



Patient motivations for non-adherence to lung cancer screening in a military population

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Background: Lung cancer remains the leading cause of cancer deaths in the United States, and lung cancer screening has been shown to decrease this mortality. Adherence to lung cancer screening is paramount to realize the mortality benefit, and reported adherence rates vary widely. Few reports address non-adherence to screening, and our study sought to understand the non-compliant patients in our military population.

Methods: This Institutional Review Board approved retrospective review of patients enrolled in our screening program from 2013–2019 identified patients who failed to obtain a subsequent Low Dose CT scan (LDCT) within 15 months of their prior scan. Attempts were made to contact these patients and elucidate motivations for non-adherence via telephone.

Results: Of the 242 patients enrolled, 183 (76%) patients were adherent to the protocol. Significant predictors of non-adherence versus adherence were younger age ($P=0.008$), female sex ($P=0.005$), and enlisted officer rank ($P=0.03$). There was no difference with regards to race, smoking status, pack-years, negative screens, lung-RADS level, or nodule size. 31 (52%) non-adherent patients were contacted, and 24 (77%) reported their reason for non-adherence was lack of follow-up for a LDCT. Twenty (64%) were interested in re-enrollment. Of the total screening cohort, 15 interventions were performed, with lung cancer identified in 5 (2%)—a 67% false positive rate. One stage IV lung cancer was found in a non-adherent patient who re-enrolled.

Conclusions: Lack of perceived contact for follow-up was expressed as the primary reason for non-compliance in our screening program. Compliance is critical to the efficacy of any screening modality, and adherence rates to lung cancer screening may be increased through improved contact with patients via multiple avenues (i.e., phone, email, and letter). There is benefit in contacting non-adherent patients as high rates of re-enrollment are possible.

Keywords: Lung cancer screening; low dose CT scan (LDCT); adherence; enrollment; smoking

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Introduction

Lung cancer remains the leading cause of cancer deaths in the United States, accounting for roughly 1 in 4 deaths from cancer in 2019 (1,2). Given the low survival rate and late presentation of the majority of lung cancer cases, efforts have been made to identify early lung cancers via screening low dose CT scan (LDCT). Detection of lung cancer earlier in the disease course allows for more effective treatment, as in the successful screening campaigns for other cancers such as cervical, breast, prostate, and colon cancer (3). Randomized clinical trials such as the National Lung Screening Trial (NLST) and the Dutch-Belgian Randomized Lung Cancer Screening Trial (NELSON trial) have demonstrated decreased mortality from lung cancer through effective screening (4-11). It is estimated that lung cancer screening can prevent greater than 12,000 premature cancer deaths yearly (12).

Lung cancer screening has been endorsed by several major U.S. medical societies in addition to the International Association for the Study of Lung Cancer (13). In 2013, the U.S. Preventative Services Task Force (USPSTF) recommended annual LDCT in asymptomatic patients aged 55–80 years with a 30 pack-year or more smoking history who are current smokers or who have quit less than 15 years ago. This recommendation requires insurers to cover screening with no cost sharing under the Affordable Care Act, and is a preventative service benefit under the Medicare program (13,14). The appropriate duration of screening and the age at which screening is inappropriate is unknown (15,16).

Despite these recommendations, enrollment of eligible patients for screening is exceedingly low. Only 4.4% of eligible smokers in the U.S. received LDCT in 2015 as compared to 71.5% for breast cancer, and 62.4% for colorectal cancer (17,18). Significant challenges to implementing a screening program exist, as demonstrated by the Veterans Health Administration, and screening has not been widespread (19). Once patients are enrolled, adherence to lung cancer screening protocols is paramount to realize the overall mortality benefit. Adherence to screening was high in the NLST (95%) and NELSON trials (90%), but varies in the literature from 51–85% outside of these major trials (4,7,11,20,21). Few reports address patient non-adherence to lung cancer screening (20,22-25). Our study sought to understand the behavior of non-compliant lung cancer screening program patients in our unique Department of Defense health beneficiaries

in an effort to identify areas to improve our program and adherence to lung cancer screening.

We present the following article in accordance with the SQUIRE reporting checklist (available at <http://dx.doi.org/10.21037/jtd-20-1841>).

