

Adherence to Post-treatment Surveillance Guidelines in Non-small Cell Lung Cancer - A Veteran's Health Administration Cohort

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Abstract

Background: Several guidelines recommend post-treatment surveillance for non-small cell lung cancer (NSCLC). However, studies evaluating surveillance patterns often cannot distinguish between imaging ordered for surveillance versus symptoms suggestive of recurrence. Moreover, early recurrences and other competing events hamper efforts to determine true surveillance rates.

Objective: Leveraging comprehensive Veterans Health Administration data, we develop a novel competing risks framework to describe patterns and predictors of NSCLC imaging surveillance.

Methods: The study cohort comprised 1,888 patients treated for Stage I-III NSCLC between 2008-2016 who survived ≥6 months. Clinical documents and radiology reports were abstracted for image indication and clinical information. We estimated the cumulative probability of receiving guideline-concordant surveillance defined as chest CT within 4-9 months after treatment, accounting for competing risks and censoring. Multivariable cause-specific Cox regression estimated associations between patient factors and guideline-concordant surveillance and were subsequently adjusted for multiple comparisons.

Results: Among 1,888 patients, 43.8% (CI, 41.6%-46.1%) received guideline-concordant surveillance within 9 months of treatment, whereas 15.2% (CI, 13.7%-16.9%) received non-concordant surveillance and 33.4% (CI, 31.3%-35.5%) received no surveillance. The remaining 7.6% of patients were ineligible for surveillance due to recurrence or death. Compared to years 2008-2010, patients treated for NSCLC from 2014-2016 had a significantly higher likelihood of receiving guideline-concordant surveillance (HR 1.42, P=0.0002).

Conclusions: In this unique application of a competing risks framework, the rate of guideline-concordant surveillance in this national cohort was lower than many previously reported studies. These data highlight a significant gap in surveillance among eligible, asymptomatic lung cancer survivors emphasizing the need to develop efficient strategies to ensure these patients continue to be monitored.

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Original Manuscript

Original Paper

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Abstract

Background: Several guidelines recommend post-treatment surveillance for non-small cell lung cancer (NSCLC). However, studies evaluating surveillance patterns often cannot distinguish between imaging ordered for surveillance versus symptoms suggestive of recurrence. Moreover, early recurrences and other competing events hamper efforts to determine true surveillance rates. Leveraging comprehensive Veterans Health Administration data, we develop a novel competing risks framework to describe patterns and predictors of NSCLC imaging surveillance.

Methods: The study cohort comprised 1,888 patients treated for Stage I-III NSCLC between 2008-2016 who survived ≥ 6 months. Clinical documents and radiology reports were abstracted for image indication and clinical information. We estimated the cumulative probability of receiving guideline-concordant surveillance defined as chest CT within 4-9 months after treatment, accounting for competing risks and censoring. Multivariable cause-specific Cox regression estimated associations between patient factors and guideline-concordant surveillance and were subsequently adjusted for multiple comparisons.

Results: Among 1,888 patients, 43.8% (CI, 41.6%-46.1%) received guideline-concordant surveillance within 9 months of treatment, whereas 15.2% (CI, 13.7%-16.9%) received non-concordant surveillance and 33.4% (CI, 31.3%-35.5%) received no surveillance. The remaining 7.6% of patients were ineligible for surveillance due to recurrence or death. Compared to years 2008-2010, patients treated for NSCLC from 2014-2016 had a significantly higher likelihood of receiving guideline-concordant surveillance (HR 1.42, $P=0.0002$).

Conclusions: In this unique application of a competing risks framework, the rate of guideline-concordant surveillance in this national cohort was lower than many previously reported studies. These data highlight a significant gap in surveillance among eligible, asymptomatic lung cancer survivors emphasizing the need to develop efficient strategies to ensure these patients continue to be monitored.

Keywords: Non-Small Cell Lung Cancer, Surveillance, CT Imaging

Introduction

Lung cancer is one of the most common cancers worldwide and remains the leading cause of cancer death¹. Following treatment for lung cancer, patients remain at risk both for cancer recurrence as well as the development of second primary lung cancers (SPLC). Surgery remains the mainstay of curative-intent therapy in early-stage disease. However, patients can have recurrence rates ranging from 30-68% despite complete resection^{2,3}. As a result, several expert bodies have published guidelines recommending routine surveillance following treatment to detect recurrence and SPLC⁴⁻⁶. Many of these guidelines recommend some form of imaging surveillance within 6 months following treatment.

Despite several recommendations for post-treatment surveillance, there is wide variability in guideline adherence in clinical practice. Previous studies have evaluated rates of adherence to these recommendations for post-treatment surveillance, with rates ranging widely from 25-71%⁷⁻¹⁰. The cause of this variability remains unknown, though differences in patient population and provider practice are likely factors. Moreover, we contend that incomplete information on imaging indication is a large potential contributor to the observed variability in adherence. Imaging after definitive treatment can occur for multiple reasons, including non-surveillance indications like a chest CT ordered for a traumatic injury. Previous studies that have included information on imaging indication have been limited to single-center experiences, whose findings are likely influenced by these population differences and varying institutional practices^{8,11}. Large population-based studies that assess surveillance across provider and patient characteristics have lacked information on imaging indication by relying on administrative claims-based data^{7,9,10,12}. Patients may have imaging procedures captured by these claims data despite competing events (i.e., early recurrence) that exclude patients from undergoing true surveillance, thereby leading to inaccurate estimates of post-treatment surveillance. Each of these limitations have hampered efforts to evaluate true surveillance rates and the effectiveness of surveillance programs more broadly.

Herein, this study examines post-treatment surveillance using detailed national Veterans Health Administration (VHA) data to estimate the true rate of adherent surveillance and predictors of guideline-concordant care in early-stage NSCLC patients. We use a novel annotation methodology to abstract imaging indications from national data at scale. Information on imaging indications and clinical documentation allow us to employ a competing risk analysis for estimating the cumulative probability of surveillance. In contrast with previous literature, this form of time-to-event analysis offers the opportunity to account for events – as well as describe the factors – that preclude or alter the likelihood of performing guideline-concordant surveillance (e.g., death, recurrence, non-concordant surveillance imaging)^{13,14}. We expect that this will provide a more accurate estimate of the rates and predictors of guideline-concordant post-treatment surveillance.

