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REVIEW ARTICLE

Errors in Cancer Diagnosis: Current Understanding and Future Directions

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ABSTRACT

Purpose
Errors in cancer diagnosis are likely the most harmful and expensive types of diagnostic errors. We reviewed the literature to understand the prevalence, origins, and prevention of errors in cancer diagnosis, focusing on common cancers for which early diagnosis offers clear benefit (melanoma and cancers of the breast, colon, and lung).

Methods
We searched the Cochrane Library and PubMed from 1966 until April 2007 for publications that met our review criteria and manually searched references of key publications. Our search yielded 110 studies, of which nine were prospective studies and the remaining were retrospective studies.

Results
Errors in cancer diagnosis were not uncommon in autopsy studies and were associated with significant harm and expense in malpractice claims. Literature on prevalence was scant. For each type of cancer, we classified preventable errors according to their origins in patient-physician encounters in the clinic setting, diagnostic test or procedure performance, pathologic confirmation of diagnosis, follow-up of patient or test result, or patient-related delays.

Conclusion
The literature reflects advanced knowledge of contributory factors and prevention for diagnostic errors related to the performance of procedures and imaging tests and emerging understanding of pathology errors. However, prospective studies are few, as are studies of diagnostic errors arising from the clinical encounter and patient follow-up. Future research should examine further the system and cognitive problems that lead to the many contributory factors we identified, and address interdisciplinary interventions to prevent errors in cancer diagnosis.

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INTRODUCTION

Diagnostic errors, defined as missed, delayed, or wrong diagnoses, are a frequent cause of medical errors in the United States.[1-3] Malpractice claims related to diagnosis are overall the most frequent and expensive of all claims (accounting for approximately 40% of all malpractice payments in 2003, with an average payment of approximately $300,000 per claim).[4] Two recent landmark studies have brought increased attention to errors in cancer diagnosis in the settings of ambulatory care and pathology.[5,6] The first of these, a study of ambulatory malpractice claims abstracted from a large risk management database, found that the majority of claims related to diagnostic errors (59%) pertained to cancer diagnosis.[5] In the second study, errors in cancer diagnosis were apparent in almost 12% of all reviewed cytologic-histologic specimen pairs. These studies establish that errors in cancer diagnosis are a significant health problem and have a tremendous impact in terms of disability and cost.[1,6-12] In many types of cancer, early diagnosis provides a clear survival benefit,[13] and diagnostic errors may result in grave consequences.[5] Preliminary data suggest that some missed and delayed cancer diagnoses are preventable.[5]

Diagnostic errors are those involving diagnoses that were unintentionally delayed (sufficient information to make a diagnosis was available earlier), wrong (another diagnosis was made before the correct one), or missed (no diagnosis was ever made), as judged from the eventual appreciation of more definitive information.[14] Examples of events leading to diagnostic error include failure to use an indicated diagnostic test, misinterpretation of test results, and failure to act or follow-up on abnormal results.[15] Although no-fault diagnostic errors (nonpreventable errors) may occur when signs of a disease are atypical or absent, diagnostic errors are often

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attributable to preventable factors such as cognitive errors (eg, faulty information synthesis or clinical reasoning) and/or systems-related factors (eg, problems with policies and procedures, inefficient processes, organizational issues, and poor communication).[5,14,16-18]

Despite being a frequent cause of medical errors, diagnostic errors have received surprisingly little attention until recently and are poorly understood. Understanding of cancer diagnostic errors is especially limited because the ultimate diagnosis may depend on multiple points of care and coordination among several disciplines. Errors in cancer diagnosis may thus originate in several domains of care (eg, the primary care practitioner's office, the specialties of radiology and pathology[6,10]) and in navigation of patients through several systems of care.[19] Hence, diagnostic errors in cancer have complex origins that require better understanding to design strategies to reduce their occurrence.[6,20,21] To our knowledge, there are no published reviews that outline a comprehensive approach to preventing errors in cancer diagnosis, taking into account several settings of care and navigation of patients between these settings. The objective of this article is thus twofold: to review systematically the published research on the prevalence, burden, origins, and prevention of diagnostic errors in cancer; and to discuss our perspective on future areas of research and prevention given the current state of the scientific evidence.

