Patients Diagnosed With Advanced-Stage Colorectal and Lung Cancer Experience Frequent Missed Opportunities For Earlier Diagnosis

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Abstract

Importance: Missed and delayed cancer diagnoses worsen patient outcomes. Missing signals of cancer may result in advanced-stage presentations.

Objective: To develop and implement a digital quality measure (dQM) of the proportion of advanced-stage cancer diagnoses in the U.S. and to determine the rate of missed diagnostic opportunities.

Design: Retrospective cohort study using electronic health records and cancer registry of patients diagnosed during 2016-2020. Clinical experts reviewed chart review data using a two-year look-back period.

Setting: Two integrated healthcare systems: Veterans Affairs (VA) and Geisinger.

Participants: Patients with incident colorectal or non-small-cell lung cancer, with at least one primary care visit in the two years before cancer diagnosis. A random sample of 100 advanced-stage cases per cancer type and health system was manually reviewed.

Main Outcome(s) and Measure(s): Descriptive analysis (stratified by health system and cancer type) of the presence of missed opportunities in diagnosis, dates of investigation initiation and completion, and factors contributing to missed opportunities.

Results: We found 37,961 and 2,914 lung cancer cases (VA and Geisinger, respectively) and 14,674 and 627 colorectal cases (VA and Geisinger, respectively). For lung cancer, advanced stage comprised 46% at VA and 58% at Geisinger. For colorectal cancer, advanced stage was 33% at VA and 36% at Geisinger. Notably, 58% (95% CI 47.5-67.5) and 76% (95% CI 66.8-83.3) of advanced-stage lung cancers (VA and Geisinger, respectively) had missed opportunities in diagnosis. For colorectal cancer, 66% (95% CI 56.3-75) and 68% (95% CI 58.3-76.3) had missed opportunities (VA and Geisinger, respectively). Patients with missed opportunities had

notable delays in diagnosis (e.g., median time from cancer signal to workup completion ranged 1–20 months). Missed screening comprised 9–29% of missed opportunities across the two institutions and cancers. The primary contributors to missed opportunities were problems performing and interpreting diagnostic tests and patient-provider encounters for lung cancer, while colorectal cases were primarily affected by patient-related factors and problems performing and interpreting diagnostic tests.

Conclusions and Relevance: We found high rates of missed opportunities in diagnosis among patients with advanced-stage cancer. By using advanced stage as a dQM, health systems can better identify care gaps and track improvement initiatives to reduce preventable delays in cancer diagnosis.

Introduction

Missed and delayed cancer diagnosis is common, impacting more than a third of patients with colorectal or lung cancer.[1,2] However, measurement of delays in cancer diagnosis poses methodological challenges. In England, the "Routes to Diagnosis" program uses emergency cancer presentation as a quality measure of the diagnostic process,[3] and a recent study demonstrates the potential of such a measure in the US.[4] Another measure reported at the level of sub-national populations in England focuses on advanced-stage (III or IV) cancer.[5,6]

Some advanced-stage diagnoses result from missed opportunities in diagnosis, such as lack of recognition or follow-up of signs, symptoms, and tests suggestive of cancer. The concept of *missed opportunity in diagnosis* has been defined as an instance "in which *post-hoc* judgement indicates that alternative decisions or actions could have led to more timely diagnosis."[7] In this conceptualization, the focus is on the diagnostic process and evidence available at a particular time and whether something different could have been done then, rather than the strict accuracy of the initial diagnosis or patient outcomes.[8]

There is limited US literature on advanced-stage cancer as a quality measure, however, or on its association with missed opportunities in diagnosis. The US Centers for Medicare and Medicaid Services has highlighted the potential of digital quality measures (dQMs), i.e. "quality measures that use standardized, digital data from one or more sources of health information".[9] Increasing electronic health record (EHR) interoperability may enhance the measurement of the diagnostic process. To investigate the potential of such a dQM for quality monitoring and improvement, we developed, validated, and implemented a dQM of the proportion of cancer diagnoses at advanced stage in the US, and we determined the rate of missed opportunities preceding advanced-stage cancer diagnosis.