Materials and Methods

Cohort and Definitions

Using VHA electronic health records databases, we identified 20,532 Veterans treated with curative intent for non-metastatic primary NSCLC diagnosed between 1/1/2008-4/30/2016. We used the International Classification of Diseases - 9th/10th Edition (ICD-9/10) diagnosis codes (Supplemental Table 1). We also retrieved demographic, clinical, and vital status information for these patients. For inclusion, patients must have had either ≥ 2 outpatient or ≥ 1 inpatient NSCLC diagnosis codes, and the date of diagnosis was the date of the earliest code demonstrating connectedness to care¹⁵. Curative intent treatment was classified based on ICD-9/10 procedure codes and Current Procedural Terminology (CPT) codes (Supplemental Table 2) within 6 months of diagnosis. NSCLC stage was classified according to American Joint Committee on Cancer (AJCC) TNM Staging system (7th Edition in effect during the observation period). We excluded patients who did not receive curative intent therapy, received chemotherapy only, died within 6 months of initiating therapy, had stage 4 cancer, had a non-skin cancer diagnosis (except melanoma and cervical

cancer) within 5 years prior to NSCLC diagnosis, or any diagnosis of lung cancer prior to 2008. Participant follow-up ended 12/31/2016.

The study cohort included 1,890 eligible patients with completely abstracted radiology reports and clinical notes from a 9,238 sample cohort. An additional 369 patients from the sample cohort had no radiology reports directly relevant to NSCLC surveillance (Figure 1). To avoid overrepresentation of patients without abstractable radiology reports in our analysis, we weighted these patients so that their proportion in the study cohort was the same as their proportion among all eligible patients in the sample cohort – bringing the final analysis sample to 1,888.

Radiology Abstraction

We abstracted image indication (surveillance, symptoms, abnormality follow-up, other, unknown) and modality (PET, chest X-Ray (CXR), Chest CT, and Other [MRI, non-chest CT, Bone Scan]) from radiology reports. Imaging indications were identified in the report text and recorded as documented.

We utilized the previously published semi-automated chart abstraction protocol by our group for obtaining detailed radiology data¹⁶. A searchable radiology index was created, which included full-text radiology reports that were then queried using SQL to identify all radiology-related text documents to be indexed. VISA, a Lucene-based open-source full-text search engine written in Java, was used to search the radiology reports for text relevant to the user query. VISA then returns the user-defined relevant full-text radiology reports with highlighted relevant text snippets, which were then manually reviewed, annotated, and coded by an abstractor.

Clinical Abstraction

Clinical notes from patient charts were used to abstract any missing data on Stage, Smoking Status as well as NSCLC recurrence and/or second primary cancer, and tumor histology. Final pathologic staging took precedence during chart abstraction. Smoking at the time of diagnosis or initial presentation was considered “current”. The presence of recurrent NSCLC or a second primary

cancer was determined based on documentation by a treating clinician. Histologic subtype was identified directly from pathologic reports when available, or collected from other clinical note types (e.g., progress notes). Patients who were found to have small cell histology, had recurrence or second primary cancer other than lung prior to 120 days post-treatment, or did not undergo curative-intent treatment were additionally excluded based on this clinical abstraction.

Outcomes of Interest

The primary outcome was receipt of guideline-concordant surveillance imaging. National Comprehensive Cancer Network (NCCN) recommendations for post-treatment surveillance imaging were used as a base set of guidelines¹⁷. Although updated periodically, they have consistently recommended routine post-treatment surveillance chest CT imaging approximately every 6 months during this study period (recommended intervals range from every 3-6 to 6-12 months during the first 24 months). We defined guideline-concordant surveillance as receiving chest CT performed for surveillance purposes (as documented by the image indication) within 120-270 days following the first day of treatment or first day of last treatment with multimodality therapy. Imaging performed explicitly for surveillance via other imaging modalities (e.g., PET) were considered non-concordant surveillance. The 120-270 day (4-9 months) post-treatment interval was adopted to represent the first surveillance window, with the intent to create a more liberal window with a 2-3 month buffer on either end of the published 6-month guideline.

This study was approved by the Institutional Review Boards of Stanford University and the Department of Veterans Affairs.

Statistical Methods

In estimating the cumulative probability of patients receiving guideline-concordant surveillance imaging within the initial 120-270 day surveillance window after curative-intent therapy, we used a competing risks framework to correctly estimate the cumulative probability by accounting for competing events. This can help provide unbiased estimates of patients experiencing

the event of interest, given that competing events materially alter their probability or preclude them entirely. For example, receiving a diagnosis of recurrent NSCLC prior to scheduled surveillance precludes guideline concordant surveillance – given imaging after recurrence can no longer be deemed to be for surveillance. Recurrences discovered during surveillance imaging were coded as surveillance events. An example schematic of the time-to-event analysis helps visualize a few of these relatively common clinical scenarios (Supplemental Figure 1).

We used the Aalen-Johansen estimator and corresponding confidence intervals to analyze the primary outcome, the receipt of guideline-concordant surveillance imaging within the 120-270 days after curative-intent treatment. Death, recurrence, second primary cancer, and non-concordant surveillance were treated as the competing events in this analysis.