METHODS

We searched the Cochrane Library and PubMed for publications related to diagnosis of four common types of cancer in adults for which early diagnosis could be of potential benefit: breast cancer, colorectal cancer (CRC), lung cancer, and melanoma. We searched the Cochrane Library with the terms "cancer diagnostic errors" and "missed and delayed cancer diagnosis" but did not find any relevant reviews on the topic. We searched PubMed for articles with a combination of at least one term (keyword) related to cancer ("cancer," "breast cancer," "colorectal cancer," "melanoma," "lung cancer," "skin cancer," "colon cancer," "malignancy") and one term from a second category ("diagnostic errors," "missed diagnosis," "delayed diagnosis," "false negative cancer," "pitfalls in cancer diagnosis," "malpractice claims," "autopsy," "primary care," "pathology," and "radiology"). We limited the results to cancer-related studies or reviews conducted in humans, age ≥ 19 years and published in English between 1966 and April 2007.

Starting with 4,089 initial hits in PubMed, we pulled 389 titles and abstracts of interest for additional review based on their potential relevance to our objectives. Two authors reviewed each abstract independently (if needed, the entire article text was reviewed) to determine eligibility, and met to discuss and reach a consensus. Criteria for inclusion included those articles that described epidemiologic characteristics such as prevalence and demographics, burden, contributory factors, and preventive strategies of errors in cancer diagnosis.

The reviewers screened (in order) the titles, abstracts, and text of the selected articles, using the standard definition of diagnostic errors (missed, delayed, or wrong diagnosis) in evaluation of the literature. We excluded publications limited to success rates of specialized methods, specific types of new pathologic and radiologic techniques not conventionally used in current practice (such as use of computed tomography for colon cancer), and diagnosis of metastasis from the primary neoplasm. Also excluded were publications that focused only on delays associated with treatment, health care disparities, screening behaviors of physicians, false-positive cancer diagnosis, and the impact of diagnostic delays on prognosis. The search yielded several types of articles including retrospective cohort studies, retrospective case series, retrospective reviews, observational cohort studies, population-based observational case series, prospective studies, and review articles. We also manually searched the reference sections of relevant papers and obtained 26 additional articles. After using the above inclusion/exclusion criteria, we reviewed a final sample of 110 original studies and seven review articles that offered additional useful information.

RESULTS

Prevalence and Burden of Errors in Cancer Diagnosis

Aside from a population-based study from Germany that found provider delay of more than 3 months in 11% of all breast cancer patients,[22] we did not find any studies that reported the prevalence of errors in cancer diagnosis. Autopsy data suggested an overall cancer-related diagnostic error rate between 4.1% and 44%,[23-29]but the heterogeneous and highly selected samples of autopsy studies do not represent the true prevalence rate in the population.[30]

Although malpractice studies cannot be used to estimate the incidence or prevalence of errors, they may provide other types of useful data.[30] In the absence of other types of studies, we used many of the malpractice claims studies to estimate the burden and significance of diagnostic errors in cancer, which we found to be high. Cancers of the breast, colon, lung, and skin were found most frequently involved in these studies.[1,5,9,10] Given the tremendous impact of early diagnosis on the 5-year survival in these cancers,[13] these data are not unexpected. Cancer-related claims were seldom found to be defensible.[9]

We also found several specialties involved in malpractice claims studies. Overall, approximately 70% of all medical malpractice lawsuits filed against medical imaging professionals relate to missed diagnosis, and cancer-related claims are the most frequent.[31] In one study, approximately half (52.4%) of radiologists reported a prior malpractice claim and 14.8% reported mammography-related claims.[32] The same study found that about one in three radiologists (35.3%) had considered withdrawing from mammogram interpretation because of malpractice concerns.[32] In malpractice claims related to breast cancer, obstetricians and gynecologists were involved in the greatest number of cases (41% to 50%), followed by family practitioners and internists, general surgeons, and radiologists.[33,34] In lung cancer malpractice litigation, primary care physicians (60% of cases) and radiologists (20% of cases) were named as defendants in more than 75% of lawsuits.[35] For skin cancer-related claims, dermatologists and general practice physicians most often faced allegations of failure to diagnose, and pathologists were most likely to receive allegations of misdiagnosis.[36] In a study of pathology-related malpractice claims, cancer-related claims involving a pathologist were most common for breast cancer, followed by melanoma.[37]

Origins and Prevention of Errors in Cancer Diagnosis

In the malpractice study by Gandhi et al,[5] breast, colorectal, and skin cancers were the most common types of cancer involved (in that order), but diagnostic error origins were not categorized by type of cancer. In this study, breakdowns in the diagnostic process were (in order from most common) failure to order an appropriate diagnostic test, failure to create a proper follow-up plan, incorrect interpretation of diagnostic tests, and failure to perform an adequate history or physical examination. The leading contributory factors were knowledge, patient-related factors, handoffs (information transfer problems), and failures in judgment, vigilance, or memory.

