Initial Presentation of Lung Cancer through the Emergency Department: A Complete Provincial Cohort Review

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ABSTRACT

Background: Lung cancer is the leading cause of cancer-related mortality in Canada. International literature indicates that a significant proportion of lung cancer patients are diagnosed as a result of an Emergency Department (ED) visit, and that this diagnostic route is associated with poor survival. There is no published population-based Canadian data regarding diagnostic route for lung cancer.

Methods. All primary lung cancer cases diagnosed in Nova Scotian residents in 2014 were identified through the provincial registry. Extracted registry data included diagnostic data and date of death to August 31, 2016. Linked hospital records, including lab and imaging, were reviewed to identify the first positive diagnostic study and presentation route (ED yes/no). The cohort, stratified by route to diagnosis, was compared on the basis of demographics, stage at diagnosis, and survival.

Results. A total of 951 cases were identified. Of these, 336 (36%) were diagnosed via the ED. There were no differences in age or sex by route to diagnosis. Cases diagnosed via the ED were more likely to be at advanced stage (Stage IV: 60% vs. 43%) and experience shorter survival (1-year survival: 28.4% vs. 49.5%). Very few (7%) of the patients presenting via the ED had no family physician.

Interpretation. The ED is a common route of presentation for lung cancer and is associated with advanced stage at diagnosis and reduced survival time. Strategies are needed to encourage diagnosis prior to emergency and to ensure that ED providers are supported in the initial care of lung cancer patients.

Key Words: lung cancer, route to diagnosis, emergency department

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Introduction:

Lung cancer remains the leading cause of cancer-related mortality in Canada, estimated to account for 26% of all cancer-related deaths (1). There will be an estimated 28,600 incident cases of lung cancer in 2017, accounting for 14% of all new cancer cases. It is projected that there will be 950 new cases of lung cancer in Nova Scotia for the same period (1). Early detection of lung cancer and guidelines for diagnosis and treatment is an important public health issue aimed at improving care, improving quality of life, and reducing patient mortality.

The high mortality rate of lung cancer is due in large part to presentation at advanced stage, which may be caused by the non-specific nature of early respiratory symptoms in this population (2). A majority (67%) of lung cancer patients present with general respiratory complaints, of which less than one-third report hemoptysis (a clinical sign prompting more rapid evaluation). Delays are exacerbated by the lack of perceived significance of symptoms and stigma associated with smoking-related diseases (3-6). Delays in seeking treatment contribute to later stage presentation. In Canada, 65.4% of non-small cell lung cancer cases diagnosed in 2013 were at an advanced stage (III or IV) and most of these patients die within one year (7).

Consensus guidelines are often designed with the assumption that evaluation of lung cancer is initiated via primary care avenues; usually through a family physician requesting diagnostic imaging or occasionally precipitated by an asymptomatic screening examination, although uncommon in Canada (8-10). The natural history of lung cancer and its propensity to present at late stage, suggests that diagnosis may also occur in an emergent environment (11, 12). This under-recognized alternative route to diagnosis has implications for both patients and care providers. The emergency department (ED) is not always well equipped to deliver a lung cancer diagnosis in terms of initiating work up, ensuring follow-up and providing patient support for the immediate questions regarding the diagnosis. This is of particular importance for the growing number of patients without a primary care provider. Thus, the ED route of lung cancer diagnosis has implications for knowledge transfer activities including the development and

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implementation of consensus guidelines regarding lung cancer diagnosis, referral and treatment.

To date, there has been no published population-based analysis of route to lung cancer diagnosis in Canada. Therefore, it has been difficult to determine the need for appropriate resources for lung cancer management in the ED. This study examined the route to diagnosis of lung cancer cases in Nova Scotia and compares the groups (ED vs. non-ED) in terms of demographics, diagnostic information, and survival.

Methods:

This is a descriptive provincial study of the route to diagnosis of all primary lung cancer cases diagnosed in Nova Scotia residents in 2014. The cohort was identified through the provincial cancer registry, which follows Canadian Council of Cancer Registries standards for deriving date and site of diagnosis making use of multiple sources of information, including histology/pathology, cancer clinic visits and death certificates (13). Both method and date of diagnosis for lung cancer cases is prioritized in the following manner: cytology, pathology, imaging, clinical, and date of death. This implies that lung cancer cases that are first diagnosed through imaging but are later confirmed through resection will be registered with a diagnosis date consistent with the resection. Data were extracted for all cases diagnosed in the calendar year 2014 with death data current to August 31, 2016. Data elements extracted from the registry included: age at diagnosis, sex, histology, stage at diagnosis and date of death. Personal identifiers were also extracted to enable linkage of diagnostic imaging and pathology data from hospital records and the provincial radiology archive.