Methods

We implemented the advanced-stage dQM in two integrated US health systems: Veterans Affairs (VA, with >130 facilities and >9 million patients) and Geisinger (with 10 hospital campuses, 133 clinic sites, and >3 million patients), focusing on colorectal and non-small-cell lung cancer. Data were retrieved from EHR data warehouses and cancer registries. The measure was defined as the number of patients with incident stage III or IV cancers divided by the number of patients with incident cancer (any stage, limited to patients with known stage data) in 2016–2020. To focus on patients established within each system, we included only patients with at least one primary care visit within two years before cancer diagnosis.

Of all charts flagged as advanced stage, experts reviewed a random sample of 100 per health system using a standardized data-collection instrument. This was drawn as a simple random sample with no weighting or oversampling. The sample size was chosen to allow a 2-sided 95% confidence interval to be +/- 10 percentage points (or less) from the measured proportion.

Reviewers abstracted the date and type of any *cancer-related diagnostic signal*, which could be any finding from history, exam, and testing that rises to the level of warranting additional guideline-recommended investigation. To minimize hindsight bias, reviewers were trained to abstract only signals that reasonably warranted investigation and cancer signals were narrowly defined (e.g., not every cough or low hemoglobin count requires workup, but a new cough lasting over 8 weeks or new and unexplained iron deficiency anemia may). A missed opportunity would then be a cancer signal that lacked initiation or completion of investigation in the appropriate timeframe. Reviewers used a look-back period of 2 years to determine the presence and absence of missed opportunities.

We trained two physician chart reviewers at each health system (UM, UM, SK, RMR), with the 100 charts divided between two reviewers, with 20% reviewed by both to ensure reliability. All reviewers had a general medical background. If reviewers were unsure about the presence of a missed opportunity, they could discuss the case with the larger research team.

There are no national targets for the time taken to work up or diagnose these cancers, so we used timeframes previously developed and validated by chart review,[2] existing policies and standards on the timely diagnosis of suspected cancer,[10] and other prior literature.[11-20] Specifically, the upper limit of time to initiate investigation (*e.g.,* to place an advanced imaging order) from cancer signal was 7 days. The upper limit of time to complete the investigation was 30 days for lung and 60 days for colorectal cancer. In addition, we used a patient-centered approach (vs. tumor progression likelihood) in determining our follow-up timeframes. National VA policies require communication of abnormal test results to patients within 7 days of the test results.[21] Most patients prefer communication as soon as the result is available.[22]

The time to completion here refers to the first step in a multi-step sequence of investigations. For instance, if a patient presented with concerning lung symptoms, our standard would be satisfied by a chest CT ordered within 7 days of the index visit and completed within 30 days of ordering. Any subsequent steps in the investigation (consultations, tissue biopsy, staging, *etc.*) are not required to be completed within 30 days. Instances where a patient who qualified for guideline-directed screening but was not offered it or did not complete it were considered as failures to initiate investigation (but with no cancer signal).

For any missed opportunity in diagnosis, reviewers also assessed and recorded factors contributing to it, using a previously described five-dimensional framework of the diagnostic process.[23] This framework comprises factors related to the patient, patient-provider encounter,

diagnostic test performance/interpretation, follow-up and tracking, and referrals. Thus, if a patient did not keep a colonoscopy appointment, reviewers considered this a missed opportunity (patient-related factor), but if a patient specifically declined to have follow-up testing, it was not considered a missed opportunity. Reviewers tracked whether patients had declined cancer-specific screening in the past.

We examined large-scale descriptive statistics for variables available as structured data, such as the presence or absence of advanced cancer stage. We also examined descriptive statistics for variables manually abstracted from the chart review sample and estimated proportions using Wilson confidence intervals (score CI). For manually abstracted continuous variables (time intervals from cancer signal to initiation or completion of workup), we examined distributions using box and whisker plots. For Geisinger data, demographics could not be obtained and analyzed on the full cohort of patients with cancer, so they are measured on the random sample of manually reviewed charts. We stratified descriptive analyses by cancer type and health system.