In our evaluation of additional literature, we identified several other contributory factors for the four types of cancers. We first classified factors as preventable (including factors related to systems and cognitive problems)[14] or nonpreventable (those considered

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no-fault[14]) for each type of cancer (Tables 1 to 6). We then classified the preventable factors into five subcategories, when applicable, according to the setting of care in which the error occurred: patient-physician encounters in the clinic setting (eg, history, physical examination); performance of a diagnostic test or procedure (eg, imaging tests or colonoscopy); pathologic confirmation of diagnosis; follow-up of patients or their test results; or patient-related delays such as those related to noncompliance. These subcategories represented the domains of care in which diagnostic errors would have the most clinical impact, and allowed us to classify comprehensively the identified factors. In the following sections we present an overview of contributory factors categorized by the four types of cancers.

Breast Cancer

Four studies used a prospective design to evaluate errors in breast cancer diagnosis.[38-41] Of the remaining publications we selected, the majority were retrospective studies (including one that used some prospective enrollment[42] and several that used malpractice claims data; Table 1) and four were review articles related to mammography and needle biopsy.[31,43-45] Retrospective studies evaluated missed and delayed diagnoses of breast cancer through medical record reviews, surveys, or interviews.

Preventable factors. Missed breast cancer was one of the most frequent cancer-related diagnostic errors implicated in malpractice claims (Table 1).[5,31] Studies revealed a large number of preventable factors, with mammography-related variables most frequently cited. There is wide variation in the rates at which radiologists recommend biopsy on the basis of mammogram interpretation,[59] and reported rates of mammography error range from 5.2% to 75%.[46-48,60-66] The majority of studies we reviewed implicated cognitive (perception and interpretation) errors by radiologists,[8,33,34,38,44-53] although system and training-related factors were also noted in several studies. For

Table 2. Factors Contributing to Errors in Breast Cancer Diagnosis: Nonpreventable Variables

Variable	Description
US/biopsy-related technical/sampling errors	Poor lesion or needle visualization, deeply located lesion, dense fibrotic tissue causing inaccurate sampling during US-guided core needle biopsy[43,53]
Lesion characteristics on mammogram	Unusual lesion characteristics, poor lesion positioning, small size of lesion, deep retroglandular location or at the edge of glandular tissue, visibility of lesion in only one projection, benign disease simulating neoplasm, overlapping tissue, lesion site in relation to corpus mammae, lesion in central and subareolar location, site where visualization is difficult, lack of a desmoplastic reaction, disease in initial stages or showing slow growth[44,46,48,50,60,61,68-72]
Patient characteristics	False-negative mammograms (low body mass index, previous breast surgery, current hormone replacement therapy use, younger age, dense breast parenchyma, breast augmentation); difficult to palpate on clinical breast examination due to size of breast, higher body mass index[40,46,61,50,68-74]

Abbreviation: US, ultrasound.

Table 1. Factors Contributing to Errors in Breast Cancer Diagnosis: Preventable Variables