To evaluate the factors associated with the primary outcome, we used multivariable cause-specific Cox regression to estimate hazard ratios (HRs) and confidence interval (CIs). We considered various demographic factors (e.g., sex, age, race, marital status, year of diagnosis) and clinical factors (e.g., treatment, histology, disease stage) in this model. To adjust for multiple testing, we applied the Bonferroni correction method for 11 independent variables in each model. We reported unadjusted P-values and interpreted any below 0.004 ($< 0.05/11$) as significant. For consistency we calculated 99.6% CIs for all point estimates. Missing data were treated as a separate category in models. To avoid very small groups we combined Stage 0 and Stage I (due to the very small proportion of Stage 0 patients). Additionally, recurrences and second primary malignancies were combined as a single competing event referred to as “recurrence” for brevity. A univariable model of the primary outcome is shown in Supplemental Table 4. Statistical analysis was performed using R Version 4.2.2¹⁸

Results

Demographics of Analytic Cohort

Of 135,513 patients diagnosed with primary NSCLC between 1/1/2008 and 4/30/2016, 20,532 met the study eligibility requirements (Figure 1). The study cohort comprised a random sample of 1,890 patients with abstracted clinical notes and radiology reports, while 369 of all eligible patients had no relevant radiology reports available which was weighted to prevent overestimation. The effective study sample size was 1,888 patients after weighting (see Methods) (Table 1). The mean age of the analysis cohort was 66 years, 95.9% were male, 71.1% of patients were white, and 43.1% were married. Of the 1,888 patients, 57.0% presented with Stage I disease, and the most common treatment modality was surgery alone (56.6%).

Figure 1. CONSORT Diagram

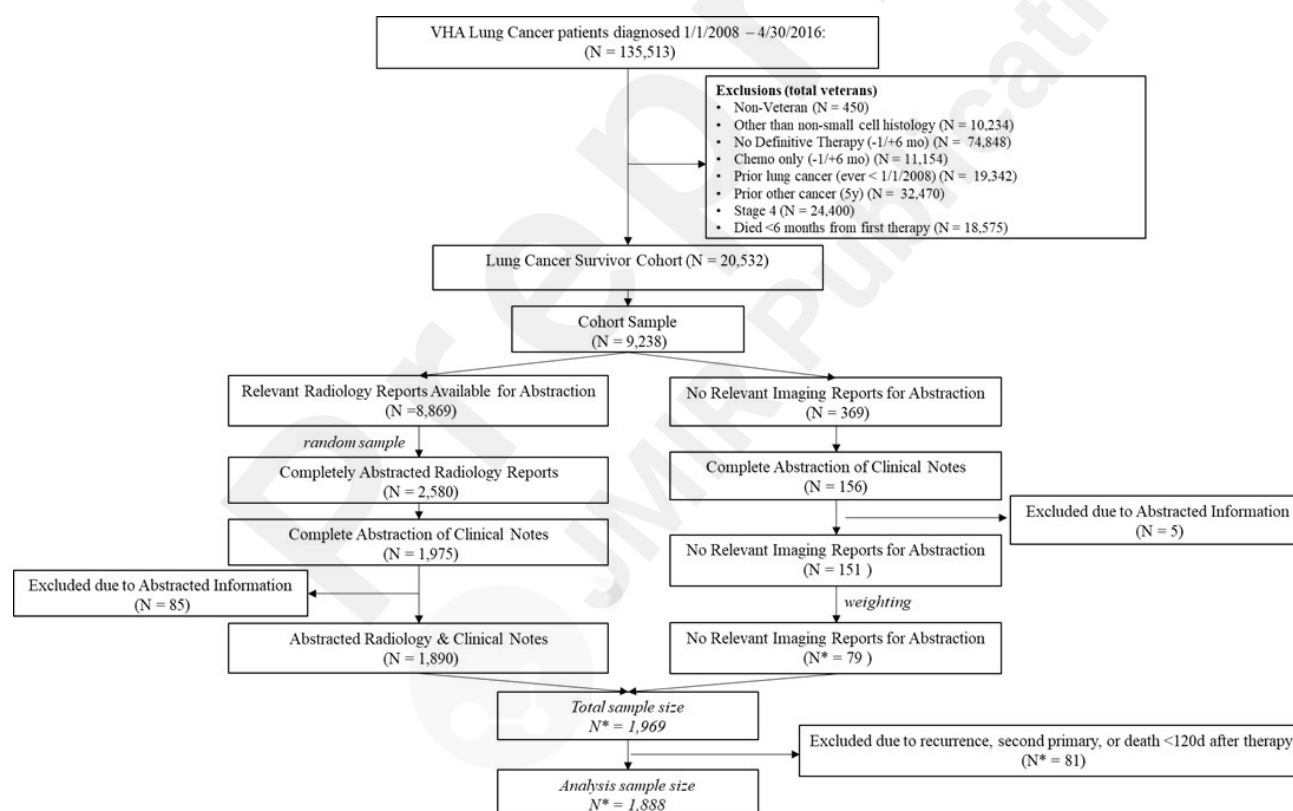


Table 1. Participant characteristics at the time of diagnosis (weighted)

	N (%)
Diagnosis Date (year)	

	N (%)
2008-2010	628 (33.3%)
2011-2013	726 (38.5%)
2014-2016	534 (28.3%)
Age(y)	
Mean (SD)	66.4 (7.9)
<65	817 (43.3%)
65-74	746 (39.5%)
75+	324 (17.2%)
Male	1811 (95.9%)
Race	
Black/AA	327 (17.3%)
Other	105 (5.5%)
White	1342 (71.1%)
Missing	114 (6.1%)
Married	814 (43.1%)
Region	
Mid-Atlantic	376 (19.9%)
Midwest	238 (12.6%)
Northeast	191 (10.1%)
South	743 (39.3%)
West	339 (18.0%)
Smoking Status	
Current	947 (50.1%)
Former	591 (31.3%)
Never	316 (16.8%)
Missing	34 (1.8%)
Charlson Comorbidity Index	
0	539 (28.6%)

	N (%)
1	597 (31.6%)
>1	752 (39.8%)
Stage	
0 or 1	1076 (57.0%)
II	329 (17.4%)
III	414 (21.9%)
Missing	69 (3.6%)
Histology	
Adenocarcinoma	876 (46.4%)
Squamous and Transitional Cell	753 (39.9%)
Other	196 (10.4%)
Missing	64 (3.4%)
Initial Therapy	
Surgery Alone	1068 (56.6%)
Radiation and Chemotherapy	251 (13.3%)
Surgery and Chemotherapy	235 (12.5%)
Radiation Alone	181 (9.6%)
Surgery, Chemotherapy, and Radiation	95 (5.0%)
Surgery and Radiation	57 (3.0%)

Distribution of Imaging Performed

The most common imaging performed during the initial 120-270 day window was chest CT at 44.5% (Table 2a). Chest X-Rays accounted for 36.3% of all images performed, while the remaining 11.8% and 18.2% were PET scans or Other image modalities, respectively. When evaluating imaging performed for the indication of surveillance, chest CT was the most common

modality. The proportion of chest X-ray imaging performed for surveillance was 12.2% (much less compared to overall imaging), while the proportion of chest CT and PET imaging done for surveillance was 70.9% and 14.4%, respectively. Chest CT remained the most common imaging procedure for surveillance across all types of primary treatment groups (Table 2b). However, PET imaging made up at least 24.0% of surveillance imaging in patients receiving some form of radiation therapy (29.5% in Radiation Alone), as opposed to just 14.4% across all treatment groups combined.

