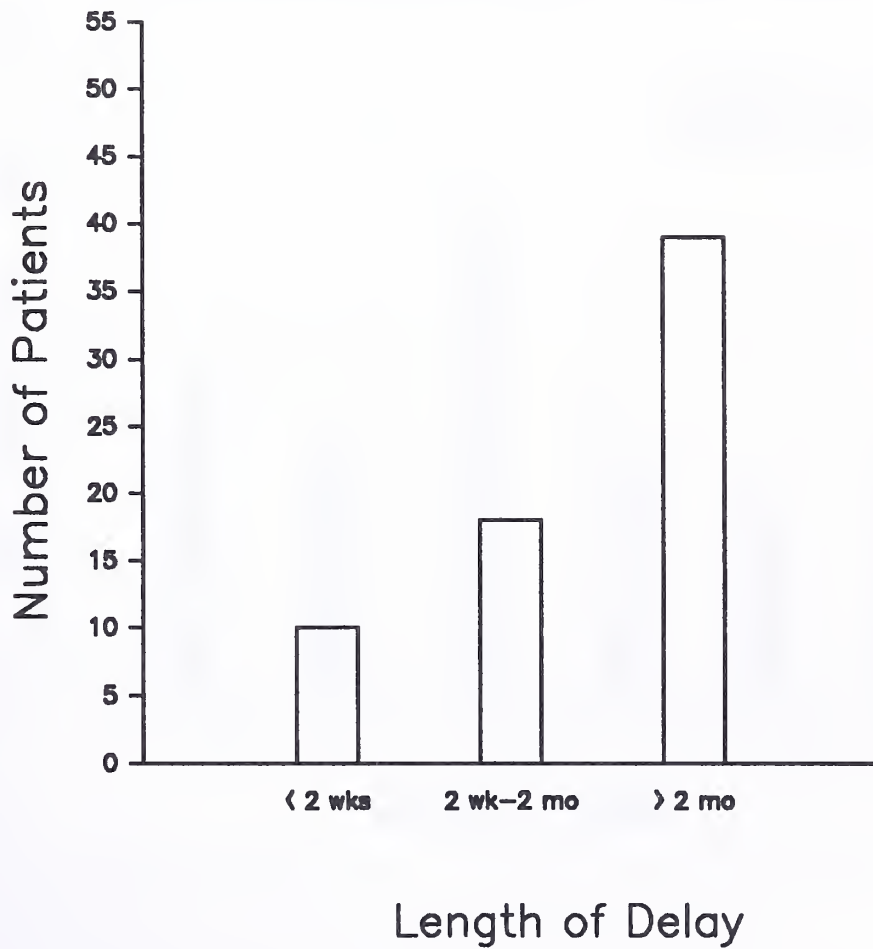


Figure 4.4

Distribution of Patient Data, using the categories of Phase 3

Comparative Delay in Evaluation

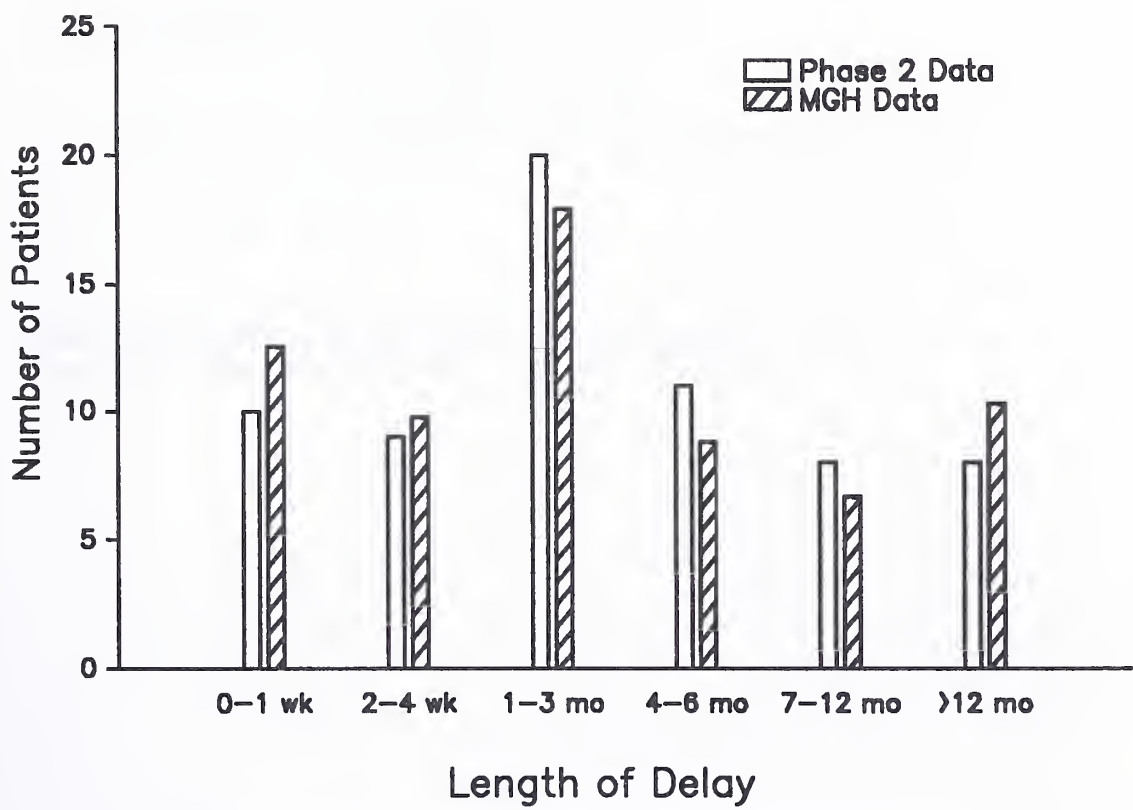


Figure 4.5

Distribution of Patient Data, using the categories of Hackett et al.

	Observed	"Expected"

0-1 wks	10	12.54 (19.0%)
2-4 wks	9	9.77 (14.8%)
1-3 mo	20	17.95 (27.2%)
4-6 mo	11	8.78 (13.3%)
7-12 mo	8	6.67 (10.1%)
> 12 mo	8	10.30 (15.6%)

totals	66	66.01 patients

6 groups - 1 = 5 degrees of freedom

Chi-squared sum = 2.150

(p = 0.05 at 11.07)

(p = 0.01 at 15.07)

This is not a significant deviation from expectation.

Expected values are based upon the proportions of the population reported by Hackett et al. (1973).

Figure 4.6

Statistical Comparison of Phase 2 Data with MGH Data

INSTRUCTIONS: Please rate the degree to which you would be vigorous in pursuing a neoplastic work-up if you were told that an individual had the findings listed.

Please rate as many of the findings as you can, leaving others blank. Indicate your ratings by marking an "S" on the lines, using the following scales:

- 4 = the individual should be admitted this week
- 3 = the individual should see a physician within 2 weeks
- 2 = this should be followed-up in the next 2 months if findings persist
- 1 = the individual should follow the usual screening exam recommendations
- 0 = this finding isn't useful for detecting cancer

Please note that questions will also be asked about demographic age, gender, race, pertinent family history) and habits (tobacco/marijuana/snuff, alcohol).