Methods

The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). This performance improvement project was approved after administrative, scientific, and ethical review by the Department of Research Programs and the Walter Reed National Military Medical Center (WRNMMC) Institutional Review Board, reference number 913214. Individual consent for this retrospective analysis was waived. The WRNMMC lung cancer screening program began in 2013 through the Department of Pulmonology, and patients are enrolled only if referred to the program. Patients are confirmed that they meet the USPSTF recommendations for screening of asymptomatic adults aged 55–80 who have a 30 pack-year history, currently smoke, or have quit within the last 15 years and have the ability/willingness to have curative lung surgery (26). When enrolled, patients are educated about lung cancer, lung cancer screening, and the WRNMMC protocol for screening. Patient data is then collected including demographics, LDCT and pathology results, interventions, timing of follow-up scans, total pack-years, and smoking status. Data are stored in a password-protected customized database for our lung cancer screening program based at WRNMMC. Once data is collected, the patient is offered smoking cessation services if currently smoking, and a LDCT is ordered and scheduled during block time with radiology, which occurs one day per week. LDCT scans are reviewed by staff radiologists who are encouraged to report results using the lung-RADS protocol (27). Results are then monitored by the program manager and discussed with a staff Pulmonologist. The next screening CT scan or intervention is then planned based on the findings and radiologist recommendations, and the patient is contacted via phone to schedule a follow-up LDCT or intervention. Patients are notified via automated letter and phone call 6 weeks before a follow-up scan is needed by the program manager or smoking cessation counselor. Patients who miss scheduled CT scans are contacted by phone where possible. To be considered adherent to the protocol, patients have to be no more than 3 months past due for their scheduled LDCT.

Table 1 Topics for review with non-adherent patients

Perception of in-office education regarding importance of screening
Any patient reservations regarding screening
Any perceived barriers to obtaining a low dose CT
Preferred method of contact
Reason for non-adherence
Desire for re-enrollment
Recommendations for improvement for the protocol and patient experience

All patients enrolled in the program from inception in 2013 until June 2019 who still met eligibility criteria for lung cancer screening were reviewed for adherence with the protocol. Those patients who met non-adherence were reviewed and attempts were made to contact these patients by phone. For patients contacted, semi-structured interviews were undertaken to discuss all topics listed in *Table 1*, and were conducted by a single provider. Patients were made aware their responses were voluntary and in no way would affect their healthcare, and questions were asked in an open-ended fashion to obtain the desired information and avoid leading patient responses. All responses to the topics in *Table 1* were immediately documented after each phone interview.

Statistical analysis

Individual categorical differences between patients who were adherent and non-adherent were initially assessed using Fisher's exact test. To assess differences in continuous variables between adherent and non-adherent individuals, the Exact Wilcoxon Rank Sum test was used. A logistic regression model was used to provide adjusted estimates for multiple covariates. Alpha was set at $P \leq 0.05$ for all analyses, and all analyses were completed in R 3.6.1 (R Core Team, Vienna, Austria).

Results

Demographic features of the 242 patients enrolled in our Lung Cancer Screening program can be found in *Table 2*. Most patients were older (median age: 67 years), male (69%), and Caucasian (58%), 183 (76%) patients were adherent to the screening protocol. *Table 2* provides

statistical tests for the association between individual features and adherence. These analyses revealed significant differences between the adherent and non-adherent groups for age ($P=0.008$), sex ($P=0.005$), and rank ($P=0.03$), with younger, female, and enlisted patients in the non-adherent group. There was no difference between the adherent and non-adherent groups with regards to race, smoking status, pack-years, negative screens, lung-RADS level, or nodule size.

An adjusted model using age, race, sex, negative screens, smoking status, and rank confirmed significant effects of age (OR, 1.43, 95% CI, 1.03–2.01, $P=0.03$) and sex (OR, 2.57, 95% CI, 1.36–4.87, $P=0.003$), but no effect of rank. Because of the identified age and sex differences, we also examined how adherence varied with age in males and females separately. Here, we observed that while men tended to increase adherence as they aged (OR, 2.38, 95% CI, 1.49–4.10), women tended to have numerically decreasing but statistically consistent adherence across the lifespan (OR, 0.71, 95% CI, 0.40–1.25).