In reverse chronological order from the cancer registry date of diagnosis, all diagnostic imaging for each case was reviewed to identify the first imaging report raising the possibility of lung cancer. The requisition point of origin was identified by examining

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the first requisition form for any of the following criteria: (i) explicit identification of patient location as ED, (ii) hand-written clinical documentation undersigned by an ED physician, or (iii) explicit documentation of verbal communication with ED physician by the reporting radiologist. If imaging was not the initial positive diagnostic test, the pathology records (cytology and tissue specimens) were reviewed in a similarly reverse chronological order. Cases were then assigned a route to diagnosis (ED or non-ED), based on the point of origin of the first requisition. For those cases diagnosed via the ED, evidence of a primary care provider was obtained from review of the ED documentation.

Details specific to each case were reviewed to establish the clinical indication for the testing leading to diagnosis (symptomatic, incidental, screening or surveillance). Cases were classified as symptomatic if the clinical history provided on the requisition included signs and symptoms of lung cancer as defined by the provincial guidelines for the diagnosis and referral of suspected lung cancer developed by Cancer Care Nova Scotia and the Clinically Detected Lung Cancer Working Group (14) (appendix A). For many of the EDs, the triage note (presenting complaint) was used as the imaging requisition. Incidental cases were defined as those for whom the clinical indication for testing prompting diagnosis met none of the aforementioned criteria (e.g. colon cancer staging, post-surgical follow-up imaging, aortic aneurysm surveillance, major trauma).

A separate designation of 'surveillance' was assigned to cases for which an incidental finding of a small pulmonary nodule of low suspicion resulted in further follow-up imaging, only later demonstrating suspicion for cancer. A small number of cases diagnosed as a result of inclusion in a nation-wide clinical trial (Pan-Canadian Early Detection of Lung Cancer Study) were indexed under the category of 'screening'. This category additionally included cases not involved in clinical trials but for whom the imaging requisition specifically stated "screening" as the clinical indication.

The clinical date of diagnosis was calculated as the date of the first definitive imaging report as determined by the level of certainty conveyed by the report. For example, the following statements were considered definitive, "highly suspicious for lung cancer" or "consistent with lung cancer", accompanied by a recommendation for referral to lung

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cancer specialist. The clinical date of diagnosis may appropriately differ from the cancer registry date of diagnosis, as described above. Files were independently reviewed by two MDs (AS and VL). Disagreements regarding clinical indication, first suspicious test and degree of report confidence were settled by a third more senior MD (DM).

Descriptive statistics were presented for the cohort, as well as stratified by route to diagnosis. Survival was calculated both from the cancer registry date of diagnosis, as well as the clinical date of diagnosis, to the date of death.

Kaplan Meier survival curves are presented for both registry date of diagnosis as well as clinical date of diagnosis. Stage-specific KM curves are also presented for cancer registry date of diagnosis. Cox regression model (Hazard Rate Ratios and 95% confidence intervals) was used to compare survival as a function of route of diagnosis, and to explore differences by stage. Statistical analysis was carried out using SPSS (IBM SPSS, version 23). This project received Institutional Research Ethics Board approval from the Nova Scotia Health Authority.

Results:

A total of 972 entries were recorded in the registry in 2014 corresponding to 951 unique cases. Data was incomplete for 5 cases: 3 cases had initial testing performed out of province and therefore unavailable for review, and 2 cases had no relevant imaging indicating suspicion for lung cancer and no alternate method of diagnosis as per registry data. Analysis was therefore performed on 946 cases. Stage specific analysis excluded cases where staging was listed as not available (14 cases), occult (3) or stage 0 (9). One case each of lymphangioleiomyomatosis, myofibroblastic tumor and carcinoid tumorlet were excluded from the stage specific analysis.

Diagnostic imaging (e.g., X-RAY or Computed Tomography (CT)) was the initial positive diagnostic test in all but five patients. One case received a lung cancer diagnosis via bone marrow biopsy initiated by hematologist consultation, prior to any relevant imaging, and another case was diagnosed incidentally on a lung wedge resection performed for

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evaluation of interstitial lung disease. In addition, while there were 8 cases included in the registry as diagnosed via 'death certificate only', the hospital record review revealed that 5 of these had CT imaging the day of death or the day prior, but the imaging reports did not meet the rigour for diagnosis required by the registry.