CONSTITUTIONAL Findings: how worrisome is/are ...

unintentional weight loss, of more than 10% ideal body weight, in less than four months?.....	4 3 2 1
please indicate if you would be more concerned about some other amount of loss or some other time frame:	
weight gain of more than 10% body weight in less than four months?.....	4 3 2 1
please indicate if you would be more concerned about some other amount of gain or some other time frame:	
fever, non-specific?.....	4 3 2 1
fever, between 101 and 104 degrees, persisting for more than two weeks, and not associated with another illness (cold, sore throat, etc.)?.....	4 3 2 1
please indicate if you would be more concerned about some other temperature range, time frame, or pattern:	
recurrent chills, not associated with another illness (cold, sore throat, etc.)?.....	4 3 2 1
recurrent night sweats which soak one's pajamas, and are not associated with another illness (cold, sore throat, etc.)?.....	4 3 2 1
fatigue (non-specific)?.....	4 3 2 1
fatigue, which affects performance at work or ability to maintain lifestyle, and not attributable to altered sleep patterns?.....	4 3 2 1
depression, not related to some upheaval in life, and which affects ability at work or relationships with friends/family?.....	4 3 2 1
loss of appetite, not related to another illness (cold, flu, etc.), and not associated with anorexia nervosa?.....	4 3 2 1
are new feelings of early satiety particularly worrisome? yes no	
feeling too cold, compared to others in the same place?.....	4 3 2 1
feeling too warm, compared to others in the same place?.....	4 3 2 1

CHEST Findings:

coughing up blood on more than two occasions?.....	4 3 2 1
changes in amount or kind of sputum?.....	4 3 2 1
bloody streaks or tingee in sputum?.....	4 3 2 1
pain on breathing deeply on more than two occasions?.....	4 3 2 1
shortness of breath, not associated with heart disease or asthma?.....	4 3 2 1
pain in neck or shoulder which is persistent and not from strain?.....	4 3 2 1
palpitations, not associated with heart disease or medications?.....	4 3 2 1

BREAST Findings:

pain, not associated with menase or injury?.....	4 3 2 1
changing breast lumps, either new ones or enlarging ones?.....	4 3 2 1
change in breast size, not associated with puberty?.....	4 3 2 1
bloody discharge from nipple?.....	4 3 2 1
milky discharge from nipple, not associated with nursing?.....	4 3 2 1
swelling in armpits?.....	4 3 2 1

GASTROINTESTINAL TRACT Findings:

nausea, persisting for over two weeks, not associated with any particular foods or another illness?.....	4 3 2 1
vomiting, recurring for over two weeks, not associated with any particular foods or other illnesses?.....	4 3 2 1
vomiting as above, but within two hours after eating a meal?.....	4 3 2 1
pain on eating which feels like the food is "sticking"?.....	4 3 2 1
recurrent hiccups, persisting for more than two weeks?.....	4 3 2 1
jaundice, not associated with pain in the right upper quadrant?.....	4 3 2 1
bulging abdomen which has enlarged rapidly (less than one month) without increased eating?.....	4 3 2 1
unusually loud rumbling sounds in belly?.....	4 3 2 1
vomiting blood repeatedly, without excessive alcohol intake?.....	4 3 2 1
vomiting material which looks like coffee grounds?.....	4 3 2 1
stool with blood, repeatedly?.....	4 3 2 1

Findings from HEENT:

HEAD	headaches of increasing frequency and duration, and not associated with other illness or trauma?.....	4 3 2
	lumps on head, not associated with recent trauma?.....	4 3 2
	fainting, not associated with stress, excessive heat or exercise?.....	4 3 2
EYES	difficulty moving eye (any defect), not associated with trauma?.....	4 3 2
	changes in ability to see (familiar objects do not look right)?.....	4 3 2
	new blind spots?.....	4 3 2
	double vision?.....	4 3 2
	drooping eyelids, not associated with fatigue or staying up late?.....	4 3 2
EARS	ringing in ears, not associated with noise exposure, and not chronic?.....	4 3 2
	poor balance, not associated with intoxication, and not chronic?.....	4 3 2
	feelings of dizziness, not from intoxication, and not chronic?.....	4 3 2
	ulcer sores on ear?.....	4 3 2
	bleeding from ear canal?.....	4 3 2
NOSE	bloody discharge (not a brisk bleeding like a nosebleed)?.....	4 3 2
	inability to breathe through both nostrils equally, not associated with a cold, sinusitis, or deviated septum?.....	4 3 2
	constant "boring" pain in nose, not associated with trauma?.....	4 3 2
MOUTH	bumps on roof of mouth, not associated with trauma or injury?.....	4 3 2
	pain in mouth on swallowing, not associated with "sore throat"?.....	4 3 2
	lip sore that doesn't heal and may bleed?.....	4 3 2
	lump in tongue, lasting more than 1 week?.....	4 3 2
	tongue pain, not associated with injury to tongue?.....	4 3 2
	hoarseness, not attributable to shouting or exposure to smoke?.....	4 3 2
	recent voice changes, not related to puberty?.....	4 3 2
	new onset of persistent or frequent drooling?.....	4 3 2
NECK	pain in throat or neck on swallowing, not attributed to sore throat?.....	4 3 2
	swelling in neck or jaw, not associated with trauma?.....	4 3 2
	gopher?.....	4 3 2
	paralysis in neck or face?.....	4 3 2

	stools are dark or tarry, repeatedly?.....	4 3 2
	bowel movements are painful, not associated with diet changes or trauma?.....	4 3 2
	recent onset (or increase) of constipation, without diet changes?.....	4 3 2
	back or abdominal pain, repeatedly over a month, not associated with other illness?.....	4 3 2
	frequent feeling of needing to move bowels, not associated with another illness, and lasting more than two weeks?.....	4 3 2
	"pencil-thin" bowel movements for more than a week?.....	4 3 2
	new or increasing problems with incontinence?.....	4 3 2

BIDRETS, BLADDER, REPRODUCTIVE TRACT: (with gender-appropriate questions)

	frequent urination (more than 3 liters per day total for one week)?.....	4 3 2
	painful urination, not associated with known venereal disease, and lasting more than two weeks?.....	4 3 2
	new trouble starting urination?.....	4 3 2
	discharge from urethra, not associated with known venereal disease?.....	4 3 2
	blood in urine for more than four consecutive days?.....	4 3 2
	penile ulcer, not associated with known VD, and persisting more than two weeks?.....	4 3 2
	vaginal or vulvar ulcers, not associated with known VD, and persisting more than two weeks?.....	4 3 2
	testicular mass or tenderness for more than one week?.....	4 3 2
	swelling of scrotum for more than two weeks?.....	4 3 2
	lumps in groin creases which persist more than two weeks?.....	4 3 2
	vaginal bleeding between periods, not associated with using oral contraceptive pills?.....	4 3 2
	post-menopausal bleeding?.....	4 3 2
	increasing abdominal girth which has enlarged in less than one month, and not associated with changes in diet?.....	4 3 2
	stool found in vagina on more than two occasions (i.e. through a fistula)?.....	4 3 2
	use of Contraceptive Pills?.....	4 3 2
	new, persistent impotence, with no erectile ability at all?.....	4 3 2
	new onset of urinary incontinence, persisting more than two weeks?.....	4 3 2

FIGURE 5.1
(PART - F)