Variable	Description
Diagnostic test or procedure performance	
Radiologist factor	Perception errors, interpretation errors; contributing factors included lack of a systematic approach to reviewing mammography films, oversight of a subtle lesion because of an obvious finding, lack of knowledge of clinical findings, and imprecise correlation with result[8,33,34,38,44-53]
Diagnostic setting of the radiologist	Suboptimal viewing conditions, distractions, unsupported/isolated imaging department[44,49]
Radiologist expertise or training of radiographic techniques	Poor radiographic technique or positioning during mammogram[39,44,46,50,54]
Clinical settings such as patient-physician encounters	
Erroneous initial suspicion of a benign breast disease	Inappropriate reassurance that the mass is benign in the absence of a biopsy; time constraints by physicians[8,22]
OCP use	Failure to recognize risk of OCPs[8,55]
Issues related to clinical breast examination	Errors during clinical breast examination (bias associated with women older than 70 years, those with multiple clinical breast examinations, and physician sex)[56]
Tests not obtained	Failure to order mammogram, ultrasound, or FNA biopsy[8,33,34,53,57]
Follow-up of patient or test results	
Follow-up failures	Follow-up failures related to system issues, lack of imaging follow-up after a benign ultrasound-guided core needle biopsy result[41-43,53,58]
Pathologic confirmation of diagnosis	
Pathology/histology issues (interpretation and sampling errors)	Biopsies inappropriately omitted, poor performance in FNA biopsy, failure to recognize or act on radiologic-histologic discordance, and specimen mixups due to negligence[6,8,36,37,43,53]
Patient-related delays	
Patient-initiated delays	Patient delays due to noncompliance (patients were responsible for follow-up); factors associated with noncompliance included old age, history of a benign mastopathy, obesity, and nonparticipation in general health screening examinations[42,53,58]

NOTE. Malpractice claim studies.[33,34,36,37,57]
Abbreviations: OCP, oral contraceptive pill; FNA, fine-needle aspiration.

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Table 3. Factors Contributing to Errors in Colorectal Cancer Diagnosis: Preventable Variables

Variable	Description
Diagnostic test or procedure performance	
Problems with colonoscopy preparation	Poor bowel preparation leads to missed diagnosis[78]
Omission of full diagnostic visualization of the large bowel during unrelated surgery	Concomitant CRC missed in three studies (laparoscopic cholecystectomy)[82-84]
Problems with colonoscopy procedure	Incomplete colonoscopy, lack of training/expertise of endoscopist, perception and interpretation errors during colonoscopy, failure to carry out adequate biopsy of lesions seen[78,79,80,82,85-87]
Barium enema	Inadequate preparation, perception and interpretation errors[81,88,89]
Clinical settings such as patient-physician encounters	
Inadequate investigation	Incorrect original diagnosis (eg, hemorrhoids, peptic ulcer disease), omission of rectal examination[12]
Patient sex bias	Fewer women were found to undergo sigmoidoscopy[90]
Follow-up of patient or test results	
Failure to follow-up on colonoscopy results[78]	
Patient-related delays	
Patient-initiated delay	Patients not concerned by their symptoms or assumed that their bleeding was due to benign causes (eg, hemorrhoids)[12]

Abbreviations: CRC, colorectal cancer.

example, radiologists specifically trained in mammography detected more early-stage cancers and more cancers overall than did general radiologists.[54]

Other commonly cited preventable factors included errors in patient-physician encounters and subsequent follow-up. Although several studies noted specific problems that impeded additional diagnostic work-up, others implicated failure to order diagnostic tests without specifying cognitive or systems-related causes. Diagnostic delays were also associated with lack of abnormal mammogram follow-up, consistent with one study's finding that 36% of abnormal mammogram results were lost to follow-up.[67]

Several studies linked diagnostic errors to problems with pathology sampling or interpretation.[6] Interpretive errors are errors of disease categorization, whereas sampling errors are made either in the pathology laboratory (in tissue processing) or during tissue procurement.[6] Finally, patient-related delays were cited in a few studies as contributing factors to missed and delayed diagnosis of breast cancer.

Nonpreventable factors. From the available literature, we identified several nonpreventable factors. These included lesion characteristics such as site and size, visualization of lesions on mammography or biopsy, and patient characteristics (Table 2).

Table 4. Factors Contributing to Errors in Colorectal Cancer Diagnosis: Nonpreventable Variables

Variable	Description
Lesion characteristics on colonoscopy	Problems related to site, size, and location of lesion (right-sided, more proximal), simulation errors, flat lesions with little intraluminal protuberance[75,76,79,80,86,91,94,95]
Lesion characteristics on barium enema	Smaller size without circumferential involvement, lesion in cecum or ascending colon, lesion in proximal colon, multiple tumors[81,88,93]
Technical errors (barium enema)	Poor coating, overlapping loops, single contrast enema, fecal residue[81,89]

CRC

Two studies used a prospective approach to study errors in diagnosis of CRC.[75,76] The remaining studies evaluated missed and delayed diagnoses of CRC retrospectively, collecting data either through medical record reviews, surveys, or interviews. One review article was included.[77]