Table 2a. Images performed during the 120-270 day surveillance window by indication and modality*

	CT-Chest (N=1460)	CXR (N=1190)	PET (N=386)	Other (N=242)	Total (N=3278)
Indication					
Surveillance	1026 (70.9%)	176 (12.2%)	209 (14.4%)	37 (2.6%)	1448 (100.0%)
Symptoms	88 (15.7%)	357 (63.5%)	8 (1.4%)	109 (19.4%)	562 (100.0%)
Follow-up	117 (39.3%)	46 (15.4%)	109 (36.6%)	26 (8.7%)	298 (100.0%)
Other/Unknown	229 (23.6%)	611 (63.0%)	60 (6.2%)	70 (7.2%)	970 (100.0%)
Total	1460 (44.5%)	1190 (36.3%)	386 (11.8%)	242 (7.4%)	3278 (100.0%)

Table 2b. Images performed for surveillance during 120-270 interval by therapy and modality*

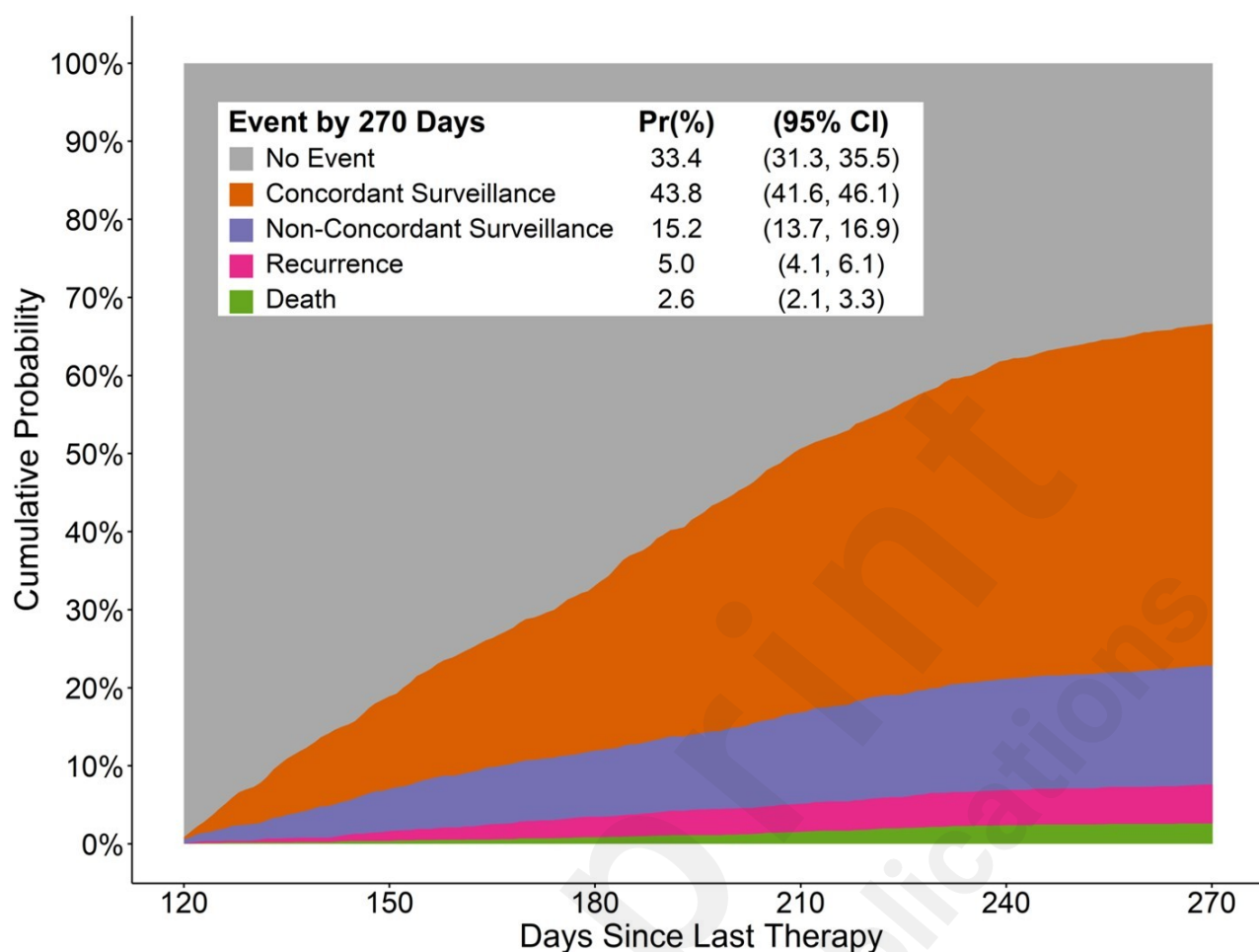
	CT-Chest (N=1026)	CXR (N=176)	PET (N=209)	Other (N=37)	Total (N=1448)
Therapy					
Surgery Alone	606 (75.3%)	119 (14.8%)	58 (7.2%)	22 (2.7%)	805 (100.0%)
Radiation +	128 (66.7%)	12 (6.2%)	46 (24.0%)	6 (3.1%)	192 (100.0%)
Chemotherapy					
Surgery +	130 (68.1%)	21 (11.0%)	34 (17.8%)	6 (3.1%)	191 (100.0%)
Chemotherapy					
Radiation	78 (60.5%)	12 (9.3%)	38 (29.5%)	1 (0.8%)	129 (100.0%)
Alone					
Surgery +	57 (68.7%)	6 (7.2%)	20 (24.1%)	0 (0.0%)	83 (100.0%)
Chemotherapy +					
Radiation					
Surgery +	27 (56.2%)	6 (12.5%)	13 (27.1%)	2 (4.2%)	48 (100.0%)
Radiation					
Total	1026 (70.9%)	176 (12.2%)	209 (14.4%)	37 (2.6%)	1448 (100.0%)

*Patients may be counted in more than one column if undergoing multiple imaging procedures
CT-Chest, computed tomography of chest; CXR, chest x-ray; Other: MRI, non-chest CT, and bone scan; PET, positron emission tomography

Cumulative Probability of Receiving Post-Treatment Imaging.