SPINE & EXTREMITIES:

new back pain (non-specific)?.....	4	3	2	1
new and persistent numbness in arm or legs?.....	4	3	2	1
bone pain which is worse at night?.....	4	3	2	1
fractures of bones with only minimal impact?.....	4	3	2	1
swollen joint, without injury or pain?.....	4	3	2	1
progressive loss of height?.....	4	3	2	1
black discoloration under fingernails or toenails, not from trauma?.....	4	3	2	1
painful red or violet spot under nail, not from trauma?.....	4	3	2	1
new persistent weakness in an arm or leg?.....	4	3	2	1
problems walking, such as foot drop, or one-sided weakness?.....	4	3	2	1

SKIN:

history of sunburning easily?.....	4	3	2	1
flushing of skin, not from blushing or a burn?.....	4	3	2	1
changes in skin color (new dark or light spots)?.....	4	3	2	1
itching, without obvious exposure to poison ivy, bee stings, etc?..	4	3	2	1
lumps under the skin, which have enlarged or are new?.....	4	3	2	1
moles which bleed or have changed in size or color?.....	4	3	2	1

HEMATOLOGIC:

swollen lymph nodes, not associated with other illness, and lasting more than two weeks.....	4	3	2	1
new onset of easy bruising.....	4	3	2	1
new onset of easy bleeding.....	4	3	2	1

One last question: Please indicate your departmental affiliation:

DEPARTMENT OF _____

Thank you very, very much for completing this questionnaire.

Please place your questionnaire in the SMALL envelope, then seal it and put it inside the larger envelope. If you would like a copy of the results, please check the box on the larger envelope.

(If you do not wish to participate in the study, please return an empty small envelope inside the larger one, as per RIC Protocol # 3856.)

Lastly, please put it into the Medical Center Campus Mail. Thank you!

FIGURE 5.1
(PART-IV)

EARLY SIGNS & SYMPTOMS OF CANCER -- Physicians' Index of Suspicion

INSTRUCTIONS: In the first column for each finding below, please rate the degree to which you would be vigorous in pursuing a neoplastic work-up, given the single, isolated finding (i.e. the patient has only that one finding). In the second column, please consider the situation of a patient having a constellation of findings suggestive of cancer, and then rate the weight you would give to a finding which fits such a constellation. (For example, one would rate "fever" alone for the first column, and "fever" as a part of "fever + adenopathy + night sweats + weight loss" for the second column.) Please base your ratings on your own patient population and experience, and leave blanks where appropriate.

Please use the following scale for these ratings:

- 4+ = the individual should be admitted this week
- 3+ = pt should see a physician within 2 weeks
- 2+ = pt should have this followed-up in the next 2 months if findings persist
- 1+ = pt should follow the usual screening exam recommendations
- 0+ = this finding isn't useful for detecting Cancer

Please note that questions will also be asked about demographics (age, gender, race, pertinent family history) and habits (tobacco/marijuana/snuff, alcohol).

<p>CONSTITUTIONAL FINDINGS</p> <p>unintentional weight loss</p> <p>weight gain</p> <p>fatigue</p> <p>depression</p> <p>fever</p> <p>chills</p> <p>night sweats</p> <p>anorexia</p> <p>feeling too cold</p> <p>feeling too warm</p> <p>Headaches with increasing frequency and duration</p> <p>lumps on head</p> <p>fainting</p> <p>difficulty moving eyes</p> <p>changes in ability to see</p> <p>new blind spots</p> <p>double vision</p> <p>drooping eyelid(s)</p> <p>ringing in ears</p> <p>poor balance</p> <p>feelings of dizziness</p> <p>ulcer sores on ear</p> <p>bleeding from ear</p> <p>bloody discharge (not brisk bleeding like nosebleeds)</p> <p>inability to breath through one nostril</p> <p>constant "boring" pain</p>	<p>Mouth</p> <p>bumps on roof of mouth</p> <p>pain in mouth on swallowing</p> <p>lip sore that doesn't heal and may bleed</p> <p>lump in tongue</p> <p>tongue pain</p> <p>hoarseness</p> <p>recent voice changes</p> <p>drooling</p> <p>pain in throat or neck on swallowing</p> <p>swelling in neck or jaw</p> <p>goiter</p> <p>paralysis in neck or face</p> <p>CHEST</p> <p>coughing up blood</p> <p>changes in amount or kind of sputum</p> <p>bloody streaks or tinges in sputum</p> <p>pain on breathing deeply</p> <p>shortness of breath</p> <p>pain in neck or shoulder</p> <p>palpitations</p> <p>BREASTS</p> <p>pain</p> <p>lumps</p> <p>recent change in breast size</p> <p>bloody discharge from nipple</p> <p>milky discharge from nipple</p> <p>swelling in armpit(s)</p>
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<p>GASTROINTESTINAL TRACT</p> <p>nausea</p> <p>vomiting</p> <p>pain on eating</p> <p>persistent hiccups</p> <p>jaundice</p> <p>bulging abdomen</p> <p>unusually loud rumbling sounds in belly</p> <p>vomiting after eating</p> <p>vomiting blood</p> <p>stool with blood</p> <p>dark or tarry stools</p> <p>painful bowel movements</p> <p>recent onset (or increase) of constipation</p> <p>back or abdominal pain</p> <p>frequent feeling of needing to move bowels</p> <p>"pencil-thin" bowel movements</p> <p>incontinence</p> <p>KIDNEYS, BLADDER, REPRODUCTIVE TRACT (with gender-appropriate questions)</p> <p>frequent urination</p> <p>painful urination</p> <p>trouble starting urination</p> <p>discharge</p> <p>blood in urine</p> <p>penile ulcer</p> <p>vaginal or vulvar ulcers</p> <p>testicular mass or tenderness</p> <p>swelling of scrotum</p> <p>lumps in groin creases</p> <p>vaginal bleeding between periods</p> <p>post-menopausal bleeding</p> <p>increasing abdominal girth</p> <p>stool found in vagina (through a fistula)</p> <p>use of Contraceptive Pills</p> <p>impotence</p> <p>incontinence of urine</p>	<p>SPINE & EXTREMITIES</p> <p>new back pain</p> <p>new and persistent numbness in arms or legs</p> <p>bone pain (worse at night)</p> <p>fractures of bones</p> <p>swollen joint, without injury or pain</p> <p>loss of height</p> <p>black discoloration under fingernails or toenails</p> <p>painful red or violet spot under nail</p> <p>weakness (one arm or leg)</p> <p>problems walking (foot drop one-sided weakness)</p> <p>SKIN</p> <p>sunburn easily</p> <p>flushing of skin</p> <p>changes in skin color</p> <p>itching</p> <p>lumps</p> <p>moles which bleed or have changed in size or color</p> <p>HEMATOLOGIC</p> <p>swollen lymph nodes</p> <p>new easy bruising</p> <p>new easy bleeding</p>
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One last question:

Please indicate your departmental affiliation:

DEPARTMENT OF _____

Thank you very much for completing this questionnaire.

Please place your questionnaire in the SMALL envelope, then seal it and put it inside the larger envelope. If you would like a copy of the results, please check the box on the larger envelope.

(If you do not wish to participate in the study, please return an empty small envelope inside the larger one, as per HIC Protocol # 3856.)

Lastly, please put it into the Medical Center Campus Mail. Thank you!