Approximately one third of the cases (336, 35.5%) were diagnosed through the ED. Differences in demographics and stage at presentation between the ED and non-ED route to diagnosis are summarized in Table 1. While there were no differences in terms of age by route to diagnosis, males were slightly more likely to be diagnosed through the ED (37% of all lung cancer diagnosed in males) than females (33%). In both the ED and non-ED route, the majority (overall 80%) of cancers were initially detected through investigation of signs or symptoms that may be caused by lung cancer. A small proportion (104, 11%) were identified through CT surveillance programs for small non-specific nodules. The lack of a primary care provider was documented for only 24 (7.1%) of individuals who were diagnosed through the ED.

Cancer detected through the ED was more likely to be of advanced stage and cases presenting through the ED had a shorter survival time than those diagnosed outside the ED (Figure 1a-b) with associated hazard rates of 1.98 (1.67,2.35) based on registry date of diagnosis and 2.27 (1.9,2.35) based on clinical date of diagnosis. The clinical date of diagnosis for the non-ED group was a mean of 88.5 days earlier than the registry date of diagnosis with a range of 0 to 1947 days. This discrepancy was less marked for the patients diagnosed through the ED route (mean 37.3 days). One-year survival from registry date of diagnosis was 28.4% in the ED route to diagnosis and 49.5% in the non-ED group. The difference in survival by route of diagnosis was evident for each stage of disease and more pronounced with advanced stages (Figure 2a-d).

Interpretation:

Over one-third of lung cancer diagnoses in Nova Scotia in 2014 were initiated through an Emergency Department visit. There were substantial differences in stage at diagnosis, with

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a disproportionate representation of advanced cancers in the ED group, and a resulting shorter survival in this group.

Although there is a lack of published comparative Canadian data, our results are similar to those of a study conducted in the United Kingdom demonstrating 39% of lung cancer diagnoses were settled following an emergency consultation (15). A 2009 New Zealand study found that 36% of lung cancer patients presented initially through the ED (2). This consistency suggests our findings are likely transferable to other jurisdictions with similar health care settings and access. Lower numbers (13% and 19%) have been found in other studies conducted in Japan (16) and the United Kingdom (17) respectively but these studies more narrowly defined ED presentation by only including patients admitted to hospital from the ED. Research from the UK has also found lower survival for patients presenting through the ED (18,19).

It has been suggested that barriers in access to primary care (i.e. orphaned patients; those without a family doctor) may drive a higher proportion of non-emergent cases to the ED (2). Our provincial data does not support this explanation, as orphaned patients accounted for only 7.1% of total ED-based diagnoses. More in-depth research from the United Kingdom has shown that patients initially presenting to the ED and later diagnosed with lung cancer are often self-referred with socioeconomic deprivation and potential financial, geographic, cultural or information barriers postulated as the attributable cause (2, 17). The nonspecific nature of lung cancer symptoms, as well as psychosocial factors such as patient guilt associated with smoking (2-6) have also been suggested as reasons for delays in seeking care. A large UK study showed that current smoking status independently reduces the likelihood of help-seeking for symptoms of lung cancer (20). In turn, these non-specific respiratory (e.g. cough, dyspnea, chest pain) and systemic symptoms (e.g. malaise, fatigue, weight loss) may be less likely to prompt expedient assessment and referral by family physicians. In our study, only 38 patients (4.0% of total) presented with hemoptysis, an alarming sign that usually generates urgent medical workup.

The late presentation of disease to the ED may present a greater drain on already stretched ED resources and by extension on diagnostic and consulting resources with many patients

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presenting after 7 pm (21). European literature emphasizes the rapidly evolving and complex nature of thoracic oncology as the reason a multidisciplinary subspecialist approach is required for optimal patient treatment (22,23). Already extremely limited in Canada outside urban centres, access to experts (including subspecialty thoracic radiology, thoracic oncology and thoracic surgery) is further restricted when required "after hours" in an emergency setting.