In estimating the cumulative probability of patients receiving guideline-concordant surveillance imaging within the initial 120-270 day surveillance window after curative-intent therapy, we used a competing risks framework to correctly estimate the cumulative probability by accounting for competing events (e.g., death or recurrence). This analysis shows that the cumulative probability of receiving guideline-concordant imaging for surveillance was 43.8% (99.6% confidence interval [CI] [41.6%, 46.1%]) (Figure 2). The cumulative probability of receiving non-concordant surveillance imaging within this window was 15.2% (CI [13.7%, 16.9%]), whereas 33.4% (CI [31.3%, 35.5%]) of patients did not receive concordant or non-concordant imaging (i.e. no imaging at all). A total of 5.0% (CI [4.1%, 6.1%]) of patients experienced recurrence, while 2.6% (CI [2.1, 3.3%]) of patients died during the post-treatment surveillance period – meaning roughly 7.6% of patients were ineligible for surveillance during this period.

Figure 2. Cumulative probability estimated from an Aalen-Johansen competing events model for receipt of guideline-concordant imaging defined as chest CT with a documented indication of “surveillance” within 120-270 days after definitive therapy. Note that the probability curves are stacked such that the sum at any time is 100%. Patients were followed only until the first event, and cumulative probability is therefore the expected proportion of patients who had the event as their first event prior to a given time. Overlaid table shows cumulative probability (Pr) and 99.6% confidence interval (CI) at 270 days post-therapy.



Factors Associated with Receiving Guideline-Concordant Surveillance Imaging.

We evaluated the association between the receipt of guideline-concordant surveillance and various demographic and clinical variables using multivariable cause-specific Cox regression (Table 3). Compared to patients treated for NSCLC between 2008-2010, patients receiving treatment from 2014-2016 were significantly more likely to receive guideline-concordant surveillance (hazard ratio [HR] 1.42, CI [1.09, 1.87], $P=0.0002$). There was a similar trend towards an increased likelihood of guideline-concordant surveillance in years 2011-2013 compared to 2008-2010, though this did not reach statistical significance. No other variables were significantly associated with receipt of guideline-concordant surveillance. Although radiation alone was not significantly associated with a decreased likelihood of receiving guideline-concordant surveillance (HR 0.68, CI [0.45, 1.03], $P=0.0071$), radiation alone was associated with an increased likelihood of non-concordant

surveillance in the same model (HR 1.93, CI [1.10, 3.38], $P=0.00079$) consistent with increased use of PET for surveillance in this group (Supplemental Table 3).

Table 3. Results of multivariable cause-specific Cox regression for receipt of guideline-concordant surveillance imaging, defined as chest CT with documented indication of surveillance, within 120-270 days of definitive therapy; competing events were the earliest of recurrence or second primary cancer, death, or non-concordant surveillance imaging.

Concordant Surveillance		
	HR (99.6% CI)	P ^a
Therapy		
Surgery Alone	Ref.	
Surgery and Chemotherapy	1.08 (0.76, 1.54)	0.53
Surgery and Radiation	1.10 (0.60, 2.01)	0.66
Surgery, Chemotherapy, and Radiation	1.07 (0.64, 1.79)	0.72
Radiation Alone	0.68 (0.45, 1.03)	0.0071
Radiation and Chemotherapy	0.93 (0.61, 1.42)	0.61
Stage		
0 or I	Ref.	
II	0.77 (0.56, 1.06)	0.020
III	0.91 (0.65, 1.29)	0.44
Missing	0.42 (0.17, 1.01)	0.0045
Diagnosis Year		
2008-2010	Ref.	
2011-2013	1.26 (0.98, 1.62)	0.0091
2014-2016	1.42 (1.09, 1.87)	0.0002*
Age		
<65	Ref.	
65-74	1.06 (0.84, 1.34)	0.50
75+	1.17 (0.86, 1.59)	0.15
Male v. Female	1.46 (0.81, 2.62)	0.06
Histology		
Adenocarcinoma	Ref.	
Squamous and Transitional Cell	0.95 (0.76, 1.18)	0.49
Other	1.03 (0.73, 1.45)	0.82
Missing	0.99 (0.45, 2.19)	0.97
Married v. Unmarried	1.11 (0.90, 1.37)	0.14
Race		
Black	Ref.	
White	1.01 (0.77, 1.34)	0.90
Other	1.19 (0.74, 1.91)	0.30
Missing	0.78 (0.46, 1.32)	0.17
Region		

Mid-Atlantic	Ref.	
Midwest	0.98 (0.69, 1.39)	0.85
Northeast	1.41 (1.00, 2.00)	0.0040
South	0.77 (0.57, 1.02)	0.0076
West	0.98 (0.71, 1.36)	0.88
Smoking		
Current	Ref.	
Former	0.94 (0.75, 1.20)	0.48
Never	0.79 (0.58, 1.07)	0.024
Missing	0.92 (0.44, 1.91)	0.73
Charlson		
Comorbidity Index		
0	Ref.	
1	0.91 (0.70, 1.17)	0.28
>1	0.99 (0.77, 1.27)	0.92

^a To account for multiple hypothesis tests, $P < 0.004$ was interpreted as statistically significant and 99.6% CIs estimated; displayed P-values were not adjusted.