Preventable factors. The majority of studies we reviewed described problems with colonoscopy performance (Table 3). A recent study found a 2% to 6% rate of missed CRC, mostly attributed to older age, concomitant diverticular disease, right-sided or transverse CRC, colonoscopy by an internist or family physician, and office-based procedures.[91] The overall miss rate for colorectal carcinomas at colonoscopy ranged from 2.3% to 17%,[78-80,92] and miss rates at barium enema were between 4.7% and 6.7%.[81,93] Right-sided adenomas were found to be missed more often, at rates of 4% to 27%.[75,94] In addition to problems with routine diagnostic test performance, we found three studies describing missed CRC during laparoscopic cholecystectomy,[82-84] a procedure in which full diagnostic visualization of the large bowel is recommended intraoperatively to avoid missing coexisting CRC.[82,84]

We found only one study addressing delays in CRC diagnosis before colonoscopic procedure due to factors such as inadequate investigation.[12] In this retrospective study from Australia that evaluated 100 patients presenting with colorectal CRC during a year, 34 had a delay in diagnosis, and about half of these delays could be attributed to physicians.[12] Likewise, we found only one study that documented diagnostic errors related to follow-up.[78] Although patient-related delays may not be unexpected in CRC diagnosis because its nonspecific early abdominal symptoms are prevalent in the general population, only one study specifically addressed patient-related delays.[12]

Nonpreventable factors. Most nonpreventable variables were related to lesion characteristics on colonoscopy and barium enema (Table 4).

Lung Cancer

Three studies approached diagnostic errors in lung cancer prospectively,[96-98] whereas the remaining retrospective studies

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Table 5. Factors Contributing to Errors in Lung Cancer Diagnosis: Preventable Variables

Variable	Description
Diagnostic test or procedure performance	
Presence of unrelated major abnormalities at CT	Presence of other major abnormalities distracts many radiologists[106]
Misinterpretation of chest x-ray[11,96,101,103,107]	
Clinical settings such as patient-physician encounters	
Waiting times for investigations at primary care[103]	
Overlooked due to either coexisting comorbidities or nonrespiratory symptoms[103,108]	
Over-reliance on negative x-ray results (tumors not visualized initially but seen in retrospect)[99,101,103,104]	
Delays in consultation and referral, work-up not aggressive enough, performing numerous other procedures before biopsies	Lack of multidisciplinary team[97,98,104,105,107-112]
Follow-up of patient or test results	
Imaging follow-up failure	Chest x-ray and CT scan–related follow-up[103,105]
Pathologic confirmation of diagnosis	
Pathology interpretation and sampling errors[6]	
Patient-related delays	
Patient-initiated delays	Patient refusal of closer examination, patient delays, patient beliefs about health changes[97,102,105,107,110,111,113,114]

Abbreviation: CT, computed tomography.

collected data through traditional methods. Two imaging-related review articles were also included.[99,100]

Preventable factors. Several studies implicated problems with imaging test performance in diagnostic errors related to lung cancer (Table 5). Similar to mammography, chest radiography is subject to wide variability in radiologic interpretation.[115] Radiologic errors can be categorized as either perceptual (abnormality readily detectable retrospectively but not seen earlier) or cognitive (abnormality is seen but misinterpreted due to faulty reasoning).[116] Errors in perception seem to be the greater threat to accurate lung cancer diagnosis.[100,117] Imaging-related errors (especially those pertaining to chest x-rays) were frequent, with an overall miss rate of lung cancer between 10% and 22%,[96,101] although substantially higher rates were reported in older studies.[118-121] Most often, structures superimposed on the tumor are responsible for missed lesions on chest x-ray, leading to a miss rate of 71%.[99] In one study, it was revealed that a clavicle obscured 22% of the missed cancers.[122]

Also widely cited were delays in lung cancer symptom recognition by general practitioners,[97,102] apparent in observations of insufficient or ineffective work-up (eg, performing numerous other procedures before biopsy). Importantly, however, a number of studies also implicated patient-related delays in diagnostic assessment. It is significant that several studies implicated physicians' over-reliance on chest x-rays to diagnose lung cancer[99,101,103,104]; nearly one fourth of chest x-rays requested from primary care in lung cancer patients are negative.[101] Furthermore, two studies revealed problems of follow-up for imaging results.[103,105] These findings are consistent with those of our own, in which we found several imaging reports indicating suspected lung neoplasm were lost to short-term follow-up in a multispecialty ambulatory clinic.[123]

Few studies addressed problems in the pathologic confirmation of lung cancer diagnosis. However, Raab et al[6] found error rates up to 12% related to pathologic confirmation of lung cancer diagnosis that originated from misinterpretation or poor tissue sampling.