Figure 5.2

Brief Questionnaire Form for Physicians

- 4+ the individual should be admitted this week
- 3+ the individual should see a physician within 2 weeks
- 2+ this should be followed-up in the next 2 months
if findings persist
- 1+ the individual should follow the usual screening exam
recommendations
- 0+ this finding isn't useful for detecting Cancer

Figure 5.3

Clinimetric Scale used for Physicians' Questionnaires

Department	Eligible	Responded	Participated		% Long	% Total
			N (long)	N (brief)		
Medicine	101	65 (64%)	41	5	41%	46%
Ob-Gyn	16	10 (63%)	5	1	31%	38%
Pediatrics	47	39 (83%)	17	4	36%	45%
Surgery	46	26 (57%)	21	3	46%	52%
.....
totals	210	145 (69%)	84	13	40%	46%

Figure 5.4

Return rates for the Physicians' Survey

Final summary statistics		for All Questionnaires & All Extended Questionnaires				
finding.....	Mean	StDev	N	Mean	StDev	N
Wt loss	2.980	0.499	94	3.001	0.407	81
Wt gain	1.188	0.943	93	1.269	0.937	80
fever nonspec	2.405	0.948	85	2.408	0.929	77
fever spec	3.187	0.884	89	3.285	0.774	76
chills	2.411	1.046	90	2.487	0.988	78
night sweats	2.882	0.703	90	2.941	0.594	78
fatigue nonspec	1.800	0.646	89	1.825	0.619	79
fatigue spec	2.411	0.758	92	2.466	0.714	79
depression	1.752	0.953	92	1.838	0.880	79
anorexia	2.331	0.719	91	2.267	0.715	79
feeling warm	1.387	0.883	91	1.451	0.868	78
cold	1.378	0.876	91	1.441	0.860	78
headaches	2.863	0.674	83	2.786	0.645	72
head lumps	2.758	0.751	83	2.779	0.842	73
fainting	2.438	1.162	78	2.496	1.059	69
FOM dysf	3.151	0.889	80	3.173	0.819	70
loss of vision	2.886	0.903	80	2.870	0.904	70
blind spots	3.212	0.797	80	3.171	0.805	70
diptopia	3.283	0.813	81	3.224	0.818	71
ptosis	2.943	0.790	82	2.907	0.806	72
tinitis	2.227	0.900	79	2.256	0.875	70
poor balance	2.914	0.839	80	2.931	0.793	71
dizziness	2.416	0.894	81	2.426	0.855	72
ear ulcers	2.430	0.883	80	2.456	0.842	71
blf fm canal	2.836	1.004	78	2.858	0.980	69
blid nasal dc	2.617	0.887	78	2.630	0.855	70
uneq nostrils	2.059	0.813	78	2.094	0.884	70
nasal pain	2.477	0.857	77	2.467	0.818	70
mouth bumps	2.643	0.711	75	2.621	0.734	68
mouth pain	2.653	0.815	77	2.657	0.773	69
lip sore	2.909	0.629	79	2.911	0.590	70
tongue lump	2.956	0.586	78	2.936	0.585	69
tongue pain	2.431	0.704	77	2.400	0.724	68
hoarseness	2.925	0.582	79	2.930	0.559	70
voice changes	2.783	0.654	78	2.770	0.642	69
drooling	2.751	0.825	77	2.762	0.770	68
neck pain	2.756	0.711	78	2.754	0.721	69
neck swelling	3.022	0.493	78	3.010	0.511	69
goiter	2.521	0.795	78	2.545	0.751	69
neck paralysis	3.314	0.825	77	3.307	0.838	69
hemoptysis	3.410	0.590	77	3.376	0.571	68
sputum change	2.514	0.706	76	2.509	0.618	67
bloody sputum	3.003	0.650	76	3.003	0.624	67
pain on inspir	2.551	0.970	75	2.459	0.940	66
SOB	2.679	0.867	75	2.589	0.853	66
pain in shoulder	2.558	0.751	74	2.520	0.758	66
palpitations	2.088	1.074	75	2.115	0.994	66
breast pain	2.316	0.882	73	2.330	0.858	64
chng breast lump	3.144	0.592	77	3.151	0.547	67

ch in breast size	2.893	0.605	74	2.877	0.573	64
bloody nipple dc	3.368	0.657	77	3.378	0.659	67
milkly dc	2.741	0.591	75	2.748	0.583	65
axillary swelling	2.991	0.660	77	2.945	0.650	67
nausea	2.405	0.845	80	2.491	0.787	70
vomiting	2.975	0.837	80	3.057	0.716	70
postpran vomiting	2.959	0.851	76	2.984	0.764	67
dysphagia	2.961	0.669	77	3.045	0.605	67
hicups	2.695	0.898	78	2.738	0.853	68
jaundice	3.680	0.521	81	3.706	0.430	71
bulging abdomen	3.453	0.690	81	3.503	0.584	71
bor-borygmi	1.748	0.858	79	1.799	0.765	69
hematemesis	3.705	0.704	81	3.692	0.717	71
coffee grounds	3.704	0.544	71	3.704	0.544	71
bloody stool	3.510	0.516	81	3.511	0.490	71
melena	3.591	0.541	79	3.604	0.518	69
painful bm	2.623	0.738	78	2.675	0.652	69
constipation	2.478	0.679	78	2.526	0.586	69
back/abd pain	2.487	0.676	77	2.543	0.626	68
tenesmus	2.474	0.656	76	2.456	0.602	68
pencil thin stool	2.933	0.742	78	2.954	0.671	69
fecal incont	2.922	0.682	76	2.957	0.654	67
polyuria	2.429	1.006	78	2.478	1.034	68
dysuria	2.571	0.892	78	2.625	0.882	68
trbl strtg urine	2.762	0.669	79	2.786	0.667	69
urethral dc	2.610	0.864	77	2.691	0.838	68
hematuria	3.346	0.588	79	3.367	0.557	69
penile ulcer	3.122	0.590	77	3.168	0.486	68
vaginal ulcer	3.101	0.602	80	3.144	0.513	70
testicular mass	3.399	0.532	78	3.364	0.529	69
scrotal swelling	3.242	0.494	77	3.226	0.493	69
lumps in groin	3.060	0.639	78	3.025	0.627	69
intermenstr bld	2.862	0.673	78	2.814	0.664	69
post menop bld	3.007	0.650	76	2.978	0.647	67
incr girth	3.203	0.519	79	3.214	0.538	70
stool in vagina	3.691	0.467	79	3.680	0.472	70
use of OCP	1.137	0.661	71	1.122	0.635	63
impotence	1.979	0.838	72	2.023	0.837	65
urinary incont	2.699	0.998	77	2.711	1.006	70
back pain	2.209	0.762	81	2.125	0.745	71
extr numbness	2.879	0.878	80	2.819	0.874	70
bone pain	2.926	0.609	80	2.857	0.573	69
pathological fx	3.491	0.612	80	3.476	0.554	70
swollen joint	2.567	0.849	79	2.526	0.862	68
height loss	2.051	0.890	79	2.058	0.839	69
blk nailbed spots	2.486	0.945	78	2.506	0.912	69
red nailbed spots	2.555	0.926	74	2.571	0.886	65
extr weakness	3.187	0.813	79	3.140	0.834	70
walking probs	3.303	0.784	80	3.289	0.799	70
sunburning hx	1.289	0.739	74	1.339	0.717	66
flushing hx	1.847	0.844	74	1.935	0.770	66
ch skin color	2.321	0.745	75	2.345	0.695	67
itching	2.080	0.823	74	2.150	0.750	66
cutaneous lumps	2.880	0.645	74	2.895	0.617	66
changing moles	3.387	0.624	75	3.343	0.629	67
adenopathy	3.222	0.535	76	3.204	0.510	68
easy bruising	3.100	0.658	77	3.097	0.685	69
easy bleeding	3.179	0.654	77	3.157	0.667	69