Of the 59 (24%) non-adherent patients, they were overdue for LDCT by an average of 29 months, and 31 (52%) were able to be contacted via phone (*Table 3*). Of the patients contacted, 93% stated their education about the importance of screening and the protocol in office were adequate, and no patients reported having any reservations about undergoing and continuing lung cancer screening. 24 (77%) reported their reason for not following through with lung cancer screening was that they were not contacted to schedule a follow-up LDCT, 4 (13%) reported screening was not a priority as they were dealing with more pressing medical issues, and 3 (10%) reported they were continuing screening at another facility. Twenty (64%) reported they were interested in being re-enrolled after being contacted. When asked about their preferred method of contact, 14 (45%) preferred phone calls, 13 (42%) preferred emails, 3 (10%) had no preference, and 1 (3.2%) preferred letters.

Of the entire cohort, 15 interventions have been performed as a result of screening, including bronchoalveolar lavage, bronchoscopy with or without biopsy, percutaneous biopsy and/or surgical resection. Lung cancer was identified in 5 cases (2% of total study population), and there was a 67% (10/15) rate of negative or non-diagnostic intervention after a purportedly concerning LDCT study (*Table 4*). Of the identified cancers, 1 (20%) was stage I, 1 (20%) was stage II, and 2 (40%) were stage III according to the American Joint Committee on Cancer 8th edition (28). One of the patients who was re-enrolled

Table 2 Demographics of adherent versus non-adherent patients

	All Enrolled	Adherent	Non-Adherent	P value
Enrolled patients	242	183/242 (76%)	59/242 (24%)	
Sex				0.005
Male	168/242 (69%)	136/168 (81%)	32/168 (19%)	
Female	74/242 (31%)	47/74 (64%)	27/74 (36%)	
Median age [range]	67 [55–80]	67 [55–80]	63 [55–80]	0.008
Race				0.529
White	140/242 (58%)	108/140 (77%)	32/140 (23%)	
Black	49/242 (20%)	34/49 (69%)	15/49 (31%)	
Other	53/242 (22%)	41/53 (77%)	12/53 (23%)	
Rank				
Enlisted	155/242 (64%)	110/155 (71%)	45/155 (29%)	0.028
Officer	87/242 (36%)	73/87 (84%)	14/87 (16%)	
Current smoker				0.294
Yes	105/242 (43%)	83/105 (79%)	22/105 (21%)	
No	137/242 (57%)	100/137 (73%)	37/137 (27%)	
Pack-years [average, range]	41 [30–100]	41 [30–100]	41 [30–70]	0.979
Negative screen				0.84
Yes	39/242 (16%)	29/39 (74%)	10/39 (26%)	
No	203/242 (84%)	154/203 (76%)	49/203 (24%)	
Lung-RADS				0.576
Not reported	63/242 (26%)	45/63 (71%)	18/63 (29%)	
1	33/242 (14%)	27/33 (82%)	6/33 (18%)	
2	131/242 (54%)	101/131 (77%)	30/131 (23%)	
3	8/242 (3%)	6/8 (75%)	2/8 (25%)	
4	7/242 (3%)	4/7 (57%)	3/7 (43%)	
Nodule size† [median, range]	3 [0–50]	3 [0–50]	2 [0–37]	0.491

†, measured in millimeters.

from the non-adherent group was found to have squamous cell carcinoma of the lung with metastases on her updated screening LDCT. The stage I cancer was cT1aN0 in a 65-year-old male with a 30 pack-year smoking history and was treated with stereotactic body radiation therapy per the patient's preference despite surgical recommendations. The stage II cancer was stage IIB adenocarcinoma (pT2aN1) in

a 59-year-old female with a 30 pack-year history, treated with surgery followed by adjuvant chemotherapy. Regarding the stage III cancers, one was stage IIIA adenocarcinoma in a 64-year-old female with an 80 pack-year smoking history and treated with surgery, adjuvant chemoradiotherapy (CRT), and maintenance durvalumab. The other stage III cancer is a stage IIIB limited small cell lung cancer in a

Table 3 Non-adherent patient characteristics

	N
Months overdue [average, range]	29 [15–54]
Able to be contacted	31 (52%)
Adequate education	
Yes	29 (93%)
No	2 (7%)
Reservations about LCS	
Yes	0 (0%)
No	31 (100%)
Reason for non-adherence	
Not contacted to follow-up	24 (77%)
Other medical issues	4 (13%)
Being followed elsewhere	3 (10%)
Refusal to follow-up	0 (0%)
Desire to re-enroll	
Yes	20 (64%)
No	11 (36%)
Preferred method of contact	
Phone	14 (45%)
Email	13 (42%)
No preference	3 (10%)
Letter	1 (3.2%)

63-year-old female with a 60 pack-year smoking history, who is currently undergoing CRT.