* $P < 0.004$

Discussion

Despite widespread recommendations for post-treatment surveillance, we find that roughly a third of patients undergoing treatment for NSCLC before 2016 did not receive any form of surveillance in our study. Moreover, the true fraction of patients receiving guideline-concordant surveillance imaging in this study was less than half at 43.8%. In our previous study of patients' first imaging procedures within 4-8 months after resection (representing the first surveillance window) of early-stage NSCLC, 24.6% of patients received a CT-Chest while 59.6% received a CXR⁷. Like others, our work demonstrates evidence of increasing use of post-treatment chest CT for surveillance^{9,12} in line with routine surveillance guidelines.

Our current study's findings on the rate of guideline-concordant surveillance CT are substantially lower than those previously reported by Malhotra et al. (2018) and others^{9,10}. In their 2018 study, Malhotra defined adherent imaging as patient receipt of at least a CT or PET/CT scan during the 7-18, 19-30, 31-42, and 43-60 month intervals post-treatment. The rate of adherent surveillance imaging at 18 months was 70.6%. The variation in reported rates across these and other studies is likely reflected in the fact that very few large studies concerning post-treatment

surveillance contain information on the indication for post-treatment imaging. Many of these studies, therefore, likely reflect imaging done for various indications, including evaluation of symptoms (e.g., cough, pneumonia), or are unknown and do not truly reflect imaging done for surveillance. Additionally, the 2018 study by Malhotra et al. defines receipt of adherent imaging as receiving CT or PET/CT despite guideline recommendations against the routine use of PET imaging for post-treatment surveillance of NSCLC. The available literature along with our findings that chest CT only makes up 70% of initial surveillance images, provide evidence that non-concordant surveillance imaging makes up a sizeable fraction of radiology evaluations in patients treated for NSCLC. This may be due in part to practice variations in using distinct treatment modalities to monitor treatment response and/or disease progression (i.e., the use of PET/CT in patients undergoing radiation or neoadjuvant therapy). As stated previously, differences in patient population, comorbidities, and systems of care delivery also likely play some role in varying reported rates of surveillance (e.g., this study reviews VHA patient data while Malhotra and colleagues evaluate surveillance among a SEER-Medicare cohort).

An important strength of our study is the inclusion of detailed VHA data that provided insight into the indication for radiology procedures. Indeed, true rates of post-treatment surveillance were previously obscured by the fact that imaging reported from other studies may have been done for purposes other than surveillance – situations that are difficult to discern using administrative and claims data alone. Another strength of our study was the ability of the competing risk model to evaluate true surveillance rates in the presence of competing events that alter estimates put forth in other studies. Indeed, we found 7.6% of patients were not eligible to receive surveillance in our sample cohort because of death or recurrence. Accounting for competing events addresses the potential for overestimating the incidence of the event of interest, a potential weakness of utilizing the Kaplan-Meier method or claims based data in this setting. Each of these features present in this study likely describe our report of relatively lower rates of guideline concordant surveillance

compared with the literature. Thus, using the most liberal interpretation of our data, excluding those patients with competing events of early recurrence or death, 64% of our cohort received imaging with the explicit intent of surveillance (47% guideline-concordant and 16% discordant) which is consistent with other reports lacking indication data, yet 36% received no imaging at all in this initial surveillance period. This allows us to highlight the latter group of patients with no surveillance as the most important group to target for interventions.

One of the limitations of our study is the use of administrative ICD-9/10 and CPT codes to identify patients with relevant treatment procedures. Additionally, we did not have structured diagnosis dates and staging information from a cancer registry for cohort construction. We used a conservative approach to ensure patients included in the cohort were newly diagnosed with NSCLC. Thus, our approach may have missed some patients with a NSCLC diagnosis and the 20,532 patient cohort likely does not reflect the total incidence of early stage NSCLC in VHA during this period. We abstracted only radiology report information on patients receiving imaging studies at VHA facilities. Veterans who received relevant imaging studies at outside facilities do not have reports that are easily viewable in the VHA database except through an archival process requiring requesting review of any scanned reports that were provided by the community imaging clinic. In sensitivity analyses we examined the rates of non-VA care including imaging paid for by VA (fee-based care) and care Veterans received through Medicare or Medicaid. Data are not available for any community care services patients pay for out of pocket or are covered by other insurance such as a Veteran's private insurance, although dual use of care from private insurance is rare among patients who otherwise rely on VHA for the majority of their care and in particular their cancer care¹⁹. This sensitivity analysis identified that among the entire cohort fewer than 16% of Veterans had any non-VA imaging performed in the available administrative data, with 8% of these corresponding to CT scans. Thus, inclusion of these studies would still result in underutilization of surveillance overall.

In conclusion, the use of this detailed clinical database along with the novel application of a

competing risk model has provided additional clarity on the current state of adherence to post-treatment surveillance guidelines for NSCLC. More studies are needed to determine how guideline adherence and other aspects of current surveillance practices (e.g., imaging frequency and modality) influence clinical outcomes, especially given recent literature casting doubts on the survival benefits of routine surveillance^{20,21,22}.



Conflict of Interest Statement: The authors have no relevant conflicts of interest to declare.

Abbreviations:

NSCLC, Non-small cell lung cancer

CT, Computed Tomography

PET, Positron Emission Tomography

MRI, Magnetic Resonance Imaging

CXR, Chest X-Ray

SPLC, Second Primary Lung Cancer

VHA, Veterans Health Administration

AJCC, American Joint Committee on Cancer

NCCN, National Comprehensive Cancer Network

CPT, Current Procedural Terminology

ICD, International Classification of Disease

Data Availability: Data is not available. Access to individual patient data in the Veterans Health Administration (VHA) Corporate Data Warehouse (CDW) is controlled by VHA. We will share aggregate results and code used to generate results according to VHA policy.