Nonpreventable factors. Tumor characteristics on imaging were the most commonly cited nonpreventable factors (Table 6).

Table 6. Factors Contributing to Errors in Lung Cancer Diagnosis: Nonpreventable Variables

Variable	Description
Tumor characteristics on chest x-ray	Small size, peripheral and upper lobe locations, and apical and posterior segmental/subsegmental locations in an upper lobe; appearance as patchy ground-glass appearance, superimposed structures, benign looking lesion (on CT and biopsy)[99,105,122,124]
Tumor characteristics on CT scan	Endobronchial location and lower lobe predominance; very slow growth or no change at all in tumor[105,106]
Cancer obscured by clavicle[122]	

Abbreviation: CT, computed tomography.

Malignant Melanoma

All studies that were identified were either retrospective case series or studies related to malpractice claims. The frequency of melanoma-related claims was second only to claims involving breast biopsy in one study.[125]

Preventable factors. Several studies implicated patient-physician encounters in errors in melanoma diagnosis, and these were all related to physician training and experience. A Swedish study found a 15% rate of missed diagnosis among dermatologists.[126] More than 10 years of experience in dermatology and exposure to more than 10 melanomas per year was associated with greater diagnostic accuracy.[127] The accuracy of clinical diagnosis increased with the level of experience.[128] Physicians with less than 1 year of experience in dermatology were able to detect malignant melanoma as the first diagnosis in 31% of the patients, in contrast to 63% for those with more than 10 years of experience.[129]

Pathology-related problems in melanoma diagnosis were also cited in several studies. In an analysis of 378 pathology malpractice claims, a false-negative diagnosis of melanoma was the most common

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reason for filing a malpractice claim against a pathologist.[37] In a review of 218 surgical pathology and fine-needle aspiration biopsy claims from 1995 through 1997, 11% involved the misdiagnosis of melanoma.[125] In the same study, 144 surgical pathology and cytology claims from 1998 through 2001 were also reviewed and 16% of these claims involved misdiagnosed melanoma. Although specific problem lesions were identified (nevoid melanoma, Spitz nevus, desmoplastic melanoma, and dysplastic nevus), many claims involved classic melanoma misdiagnosed as melanocytic nevus without an identifiable explanation. We did not find any studies of errors in melanoma diagnosis due to factors related to diagnostic test/procedure performance, follow-up, or patient-related delays.

Nonpreventable factors. Nonpreventable factors included specific pathologic characteristics of certain melanomas (dermoscopically difficult-to-diagnose melanomas). Typical pathologic characteristics of these melanomas included the presence of streaks, absence or presence of regular pigmentation, absence of a blue-whitish veil, absence of regression structures, and presence of hypopigmentation.[130]

IMPLICATIONS FOR PREVENTION AND FUTURE DIRECTIONS

We present a comprehensive overview of the literature on errors in cancer diagnosis and their prevention, taking into account several settings of care and navigation of patients between these settings. In our analysis, we found errors in cancer diagnosis to have a substantial health and economic burden. We found few prospective studies (only nine of 110 studies we evaluated), but were able to compile several contributory factors from the other available literature that provide useful guidance for additional work. We categorized contributory factors along five major domains where care involving cancer diagnosis could be compromised. We use this evidence base, in addition to evidence from related literature, to shed light on prevention of these errors. Although new diagnostic technologies could play a role in reducing some of the nonpreventable factors identified in the literature, future strategies focusing on several key preventable factors could substantially reduce diagnostic errors in cancer. In addition, better identification of these errors, such as through reporting and tracking systems, would lead to their enhanced understanding and prevention.[131]