Conclusions

Lung cancer survival rates are significantly higher with early stage disease, and outcomes dramatically decline with increasing stage. Five-year survival is below 25% for Stage III, and only 5% for patients with distant disease—the most common presentation (2,29). Through identification of lung cancers earlier in their disease course, lung cancer screening with LDCT has been shown to reduce lung cancer mortality by 20–41% in the NLST and NELSON trials (4–11). In the NELSON trial, 59% of lung cancers were identified as stage I, compared to only 16% identified at the same stage currently in the U.S. (2,7,11). This stage

Table 4 Lung cancer screening interventions

	N	Patient details
Interventions Performed	15 (6%)	
False positive	10 (67%)	
Cancers Identified	5 (2%)	
Stage I	1 (20%)	Estimated Stage IA: cT1aN0, SBRT
Stage II	1 (20%)	Stage IIB: pT2aN1, surgery, adjuvant chemotherapy
Stage III	2 (40%)	Stage IIIA: pT1bN2, surgery, adjuvant CRT, maintenance durvalumab
Stage IV	1 (20%)	Stage IIIB: T3N2 Limited Small Cell Lung Cancer, CRT
		Updated screen found Squamous Cell Carcinoma with metastatic disease. Patient was re-enrolled after non-adherence

migration allowed a surgical intervention with curative intent rate of 68% in the treatment arm versus only 25% in the control group. The majority of cancers (60%) found during our screening program were amenable to surgical intervention. This is consistent with findings in the NSLT and NELSON trials, which is in contrast to the majority of patients presenting nationally with advanced lung cancer. Given that surgical intervention remains the mainstay of curative therapy for lung cancer, these results highlight the central importance of thoracic surgeons in the screening and treatment of lung cancer.

As demonstrated, high adherence rates are critical to realize the mortality benefit of lung cancer screening, and the adherence rate was 76% within our program. One cancer was found in a patient who was re-enrolled 54 months after her index scan, and was unfortunately found to have squamous cell lung cancer with distant disease on her updated screening LDCT. Her case illustrates the critical importance of efforts to improve patient adherence to a screening program. Our adherence rate is higher than reported rates for breast and colon cancer screening and consistent with other rates reported in the

community, however not as high as the major trials. Little is known about patient motivations for non-adherence to screening, and it has been suggested that lack of awareness or understanding of screening benefits, screening fatigue, the risks involved with screening, false-negative and false-positive results, radiation exposure, anxiety, complications from workup interventions, financial costs, patient refusal to follow-up, inability to contact the patient, male gender, and proximity to referral centers are all factors influencing adherence (20,22-25). Of the non-adherent patients that were able to be contacted from our program, 77% reported their reasoning for non-adherence was lack of contact to follow-up and schedule their next scan. This was despite 93% stating they had adequate education about the program and protocol, and 100% stating they had no reservations about continuing with screening. We suspect this lack of patient follow-up could be secondary to an inability to contact the patients reliably via phone. Our non-adherent patients reported phone calls were not the unanimously preferred method of contact, especially in light of increased telemarketing causing many patients to ignore unknown phone numbers. Many (42%) preferred email communication, and stated their emails remained stable despite changing addresses and phone numbers. Once contacted, the majority (64%) wished to be re-enrolled and scheduled for a follow-up LDCT. Although we were able to demonstrate that non-adherent patients were more likely to be younger, female, and in an enlisted rank, we believe all patients should be targeted to maintain enrollment. Based on these results, we hypothesize that additional administrative support to increase contact via multiple avenues (phone, email, and letter) with all enrolled patients regardless of age, sex, race, rank or smoking history will continue to improve and maintain adherence to screening. This is especially important in those patients who become non-adherent as many can be recaptured. Commercially available software programs that provide comprehensive tracking and reporting systems to decrease administrative burden are another consideration to augment established lung cancer screening programs.