Associations of advanced stage with categorical demographic variables were examined with the chi-squared test, and association with age was examined using the Wilcoxon test (two-sided tests, $P<0.05$ considered significant). Demographics were determined from structured EHR data. To allow for differences in data representation and demographic makeup across the two health systems, race and ethnicity were merged into one variable with four levels: white, black non-Hispanic, Hispanic/Latino (any), and other.

Results

The percentage of advanced-stage diagnoses was 46.1% and 58.3% for lung cancer at VA and Geisinger, respectively, and 33.3% to 36.2% for colorectal cancer at VA and Geisinger,

respectively (Table 1). We excluded 258 lung cancer patients and 79 colorectal cancer patients from the cohort due to a lack of primary care visits in the VA. Reviewers found missed opportunities in diagnosis in 58% and 76% of advanced-stage lung cancers at VA and Geisinger, respectively, and 66% and 68% of advanced-stage colorectal cancers at VA and Geisinger, respectively (Table 2). Based on the reviewed sample of 100 patient charts per health system, the most common contributors to missed opportunities among advanced-stage lung cancer patients were problems with performing and interpreting diagnostic tests (e.g., computed tomography clinically indicated but not performed within 60 days or per guidelines) and patient-provider encounter factors (history-taking, exam, test ordering). In the reviewed sample of patients with colorectal cancers, the most common contributors were patient-related factors (documented hesitancy to undergo invasive tests or documented access and affordability issues) and problems performing and interpreting diagnostic tests. For lung cancer, advanced stage had statistically significant but small-magnitude associations with age (mean 70.5 years in advanced-stage, 71.0 years in early-stage, $P < .001$), sex, and race (Table 3). For colorectal cancer, advanced stage was significantly associated only with race (Table 3).

Discussion

To advance the science of digital quality measurement and improvement for cancer diagnosis, we developed and validated a dQM reflecting the proportion of cancer diagnoses at advanced stage in the US and determined the rate of missed opportunities preceding advanced-stage cancer diagnosis. We implemented the dQM in two large US health systems with integrated electronic health records and found it to be associated with a high rate of missed opportunities to diagnose cancer earlier.

Our work builds on prior research that used electronic trigger (e-trigger) tools to detect delays in follow-up of diagnostic tests that may be suggestive of cancer.[24,25] These e-triggers focus only on the quality of abnormal test follow-up, not on other elements of the diagnostic process. Our dQMs, including one we recently developed for emergency cancer presentations, were developed using an electronic health record-based query methodology similar to that used to develop e-trigger tools.[26] However, such e-trigger tools function mainly as indicators of the quality of the follow-up process (not every patient with delayed test follow-up has cancer). By contrast, the advanced-stage dQM presented here represents an outcome measure downstream of the diagnostic process.

This work has several limitations. First, we examined the association of advanced-stage presentation with simple demographic factors (sex, race, age), but we did not collect other factors that may be associated with advanced stage or time to treatment. These factors may interact to influence the cancer diagnostic process, thus influencing the stage at presentation. Such factors include income, employment, insurance, transportation, social support, and distance to diagnostic services. Second, we limited the population to patients with at least one primary care visit two years before diagnosis. This focused the dQM on active health system users because we envision the measure used primarily at the health system level. However, this also has the effect of excluding patients with general difficulties accessing primary care. It is important to measure this aspect of the diagnostic process, but we did not design the current measure to assess patients without a clear established relationship with a health system.

Conclusion

A dQM related to an advanced stage of cancer diagnosis is associated with a high rate of missed opportunities to diagnose cancer earlier. Health systems could use this measure to

identify care gaps, inform interventions, and monitor improvements over time in response to initiatives to reduce preventable delays in cancer diagnosis.