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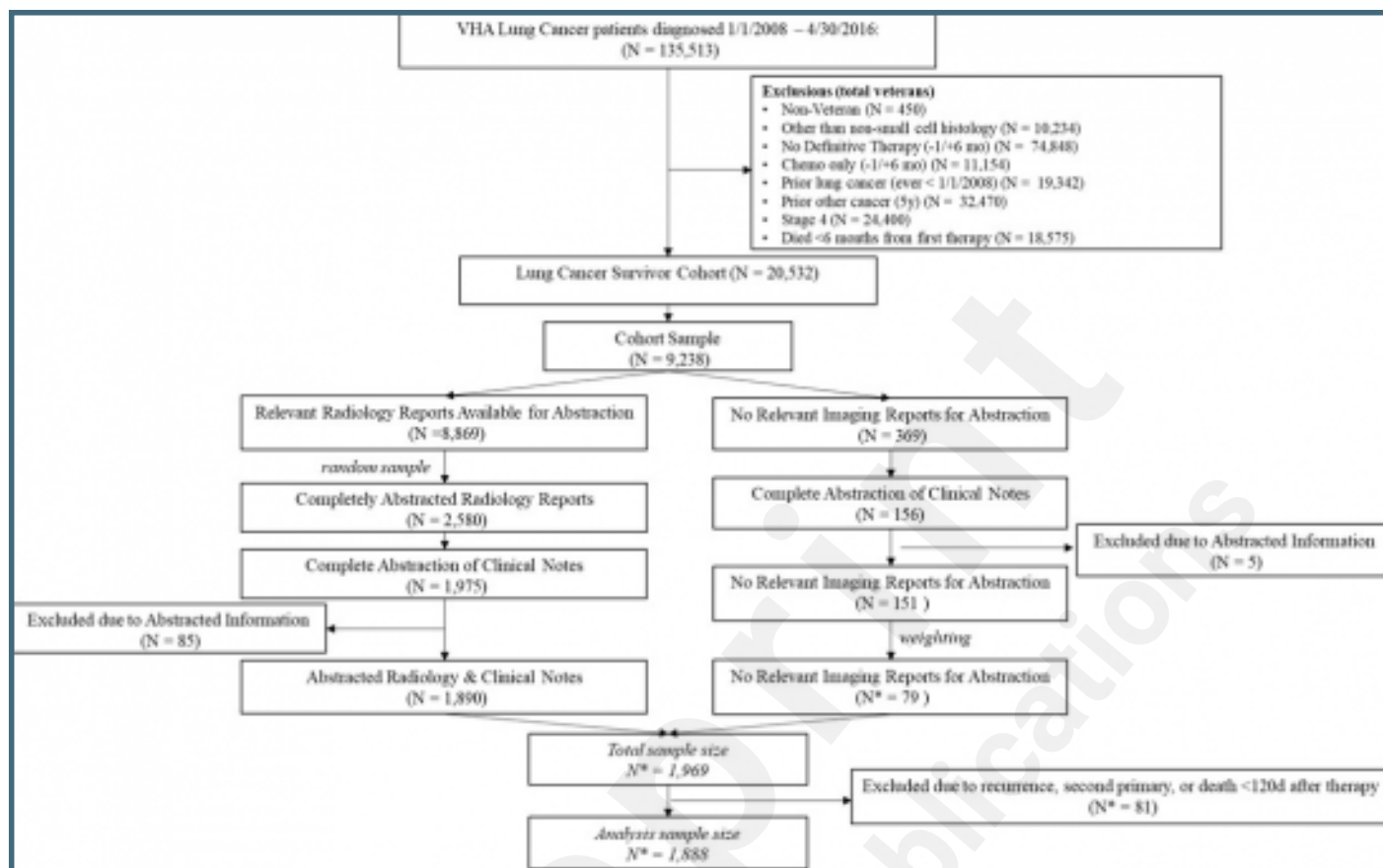
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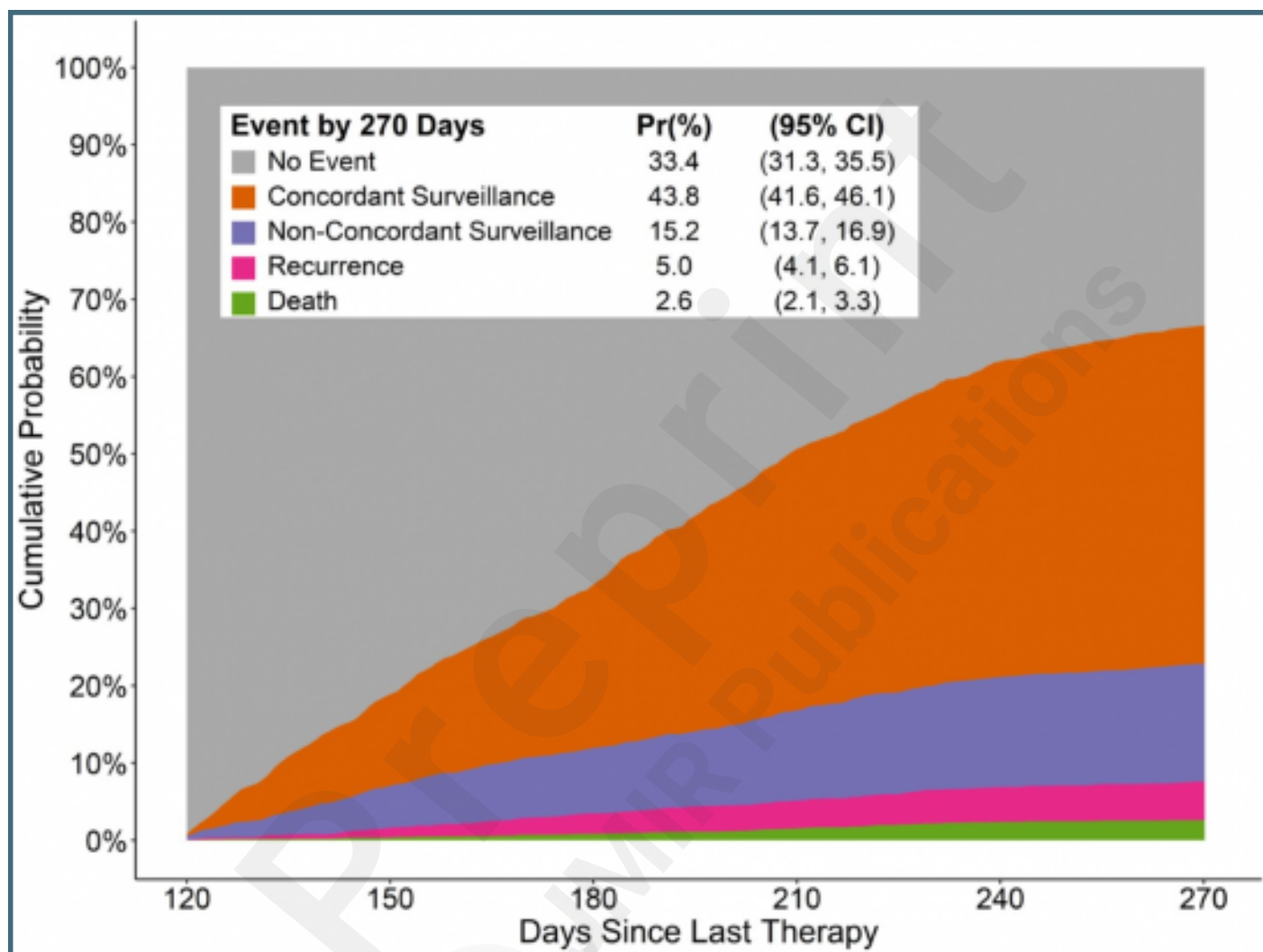
Supplementary Files