In addition to non-adherence to lung cancer screening is the issue of underutilization of screening. The military health system serves over 9 million beneficiaries, with WRNMMC being the nation's largest joint military medical center (30). Certainly more patients would qualify for our program than the currently enrolled 242 patients. This underutilization of LDCT for screening within the military health system parallels the nation as a whole with

lack of adequate implementation seen nationwide in the general U.S. population as well as the Veterans Health Administration system (18,19). The slow adoption of lung cancer screening is likely multifactorial, with one possible contribution being lack of awareness or understanding regarding screening. Currently, the American Academy of Family Physicians deems there is insufficient evidence to date to recommend lung cancer screening (31). It has also been shown that protocols used to identify eligible patients vary widely in the community and that the off-guideline use of LDCT screening may be common (32). The Lung Cancer Screening Registry sponsored by the American College of Radiology has over 4,000 participating facilities and continues to grow, but there certainly are still patients and providers that may not have access to a lung cancer screening program (33).

There may be concerns about the risk/benefit ratio, as over-diagnosis and high false positive rates leading to invasive follow-up examinations have been demonstrated in the NSLT and VA populations (4,19). A study of pulmonologists' views on LDCT for lung cancer screening in 2015 reported 52.4% had a propensity for guideline-concordant screening, 22.7% for over-screening, and 24.9% for under-screening. Pulmonologists recommending under-screening cited the harms of potential screening including false positive results, radiation exposure, unfavorable cost-benefit ratio, and also cite insufficient infrastructure and personnel as barriers to implementation (34). Additionally, the collection of lung cancer screening data from records is labor-intensive and there may be a role for automated techniques to obtain this data in the future (19,32). Re-engaging primary and specialist physicians to educate about the benefits of screening and to improve on documentation of accurate smoking histories will improve enrollment, adherence, and any attempts to use electronic health records for lung cancer screening evaluations.

To combat the high false-positive rates associated with screening, risk prediction modeling has been proposed to identify patients for screening based on individual risk as opposed to just age and smoking exposure. Many models have been developed that have retrospectively performed better (especially the PLCOm2012 model) at risk prediction than the NSLT criteria (35). Although promising, there is no information on long term mortality reduction using these models, and these models would need to prove to be effective and user-friendly across a large population. One well-established means to increase the detection of lung cancer and to decrease the rate of false positive CT results

is through the consistent utilization of the lung-RADS reporting system, the use of which is strongly encouraged at the facilities participating in our LDCT screening program (13,27,36,37).

Regarding the potential untoward psychological effects of LDCT screening such as patient anxiety, guilt or shame, none of the non-adherent patients in our study expressed that these feelings were a subjective impediment to continued screening (38). In terms of the cost effectiveness of screening, initial analyses of the NLST data found screening to be cost-effective at \$81,000 per quality-adjusted life-year (QALY) gained, and several analyses have reported on the cost-effectiveness ratio of \$100,000 or less per QALY gained for LDCT (39,40).

The results of this present study have several limitations. Firstly, there is inherent bias in semi-structured interviews from recall bias to response bias on the part of the patient, based on what they remember of their experience and also how positively they wished to respond the questions posed by the interviewer. Efforts were made to ask neutral questions, avoid leading questions, and ensure participants understood the survey would in no way affect their healthcare or relationship with their providers. Additionally, a single interviewer was used in an effort to provide a consistent format and result. Despite the inherent disadvantages of semi-structured interviews, they have been shown to provide meaningful data and insight for clinical decision making (41). Furthermore, our retrospective study not only involved a single-institution, but also our patient population is unique with regards to increased risk of smoking and occupational exposure to carcinogens, which may limit the generalizability of these results (42). Prior reports suggest lung cancer rates up to double in military veterans compared to the general U.S. population (43). Additionally, our analysis and conclusions are based off of the 52% of non-adherent patients who were able to be contacted by phone, highlighting the need for multiple accurate methods to contact patients. It is possible these patients may be getting screening in civilian institutions as 10% of those we were able to contact were being followed elsewhere.

Lung cancer screening is an important method of identifying lung cancer at early stages, allowing for earlier and more effective surgical interventions, and an associated potential for improved long-term survival. Although compliance is critical to the efficacy of any screening modality, prior studies on LDCT for lung cancer screening

reveal little about reasons for lack of patient adherence. By contacting patients in our LDCT lung cancer screening protocol who were non-adherent, we determined that the majority cited lack of follow-up to schedule the next LDCT as their reason for non-adherence. Adherence rates may be increased through improved contact with patients through multiple avenues of communication (i.e., phone, email, letter), and there is benefit in reaching out to non-adherent patients as high rates of re-enrollment are possible.

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Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by institutional review board of Walter Reed National Military Medical Center (#913214) and individual consent for this

retrospective analysis was waived.

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