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Table 1. Characteristics of incident cancer diagnoses in two health systems and two cancer types.

Characteristic	VA Lung (n=37691)	VA Colon (n=14674)	Geisinger Lung (n=2914)	Geisinger Colon (n=627)
Age, y	70 (66 - 75)	69 (63 - 75)	65 (58.8 - 72.2)	64.2 (55.3 - 73.7)
Sex: Male	36358 (96.5%)	14075 (95.9%)	56% (46.2-65.3)*	52% (42.3-61.5)*
Race				
White	28944 (76.8%)	10111 (68.9%)	100% (96.3-100)*	95% (88.8-97.8)*
Black	6175 (16.4%)	2968 (20.2%)	0%	3% (1-8.5) *
Hispanic	964 (2.6%)	870 (5.9%)	0%	1% (0.1-5.4) *
Other	1608 (4.3%)	725 (4.9%)	0%	1% (0.1-5.4) *
Advanced stage	17319 (45.9%)	4874 (33.2%)	1699 (58.3%)	227 (36.2%)

Values are presented as number (percent) or as median (quartile 1 – quartile 3), except as indicated. *: Values were determined on a 100-person sample and are presented as percent (95% CI).

Table 2. Characteristics of late-stage cancers, as determined by chart review of a random sample.

Characteristic	VA Lung	VA Colon	Geisinger Lung	Geisinger Colon
Cancer signal present	67.8% (57.6-76.5)	67.4% (57.4-76)	65.7% (55.9-74.3)	70.7% (61.1-78.8)
MOD present	57.8% (47.5-67.5)	66.3% (56.3-75)	76% (66.8-83.3)	68% (58.3-76.3)
Cancer not considered, given signal	14.8% (8-25.7)	24.2% (15.5-35.8)	63.1% (50.9-73.8)	24.6% (16-36)
Missed screening, given MOD	28.8% (18.3-42.3)	12.7% (6.6-23.1)	21.1% (13.4-31.5)	8.8% (4.1-17.9)
Declined screening	2% (0.6-7.1)	24% (16.7-33.2)	6% (2.8-12.5)	43% (33.7-52.8)
Cancer signal to workup initiation, d	2 (0 - 23)	30 (2 - 216.2)	141 (5 - 710)	8.5 (0 - 133)
Workup initiation to completion, d	1 (0 - 19)	13 (0.8 - 78.5)	5 (1 - 28)	71 (20 - 321.5)
Cancer signal to workup completion, d	16 (2 - 63)	108 (30.8 - 441.8)	426 (113 - 1229)	173.5 (60.2 - 540.8)