Figure 5.5
Composite results for all physicians

Composite	Internal Medicine	Ob-Gyn	Pediatrics	Surgery
jaundice	stool in vagina	patho. fractures	stool in vagina	hematemesis
coffee grounds	coffee grounds	walking problems	jaundice	coffee grounds
hematemesis	jaundice	coffee grounds	coffee grounds	jaundice
stool in vagina	melena	hematemesis	hematemesis	bulging abdomen
melena	hematemesis	jaundice	bulging abdomen	path. fractures
bloody stool	blood in stool	adenopathy	testicular mass	melena
bulging abdomen	bloody nipple d/c	extremity weakness	blood in stool	stool in vagina
path. fractures	hematuria	changing mole	diplopia	fever, specific
bloody nipple d/c	hemoptysis	neck paralysis	melena	blind spots
hemoptysis	bulging abdomen	black nailbed spots	path. fractures	blood in stool
hematuria	path. fractures	bulging abdomen	hemoptysis	testicular mass
testicular mass	changing mole	stool in vagina	scrotal swelling	neck paralysis

Figure 5.6

"Top Dozen" Findings

ISRs order from Highest to Lowest mean value

finding.....	Mean	StDev	N	2.814	0.664	69
jaundice	3.706	0.430	71	intermenst bld	0.667	69
coffee grounds	3.704	0.544	71	trbl strtg urine	2.786	69
hematemesis	3.692	0.717	71	headaches	2.786	72
stool in vagina	3.680	0.472	70	head lumps	2.779	73
melena	3.604	0.518	69	voice changes	2.770	69
bloody stool	3.511	0.490	71	drooling	2.762	68
bulging abdomen	3.503	0.584	71	neck pain	2.754	69
pathological fx	3.476	0.554	70	mikly dc	2.748	65
bloody nipple dc	3.378	0.659	67	hiccupps	2.738	68
hemoptysis	3.376	0.571	68	urinary incont	2.711	70
hematuria	3.367	0.557	69	urethral dc	2.691	68
testicular mass	3.364	0.529	69	painful bm	2.675	69
changing moles	3.343	0.629	67	mouth pain	2.657	69
neck paralysis	3.307	0.838	69	bid nasal dc	2.630	70
walking probs	3.289	0.799	70	dysuria	2.625	68
fever spec	3.285	0.774	76	mouth bumps	2.621	68
scrotal swelling	3.226	0.493	69	red nailbed spots	2.589	66
diplopia	3.224	0.818	71	goiter	2.571	65
incr girth	3.214	0.538	70	back/abd pain	2.545	69
adenopathy	3.204	0.510	68	swollen joint	2.526	68
EOM dysf	3.173	0.819	70	constipation	2.526	69
blind spots	3.171	0.805	70	pain in shoulder	2.520	66
penile ulcer	3.168	0.486	68	sputum change	2.509	67
easy bleeding	3.157	0.667	69	bik nailbed spots	2.506	69
chnq breast lump	3.151	0.547	67	fainting	2.496	69
vaginal ulcer	3.144	0.834	70	nausea	2.491	70
extr weakness	3.140	0.834	70	chills	2.487	78
easy bruising	3.097	0.685	69	polyuria	2.478	68
vomiting	3.057	0.716	70	nasal pain	2.467	70
dysphagia	3.045	0.605	67	fatigue spec	2.466	79
lumps in groin	3.025	0.627	69	pain on inspir	2.459	66
neck swelling	3.010	0.511	69	ear ulcers	2.456	71
bloody sputum	3.003	0.624	67	tenesmus	2.456	68
Wt loss	3.001	0.407	81	dizziness	2.426	72
postpran vomiting	2.984	0.764	67	fever nonspec	2.408	77
post menop bld	2.978	0.647	67	tongue pain	2.400	68
fecal incont	2.957	0.654	67	ch skin color	2.345	67
pencil thin stool	2.954	0.671	69	breast pain	2.330	64
axillary swelling	2.945	0.650	67	anorexia	2.267	79
night sweats	2.941	0.594	78	tinitis	2.256	70
tongue lump	2.936	0.585	69	itching	2.256	66
poor balance	2.931	0.793	71	back pain	2.150	70
hoarseness	2.930	0.559	70	palpitations	2.125	71
lip sore	2.911	0.590	70	uneg nostrils	2.115	66
ptosis	2.907	0.806	72	height loss	2.094	70
cutaneous lumps	2.895	0.617	66	impotence	2.058	69
ch in breast size	2.877	0.573	64	flushing hx	2.023	65
loss of vision	2.870	0.904	70	depression	1.935	66
bld fm canal	2.858	0.980	69	fatigue nonspec	1.838	79
bone pain	2.857	0.573	69	borborygmi	1.825	69
extr numbness	2.819	0.874	70	feeling warm	1.799	69
				cold	1.451	78
				sunburning hx	1.441	78
				Wt gain	1.339	66
				use of OCP	1.269	80
					1.122	63

Figure 5.7
 Variability in ranking findings
 (Part I - sorted by mean ISR)

ISRs order from Highest to Lowest Standard Deviation value

finding.....	Mean	StDev	N	2.754	0.721	69
fainting	2.496	1.059	69	neck pain	0.721	69
polyuria	2.478	1.034	68	hematemesis	0.717	71
urinary incont	2.711	1.006	70	sunburning hx	0.717	66
palpitations	2.115	0.994	66	vomiting	0.716	70
chills	2.487	0.988	78	anorexia	0.715	79
blid fm canal	2.858	0.980	69	fatigue spec	0.714	79
pain on inspir	2.459	0.940	66	ch skin color	0.695	67
wt gain	1.269	0.937	80	easy bruising	0.685	69
fever nonspec	2.408	0.929	77	pencil thin stool	0.671	69
blk nailbed spots	2.506	0.912	69	easy bleeding	0.667	69
loss of vision	2.870	0.904	70	trbl strtg urine	0.667	69
red nailbed spots	2.571	0.886	65	intermenst bid	0.664	69
ureg nostrils	2.094	0.884	70	bloody nipple dc	0.659	67
dysuria	2.625	0.882	68	fecal incont	0.654	67
depression	1.838	0.880	79	painful bm	0.652	69
tinitis	2.256	0.875	70	axillary swelling	0.650	67
extr numbness	2.819	0.874	70	post menop bid	0.647	67
feeling warm	1.451	0.868	78	headaches	0.645	72
swollen joint	2.526	0.862	68	head lumps	0.642	73
cold	1.441	0.860	78	voice changes	0.642	69
breast pain	2.330	0.858	64	use of OCP	0.635	63
dizziness	2.426	0.855	72	changing moles	0.629	67
blid nasal dc	2.630	0.855	70	lumps in groin	0.627	69
hiccups	2.738	0.853	68	back/abd pain	0.626	69
SOB	2.589	0.853	66	bloody sputum	0.624	67
ear ulcers	2.456	0.842	71	fatigue nonspec	0.619	79
height loss	2.058	0.839	69	sputum change	0.618	67
neck paralysis	3.307	0.838	69	cutaneous lumps	0.617	66
urethral dc	2.691	0.838	68	dysphagia	0.605	67
impotence	2.023	0.837	65	tenesmus	0.602	68
extr weakness	3.140	0.834	70	night sweats	0.594	78
EOM dysf	3.173	0.819	70	lip sore	0.590	70
diplopia	3.224	0.818	71	constipation	0.586	69
nasal pain	2.467	0.818	70	tongue lump	0.585	69
ptosis	2.907	0.806	72	bulging abdomen	0.584	71
blind spots	3.171	0.805	70	mikly dc	0.583	65
walking probs	3.289	0.799	70	bone pain	0.573	69
poor balance	2.931	0.793	71	ch in breast size	0.571	68
nausea	2.491	0.787	70	hemoptysis	0.571	68
fever spec	3.285	0.774	76	hoarseness	0.559	70
mouth pain	2.657	0.773	69	hematuria	0.557	69
drooling	2.762	0.770	68	pathological fx	0.554	70
flushing hx	1.935	0.770	66	chng breast lump	0.547	67
borborygmi	1.799	0.765	69	coffee grounds	0.544	71
postpran vomiting	2.984	0.764	67	incr girth	0.538	70
pain in shoulder	2.520	0.758	66	testicular mass	0.529	69
goiter	2.545	0.751	69	melena	0.518	69
itching	2.150	0.750	66	vaginal ulcer	0.513	70
back pain	2.125	0.745	71	neck swelling	0.511	69
mouth bumps	2.621	0.734	68	adenopathy	0.510	68
tongue pain	2.400	0.724	68	scrotal swelling	0.493	69
				bloody stool	0.490	71
				penile ulcer	0.486	68
				stool in vagina	0.472	70
				jaundice	0.430	71
				Wt loss	0.407	81