Figures

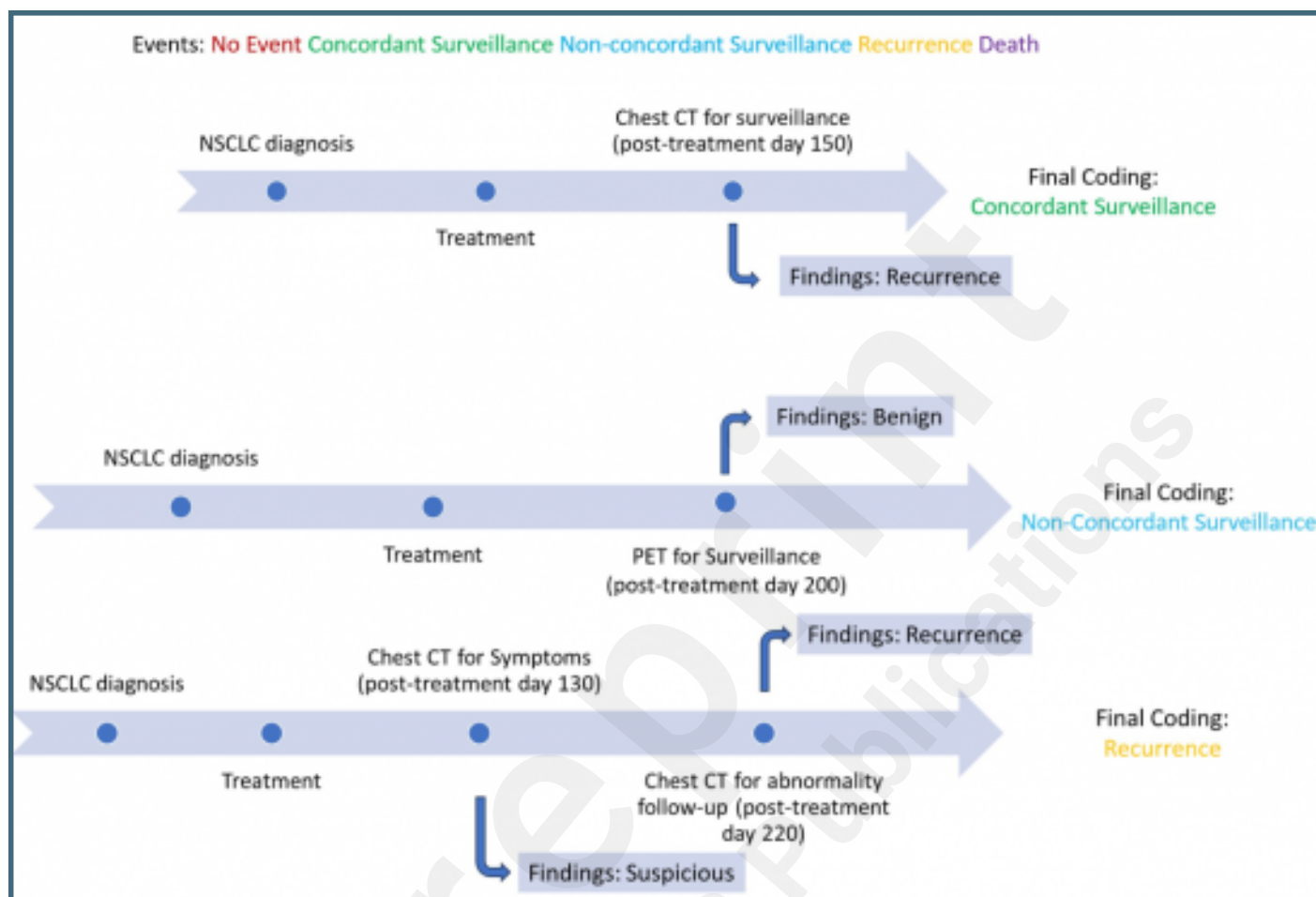
CONSORT Diagram.



Cumulative probability estimated from an Aalen-Johansen competing events model for receipt of guideline-concordant imaging defined as chest CT with a documented indication of “surveillance” within 120-270 days after definitive therapy. Note that the probability curves are stacked such that the sum at any time is 100%. Patients were followed only until the first event, and cumulative probability is therefore the expected proportion of patients who had the event as their first event prior to a given time. Overlaid table shows cumulative probability (Pr) and 99.6% confidence interval (CI) at 270 days post-therapy.



Example schematic of time-to-event analysis with competing risks. The multicolored banners represent individual models with the event of interest and their corresponding competing risks. Each horizontal arrow is a single hypothetical patient undergoing review within the 120-270 day post-treatment period.



Multimedia Appendixes

Supplementary Figures and Tables.

URL: <http://asset.jmir.pub/assets/fae8adc966e74a38073569092a510b41.docx>