Diagnostic Test or Procedure Performance

Literature suggests that providing radiologists with appropriate clinical findings can reduce errors in diagnostic radiology interpretation.[132,133] However, this practice is not well followed even in this day and age. Other factors such as consistently and carefully comparing new diagnostic radiology studies with previous studies and obtaining second opinions (double interpretation) in selected cases could also reduce these errors.[132] During the last decade, the use of digital radiography and computer-aided detection has been proposed to improve the sensitivity and decrease the variability of radiologic interpretation.[132] These techniques can reduce error by raising the radiologist's suspicion in examinations where a potential abnormality has been highlighted, and have been found to be of value in mammography. Whether these methods will produce similar results in other settings is not yet clear.[132]

Although radiologists receive regular but limited feedback regarding their interpretive accuracy in mammography, arrangements for more extensive feedback about their performance in mammography and other imaging could be useful.[134] For instance, radiologists in the United Kingdom National Health Program attend routine breast disease–related meetings and receive personal and group audit reports that include data on cancer detection rate, recall rate, and proportion of all women recommended for biopsy after mammography (the Breast Imaging Reporting and Data System category 4 or 5) who are diagnosed with breast cancer.[135,136] They also attend a 2-week multidisciplinary course with specialist training at high-volume mammography screening sites. Such activities have been cited in an increase in invasive cancer detection rate from 1.6/1,000 to 2.5/1,000. Hence, direct feedback with audit results and focused training may result in better performance.[137,138]

Performance of procedures such as colonoscopy may be aided by higher standards of training for the nongastroenterologist and by better test preparation. Readiness to perform a second test including barium enema after an incomplete colonoscopy can also reduce missed colon cancer.[77] Future studies will need to explore further the precise origins of the perceptual and cognitive errors that lead to missed lesions, and outline preventive strategies for radiologists and others who perform and interpret diagnostic tests and procedures.

Clinical Settings Such As Patient-Physician Encounters

Studies related to the patient-physician encounter were few relative to the importance of this setting in cancer diagnosis. The effect of several cognitive and system factors on the diagnostic performance of the ambulatory care practitioner was highlighted in the study by Gandhi et al.[5] Gathering adequate and meaningful data through patient encounters is a key diagnostic skill, and hence research focusing on errors arising from inadequate history-taking and physical examination would be a first start. In previous work done by our team, we found problems with data gathering (history and physical examination) to be the most common reasons for diagnostic errors in trainees.[139] Over-reliance on diagnostic tests (both laboratory and imaging) and overuse of newer technology has eroded these skills to some extent,[140] and a change in training techniques for the newer generation of physicians may be warranted.

In addition to problems in gathering data, diagnostic errors may be the result of cognitive errors related to faulty reasoning. Despite guidelines and protocols to standardize patient care and improve diagnosis, clinicians often use subjectivity, which can lead to faulty reasoning and error in everyday practice.[141,142] For example, in a study of referrals for colon cancer evaluation in which 43 clinicians were asked to assess 40 symptomatic colorectal referrals, implementation of guidelines was found to be erratic.[141] Physicians were inconsistent not only in assessing the patient's potential cancer risk (clinicians correctly diagnosed 71.3% of the cancer patients and 44% of the patients with benign conditions), but also in choosing investigations needed. Cognitive errors result from failures in perception, mental states (such as affect), use of heuristics (shortcuts in reasoning or so-called rules of thumb), and biases in the reasoning process,[16-18] and these have not been well studied in the context of cancer diagnosis. Future research should focus on the origins and prevention of the many cognitive constraints faced by practicing physicians in a diagnostic encounter. Future interventions should also focus on the system and organizational processes, policies, and procedures that contribute to errors in

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cancer diagnosis that arise in clinic settings such as primary care, which is considered a front line in the war on cancer.[143-145]