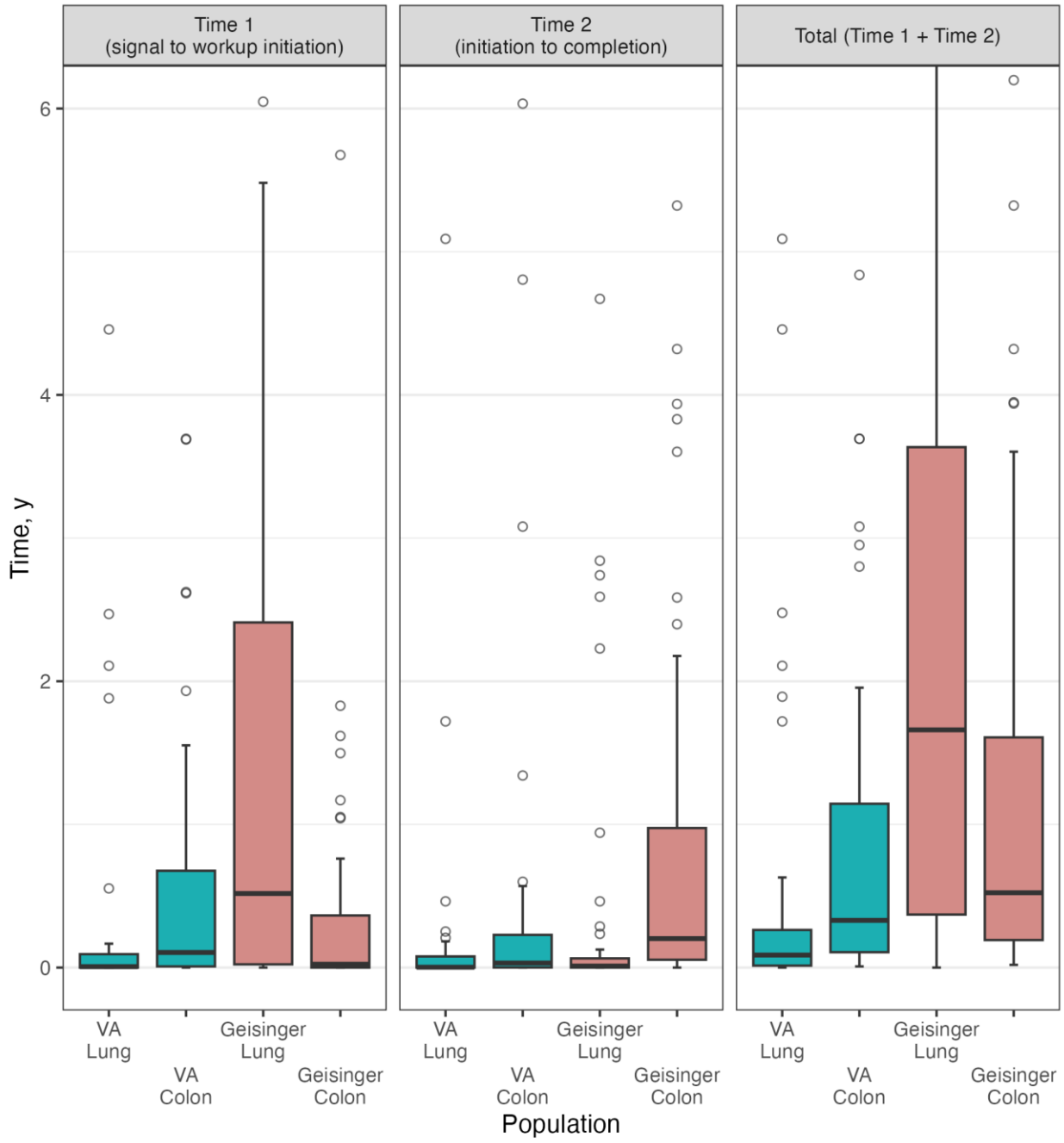
Values are presented as percent (95% CI) or as median (quartile 1 – quartile 3), as appropriate.

Table 3. Rate of advanced stage, associated with demographic characteristics.

Characteristic	VA Colorectal	*P* value	VA Lung	*P* value
Race		.003		.002
White	3440 / 10111 (34)		13190 / 28944 (45.6)	
Black	908 / 2968 (30.6)		2970 / 6175 (48.1)	
Other	251 / 725 (34.6)		712 / 1608 (44.3)	
Hispanic	275 / 870 (31.6)		447 / 964 (46.4)	
Sex		.122		.012
Male	4693 / 14075 (33.3)		16752 / 36358 (46.1)	
Female	181 / 599 (30.2)		567 / 1333 (42.5)	

Values are presented as No. with advanced-stage cancer / No. with cancer of any stage (percent)

Figure. Distributions of time intervals from cancer signal to workup initiation and workup completion in patients with missed opportunities.



Reviewers logged the dates of the first cancer signal, investigation initiation, and investigation completion. Time intervals are computed and distributions plotted (stratified by health system

and cancer type) in cases where the reviewers found a missed opportunity in diagnosis. The y axis is limited to better show details of strata with shorter time intervals. In panel one, 8 of 206 points are off scale, with a maximum of 12.2. In panel two, 7 of 202 points are off scale, with a maximum of 16.9. In panel three, 16 of 203 points are off scale, with a maximum of 16.9.