Figure 5.7
Variability in ranking findings
(Part II - sorted by standard deviation in ISR)

CN	Patient	Diagnosis	Time-lag	Findings	Rec	Delta months
1001	28 y.o. F	Melanoma	6 mo	y 3	3.3	5.5
1002	43 y.o. F	Breast mets	as soon as found	y 1	3.1	-
1003	49 y.o. F	Breast	4 wks	y 3	3.1	0.5
1004	36 y.o. F	Melanoma	6 mo	y 1	3.3	5.5
1005	48 y.o. F	Breast	7 yrs	y 1	3.1	82
1006	58 y.o. F	unknown	2 wks	y 1	2.6	-
1007	41 y.o. M	Adenocystic Car	2 mo	y 1	3.3	1.5
1008	52 y.o. F	Breast	3 mo	y 1	3.1	2.5
1009	49 y.o. F	Melanoma	2-3 mo	y 1	3.3	2
1010	25 y.o. M	Melanoma	days	y 1	3.3	-
1011	65 y.o. M	Bladder	1.5 yrs	y 1	2.6	15
1012	49 y.o. F	Breast	several months	y 1	3.1	2.5
1013	51 y.o. F	Breast	3 wks	y 3	3.1	0.25
1014	48 y.o. F	Melanoma	1 mo	y 1	2.9	0.5
1015	65 y.o. F	Breast	uncertain	y 1	3.1	N/A
1016	36 y.o. M	Hodgkins	1 mo	y 2	3.5	0.5
1017	67 y.o. M	Small Cell	1 mo	y 1	2.5	N/A
1018	53 y.o. F	Thyroid	1 wk	y 1	2.9	-
1019	44 y.o. F	Breast mets	2 wks at dx	y 2	3.1	0.1
1020	71 y.o. M	Breast	2 yrs	y 1	3.1	23.5
1021	55 y.o. F	Melanoma	found at P.E.	y 1	3.4	N/A
1022	48 y.o. F	Melanoma	5 mo	y 1	3.3	4.5
1023	62 y.o. F	Lymphoma	2 mo	y 2	2.8	1.5
1024	50 y.o. M	Melanoma	7 mo	y 1	3.4	6.5
1025	65 y.o. F	Leukemia	CLL by lab tests	n 0	---	N/A
1026	38 y.o. F	Lymphoma Non-H.	1 yr	y 1	3.0	11.5
1027	38 y.o. F	Colon	2 wks +/-	y 6	3.3	0
1028	31 y.o. F	Melanoma	3 mo	y 1	3.3	2.5
1029	31 y.o. F	Breast	3 mo	y 2	3.0	0.5
1030	21 y.o. F	Hodgkins	month	y 3	3.0	-
1031	62 y.o. F	Breast	4-5 d	y 1	3.1	N/A
1032	40 y.o. F	Breast	found at P.E.	y 1	3.0	2.5
1033	52 y.o. F	Lymphoma	2-3 months	y 2	3.0	-
1034	38 y.o. F	Lymphoma	1 wk	y 2	3.5	-
1035	57 y.o. F	Breast	3 wks	y 1	3.1	0.25
1036	70 y.o. F	Lymphoma	several months	y 1	2.9	2.5
1037	41 y.o. F	Melanoma	found at P.E.	y 1	3.3	N/A
1038	70 y.o. M	Lymphoma	6 mo	y 4	3.3	5.5
1039	39 y.o. F	Breast	1 day	y 2	3.1	-
1040	44 y.o. M	Mycosis fung.	3 yrs	y 1	2.1	34
1041	56 y.o. F	Melanoma	6 mo	y 2	2.9	5.5
1042	59 y.o. F	Melanoma	5 mo	y 1	3.3	4.5
1043	50 y.o. M	Melanoma	8 yrs	y 2	2.9	75.5
1044	34 y.o. M	NonHodgkins	6 mo (under MD)	y 6	3.0	5.5
2001	35 y.o. M	Colon	2 yrs	y 3	3.5	23.5
2002	32 y.o. F	Melanoma	1 yr	y 1	3.3	11.5
2003	45 y.o. M	Colon	6 mo	y 1	2.5	4
2004	43 y.o. F	Breast	found at P.E.	y 1	3.1	N/A
2005	54 y.o. F	unknown	2 mo	y 1	3.3	1.5
2006	32 y.o. F	Skin	long time	y 1	3.3	N/A
2007	30 y.o. F	Breast	2 months	y 2	3.1	1.5
2008	39 y.o. M	unknown	6 mo	y 3	3.0	5.5

Figure 6.1

Efficacy of computer assisted screen on time lags

CN	Patient	Diagnosis	Time-lag	Findings	Recs	Delta months
2009	42 y.o. F	Cervix	abnormal Pap	n 0	---	N/A
2010	27 y.o. F	Melanoma	3 mo	y 1	3.3	2.5
2011	59 y.o. F	Breast (Pagets)	immediate	y 2	3.0	-
2012	39 y.o. F	Breast	6 mo	y 1	3.1	5.5
2013	43 y.o. F	Breast	months	y 1	3.1	2.5
2014	93 y.o. F	Bladder	immediately	y 1	3.4	-
2015	61 y.o. M	Basal Cell	a few months	y 3	3.3	2.5
2016	54 y.o. F	Breast	1 wk	y 1	3.1	-
2017	67 y.o. F	Breast	year	y 1	3.1	11.5
2018	56 y.o. F	Breast	2-3 mo	y 1	2.3	1
2019	43 y.o. F	Breast	few months	y 4	3.1	2.5
2020	71 y.o. M	Angiosarcoma	2-3 yrs	y 1	2.9	29
2021	45 y.o. F	Breast	Ing time (month)	y 1	3.1	0.5
2022	34 y.o. F	Squamous Cell	2 wks	y 1	2.9	-
2023	56 y.o. F	Breast	5 mo	y 1	3.1	4.5
2024	45 y.o. F	Breast	mammography	n 0	---	N/A
2025	26 y.o. F	Melanoma	1 yr	y 1	3.3	11.5
2026	46 y.o. F	Breast	2 wks	y 1	3.1	0.1
2027	54 y.o. F	Breast	few wks	y 1	3.1	0.25
2028	37 y.o. F	Breast	week	y 1	3.4	-
2029	58 y.o. F	Colon	2 yrs	y 2	3.5	23.5
2030	59 y.o. F	Breast	30 yrs	y 1	3.1	360
2031	40 y.o. F	Breast	6-12 mo	y 3	3.1	5.5
2032	52 y.o. F	Breast	1 yr	y 1	3.1	11.5
2033	57 y.o. F	Breast	unaware	y 1	3.1	N/A