Follow-Up of Patients or Test Results

Recent studies have raised concern about errors related to abnormal test result communication in ambulatory care.[67,146-150] Several studies, including our own, reveal the presence of communication breakdowns among physicians, patients, and third parties such as radiologists, pathologists, and laboratories.[67,123,150-157] When we evaluated communication outcomes in a computerized test result notification system, we found that 4% of abnormal imaging results were lost to follow-up; of these, a large majority involved the diagnosis of potentially new malignancies.[123] In one study of abnormal mammograms, more than one third of the women studied did not receive appropriate follow-up.[67] Improving follow-up of patients and test results by using information technology and adoption of electronic medical records has potential to improve patient safety in this setting. For example, the Department of Veterans Affairs uses a View Alert notification system to notify clinicians of abnormal test reports. This system may have several advantages over previously used systems in that it can track acknowledgment of abnormal radiology test results; results that go unacknowledged receive a higher degree of monitoring, reducing the chance that these reports are lost in the system.[123] New policies require mammogram reports written in lay terms to be sent to patients within 30 days of the examination. Other strategies to notify patients automatically of test results are also being evaluated.[158] Systems of fail-safe follow-up related to other procedures such as colonoscopy could be redesigned similarly to ensure that patients who had incomplete procedures are called back to conduct timely investigations. Likewise, the increasing use of automated appointment reminders linked to the electronic medical records could reduce reliance on other poorly designed systems to ensure patient follow-up. The recently introduced concept of patient navigation (a process by which an individual—a patient navigator—guides patients with a finding suggestive of cancer through and around barriers in the complex cancer care system to help ensure timely diagnosis and treatment) potentially could be of great benefit to reduce errors related to follow-up.[41]

Pathologic Confirmation of Diagnosis

Recent work by Raab et al[6] has brought much-needed attention to pathology-related diagnostic errors in cancer. In their landmark study on cancer diagnosis, interpretative errors ranged from 5% to 51%; the remaining were due to clinical sampling problems. Several strategies have been proposed to reduce these errors, including immediate interpretation of fine-needle aspiration to assess the quality of samples, review of slides of specific tumor types by two pathologists, addition of qualifying statements on biopsy result reports to aid decision making by clinicians, and uniform reporting of errors in cancer diagnosis.[159-163] Increased participation in quality monitoring, auditing, and feedback programs such as Q tracks offered by the College of American Pathologists should lead to fewer errors.[164] For instance, Q tracks allows pathologists to track laboratory and individual performance, issues quarterly performance reports to assist participants in documenting improvement over time, and disseminates knowledge of practices and policies associated with improved performance of other participants. Future work should aim to increase the understanding of the origins of both cognitive errors by pathologists and tissue sampling errors, and should design interventions to reduce them.

Patient-Related Delays

We believe that this area could benefit from multidisciplinary research and interventions to improve patient adherence and involvement. Better communication strategies between the health care system and the patient and newer techniques of involving patients in their own care (such as the use of patient navigators)[41] may reduce the preventable delays related to patients.

Our review had several limitations. First, we did not capture studies of false-positive diagnostic errors that occur when a diagnosis of cancer is made in a patient without cancer. Patients incurring a false-positive cancer diagnosis can receive unnecessary testing, medical costs, emotional burden, and other potential undesirable consequences. Second, we excluded publications that mostly focused on delays associated with screening and treatment behaviors of physicians, which could potentially affect our results. Third, to address some of our review questions, we included all types of studies, including studies of malpractice claims, that may be somewhat biased and represent a collection of highly selected cases from which it is difficult to generalize. Nevertheless, these studies are a unique and rich source of data in the relatively underdeveloped field of diagnostic error.[5] Lastly, as in all reviews of the literature, our results may be affected by publication bias. However, we believe that important concepts from our findings can be used to guide and stimulate future work in this area.

In conclusion, diagnostic errors in cancer can lead to unnecessary health care expenses and to preventable morbidity and mortality. On the basis of our review of the literature, factors contributing to errors are diverse and in some cases are specific to the type of cancer. Factors that we judged to be preventable were related to one of five domains of the complex health care system: patient-physician encounters in the clinic setting, performance of a diagnostic test or procedure, pathologic confirmation of diagnosis, follow-up of patients or their test results, or patient-related delays. Our current understanding of contributory factors and prevention is fairly advanced for errors related to the performance of procedures and imaging tests, and is emerging in relation to pathology errors. More prospective studies, studies of errors arising from the clinical encounter (including system problems and cognitive errors by clinicians), and studies addressing follow-up of patients are needed. Future research should examine further the various systems and cognitive problems that lead to the many contributory factors we identified, and address interdisciplinary interventions to prevent errors in cancer diagnosis.

AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

The author(s) indicated no potential conflicts of interest.

AUTHOR CONTRIBUTIONS

Conception and design: Hardeep Singh, Saurabh Sethi, Laura A. Petersen
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