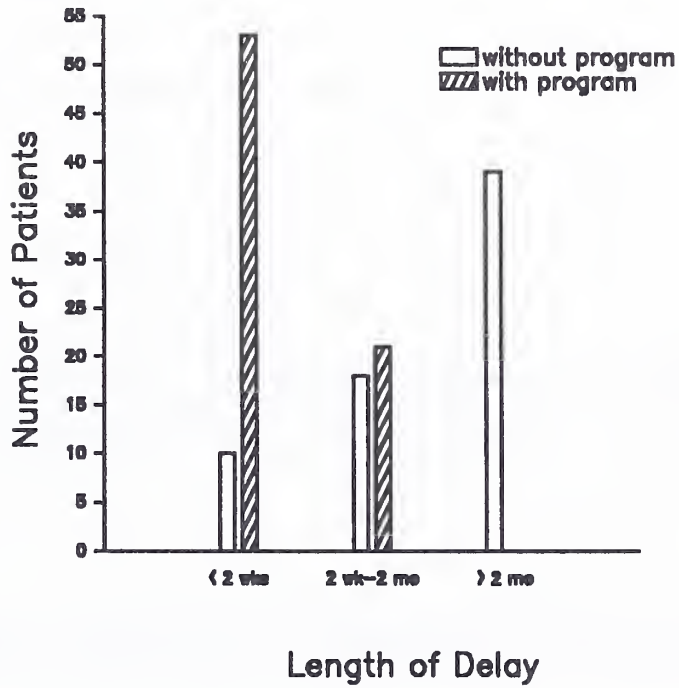
Of 76 patients who returned the questionnaire, 3 would not have been detected on clinical grounds (picked up by mammography, blood test, pap smear).

Of the 66 patients who reported a time course (between sx and dx): 53 would have been seen earlier (distributed as below)

13 would not have been helped (no change or not better)
 1 person was seen at 2 wks, as would have been recommended;
 the other 12 were seen within 2 wks

Delta interval	Number of patients helped
< 1 mo	10
1 - 3 mo	16
4 - 7 mo	13
8 - 15 mo	6
> 23 mo	8
-- total	53

Time between Symptoms and Evaluation



Efficacy of Screening Program

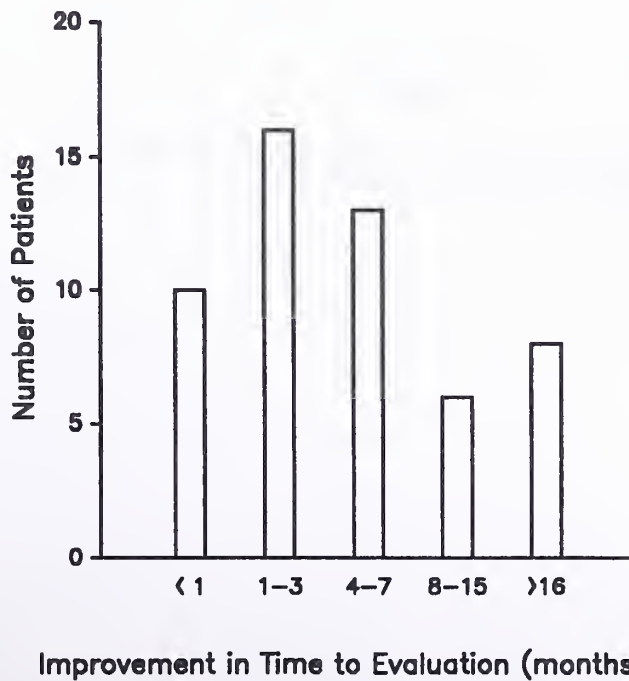


Figure 6.2
Distribution of changes in delay

category	Number of Pts, With Screening	Expected*	Chi-squared
< 2 wks	53	11.211	155.769
2 wks - 2 mo	21	20.180	0.033
> 2 mo	0	42.609	42.609
totals:	74	74.000	198.411

Degrees of freedom: 3 categories - 1 = 2 df

	p = 0.05	0.01	0.001
for 2 df, Chi-sq:	5.991	9.210	13.82

198.411 >> 13.82;

Conclusion: the screened population is significantly different from the expected results in the unscreened population of Phase 2 ($p \ll 0.001$).

* expected frequencies are based upon the Phase 2 findings of 10, 18, and 38 patients (of 66) in these three categories.

Figure 6.3

**Statistical Comparison of the Screening Recommendations
with Phase 2 Patient Data**

Appendix I
Sample Covering Letter

June 1986

SHM Mailroom / 333 Cedar St.

Dear Physician:

Could you please take a few moments of your time to share your clinical expertise with me for incorporation into a Medical School thesis?

Cancer continues to be a major health concern in this country. It is widely held that early diagnosis can lead to more effective treatment and thus to an improvement in a given patient's prognosis. My thesis involves developing a system to facilitate earlier entry into the health care system. I am assessing (a) from patients, the signs which they notice and the factors which determine when they see a physician and (b) from physicians, the findings which raise one's "Index of Suspicion" that a neoplasm needs to be worked-up.

This will form the basis for a computer program which lay people can use (e.g. at home, in the workplace) to help them evaluate their need to seek medical care for findings which are worrisome of cancer. For example, if an individual were to indicate a worrisome constellation of features*, the program would describe which findings were worrisome, and urge the person to see a physician sooner rather than later (a pre-triage function). For individuals without worrisome findings, the program would educate them as to the current recommendations for periodic screening exams (guaiac tests, mammograms, etc.) for their age group. (The program will be made available free of charge.)

The purpose of this program, thus, is to facilitate the entry of individuals with probable cancers into the health care system, not to let people "play doctor" or to replace the relationship between a patient and a physician.

I have enclosed two questionnaires, and I would ask you to complete one of them and return it to me (preferably the one entitled "Extended Questionnaire"). I have listed historical data in groups, by organ system. Where I need your help is in determining the relative importance of these features in raising your index of suspicion that some potentially serious pathology is lurking. For each organ system for which you wish to make comments, please circle the organ system name and then rate the symptoms following it. Please use the grading system described on the sheet. If you feel that additional findings should be included, please write them in.

When you are finished, please place your questionnaire into the smaller envelope, seal it, and then place it into the larger envelope and send it to me via Medical Center Mail. If you do not wish to participate in this study, please send me an empty envelope. Results of this work will be available to those who participate and indicate that they would like follow-up by checking the box next to the Control Number on the envelope. Please return your materials by the end of July, if that is possible.

Thank you very, very much for your assistance.

Sincerely,

Ian A. Cook YMS

* e.g. 50-pack year tobacco history, chronic cough with increasingly bloody sputum for 2 months, and a 20 lb weight loss over 4 months

Appendix II.

In this appendix, sample case histories are used to demonstrate how the computer program actually works. The following descriptions come from the application of the program to patients from Phase 2.

Example Case A Patient 2012, a 39 y.o. woman with breast cancer

You have reported that you are a 39 year old woman.

The following things which you reported may be abnormal:

1. lump in breast
2. feelings of fatigue

DISCUSSION:

1. LUMP IN BREAST:

A lump in the breast may be caused by a number of things. Fibrocystic breasts feel lumpy all the time, and these lumps are not cancerous. Infections can cause breast lumps as well. LUMPS WHICH CHANGE IN SIZE NEED TO BE SEEN BY A PHYSICIAN. You can help yourself by practicing the Breast Self-Examination (BSE) once a month, since the majority of breast cancers are self-detected.

2. FEELINGS OF FATIGUE:

Many, many things can cause feelings of fatigue. Inadequate amounts of sleep, excessive stress at home or at work, trouble "eating right," and many other things that are not cancer can cause fatigue. Seeing your doctor about any of these things may not be a bad idea either, and he or she may be able to help you feel better. On the other hand, feelings of fatigue can be associated with cancer, especially if accompanied by weight loss or loss of appetite. THESE THINGS SHOULD LEAD YOU TO MAKING AN APPOINTMENT.

RECOMMENDATIONS:

The physicians who contributed information to this project had the following predominant views:

1. LUMP IN BREAST:

you should try to see your physician
--> in between 1 and 2 weeks
if the problem continues

2. FEELINGS OF FATIGUE:

you should try to see your physician
--> in between 2 weeks and 2 months
if the problem continues

NOTE: Because you had specific findings (lump in breast) and "constitutional" findings (feelings of fatigue) you would be well advised to play it safe and see your physician in between 1 and 2 weeks

Example Case B. Patient 2029, a 58 y.o. woman with colon cancer

You have reported that you are a 58 year old woman.

The following things which you reported may be abnormal:

1. blood in stool
2. back or abdominal pains

DISCUSSION:

1. BLOOD IN STOOL:

Finding blood in your stool can be a sign of a number of things. Bleeding hemorrhoids, anal fissures, and abrasions around the anus can cause you to find blood ON your stool (or on the toilet paper after you've used it), but they do not cause there to be blood mixed IN with your stool. There is a test ("Occult Blood" or "Guicac" test) which your physician can help you do to determine the cause of this problem.

2. BACK OR ABDOMINAL PAINS:

Many, many things can cause back or abdominal pains. Indigestion, eating foods which upset your stomach, lifting heavy objects, and the like can cause these. These pains are more ominous if you also have problems with your stomach or intestines (blood in stool, black "tarry" stools, painful bowel movements, new or increased constipation). The presence of these findings as well should make you see your physician sooner.

RECOMMENDATIONS:

The physicians who contributed information to this project had the following predominant views:

1. BLOOD IN STOOL:

you should try to see your physician
--> in between 1 and 2 weeks
if the problem continues

2. BACK OR ABDOMINAL PAINS:

you should try to see your physician
--> in between 2 weeks and 2 months
if the problem continues

NOTE: Because you had multiple specific findings, you would be well advised to play it safe and see your physician in between 1 and 2 weeks

Example Case C. Patient 1030, a 21 y.o. woman with Hodgkins disease

You have reported that you are a 21 year old woman.

The following things which you reported may be abnormal:

1. swollen neck
2. weight loss
3. fatigue

DISCUSSION:

1. SWOLLEN NECK

A swollen neck can signify a number of things. A sore throat can sometimes produce a swelling in the neck. Other infections (like long-term acne) can cause swellings as well. You can try to feel the swelling so you can describe it: is it soft or hard, can you push it around under the skin or does it seem to be stuck to other things in your neck, is it painful to press on it? These things can help your physician decide what to do.

2. WEIGHT LOSS

With unintentional weight loss, a number of questions come to mind. Has your appetite changed, so that you aren't eating as much? Are you more physically active, so that you are burning up calories more? Are you not eating well because you're upset? Losing a lot of weight can be hazardous in and of itself, and ought to be discussed with your physician.

3. FEELINGS OF FATIGUE:

Many, many things can cause feelings of fatigue. Inadequate amounts of sleep, excessive stress at home or at work, trouble "eating right," and many other things that are not cancer can cause fatigue. Seeing your doctor about any of these things may not be a bad idea either, and he or she may be able to help you feel better. On the other hand, feelings of fatigue can be associated with cancer, especially if accompanied by weight loss or loss of appetite. THESE THINGS SHOULD LEAD YOU TO MAKE AN APPOINTMENT.

RECOMMENDATIONS:

The physicians who contributed information to this project had the following predominant views:

1. SWOLLEN NECK:

you should try to see your physician
 --> in about 2 weeks
 if the problem continues

2. WEIGHT LOSS:

you should try to see your physician
 --> in about 2 weeks
 if the problem continues

3. FEELINGS OF FATIGUE:

you should try to see your physician
 --> in between 2 weeks and 2 months
 if the problem continues

(... continued ...)

NOTE: Because you had specific findings (swollen neck), and "constitutional findings" (weight loss, feelings of fatigue) you would be well advised to play it safe and see your physician in about 2 weeks.

Example Case D. Patient 1001, a 28 y.o. woman with melanoma

You have reported that you are a 28 year old woman.

The following things which you reported may be abnormal:

1. moles which bleed or have changed in size or color
2. itching, without obvious exposure to poison ivy, bee stings, etc.

DISCUSSION:

1. MOLES WHICH BLEED OR HAVE CHANGED IN SIZE OR COLOR

Moles which change in size, shape, or color are worrisome. Fortunately, when caught early, it is very easy to treat these moles without leaving big scars. ACTING PROMPTLY IS IMPORTANT.

2. ITCHING, WITHOUT OBVIOUS EXPOSURE TO POISON IVY, BEE STINGS, ETC.

The causes of itching are many. You should decide whether the itching is all over your body or just in some spots, whether this is something new or old, and if you are taking any new medications (some of them may cause itching, but you should discuss this with your doctor before stopping to take them).

RECOMMENDATIONS:

The physicians who contributed information to this project had the following predominant views:

1. MOLES WHICH BLEED OR HAVE CHANGED IN SIZE OR COLOR:
you should try to see your physician
--> in between 1 and 2 weeks
if the problem continues
2. ITCHING, WITHOUT OBVIOUS EXPOSURE TO POISON IVY, BEE STINGS, ETC.:
you should try to see your physician
--> in between 2 weeks and 2 months
if the problem continues

NOTE: Because you had multiple specific findings (moles which bleed or have changed in size or color, itching, without obvious exposure to poison ivy, bee stings, etc.) you would be well advised to play it safe and see your physician in between 1 and 2 weeks.

Example case B. Normal control, 27 y.o. man without findings

You have reported that you are a 27 year old man.

The following things which you reported may be abnormal:

NOTHING

DISCUSSION:

You have not reported anything specifically which is worrisome for cancer.

RECOMMENDATIONS:

The physicians who contributed information to this project had the following predominant views:

You should be reminded of the Seven Warning Signals of cancer, as popularized by the American Cancer Society. They are:

- Change in bowel or bladder habits
- A sore that does not heal
- Unusual bleeding or discharge
- Thickening or lump in breast or elsewhere
- Indigestion or difficulty in swallowing
- Obvious change in wart or mole
- Nagging cough or hoarseness

NOTE: Because you had no abnormal findings you would be well advised see your physician if any of these signals develop.

CANCER CHECK PROGRAM

A part of the thesis "Computer Aided
Evaluation of Early Neoplasms."

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