The primary strength of this study is the fact that there was complete capture of all lung cancer cases in the province by way of the provincial cancer registry. In addition, there was complete ascertainment of all relevant imaging given the existence of one provincial imaging archive system. Although precipitous ED presentation may reflect diagnostic delays (i.e., delayed wait times for CT and specialist appointment) there is currently no wait time for general x-ray in the province. Provided workup was initiated with x-ray, concerning imaging reports would have been accurately identified and linked to the appropriate route of entry in our study. Cases diagnosed through the ED were therefore unlikely to be awaiting imaging workup or specialist referral via their family doctor. However, there may have been incomplete capture of patients awaiting specialist referral after a normal x-ray but before CT. Unfortunately, primary care consultation records were not accessible to determine if opportunities for earlier diagnoses would have been possible. In addition, although our results indicate that more than 80% of lung cancer presents symptomatically this is likely an overestimate. The ability to distinguish symptomatic lung cancer diagnosis from incidental diagnosis was limited due to the non-specific nature of the symptoms associated with lung cancer. Many instances were noted where lung cancer was unlikely to have been the cause of the respiratory symptoms being investigated (for example lung cancer detected on chest radiograph in a patient presenting with dyspnea and admitted for heart failure). There was no objective way to ensure that lung cancer was not responsible for at least a component of the symptoms even in a patient with a competing diagnosis.

Strategies to promote early recognition, to improve resources for patient navigation after the ED visit, and to prevent unnecessary delays along the diagnostic pathway may all be

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important for improving survival of lung cancer patients. Despite current efforts to target family doctors and lung specialists, the consistent presentation of lung cancer in our acute care facilities reinforces the need for consensus guidelines, resources and training tailored specifically for the Emergency Department.

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Figure 1.
Title: Survival of Nova Scotia Lung Cancer Cases by Route to Diagnosis, 2014.

Caption: Comparison of survival for patients diagnosed with lung cancer by an emergency department (ED) route versus those diagnosed by a route that did not involve the emergency department (non-ED) as calculated from (a) registry date of diagnosis and (b) clinical date of diagnosis.

Figure 2:
Title: Comparison of Survival of Lung Cancer Cases Parsed by Stage at Diagnosis.
Caption: Patients diagnosed by either the emergency department (ED) referral route or the non-emergency (non-ED) referral route were compared by cancer stage at time of diagnosis. Stage 0 patients were not included in this analysis.

Table 1:
Title: Characteristics of the patient populations for both ED and non-ED route to diagnosis.

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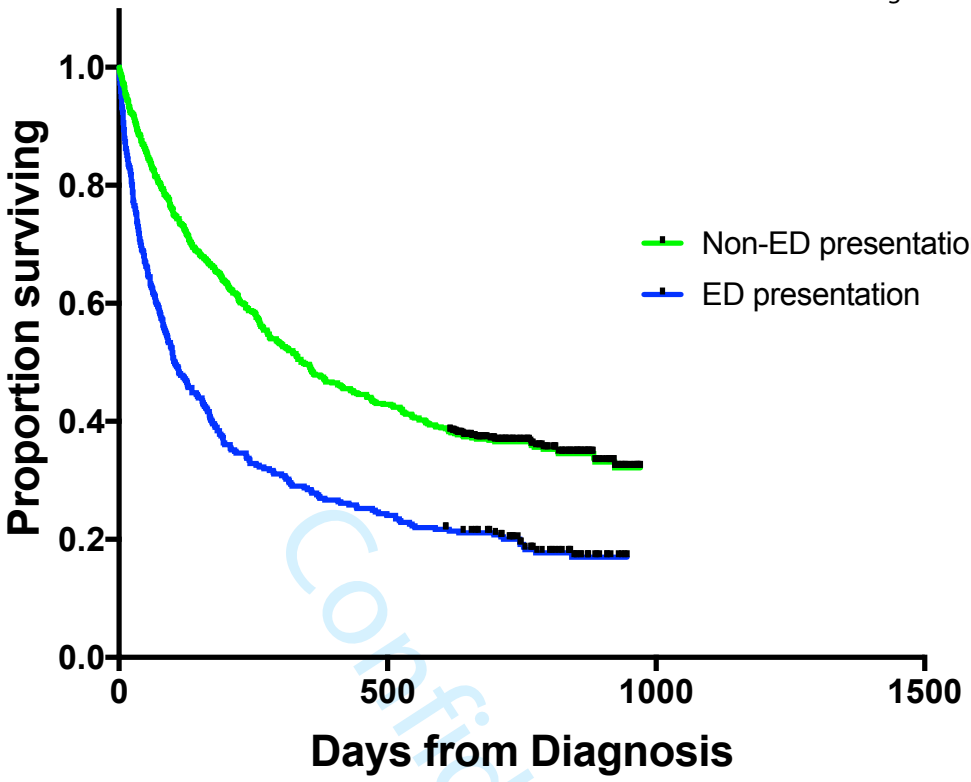
A



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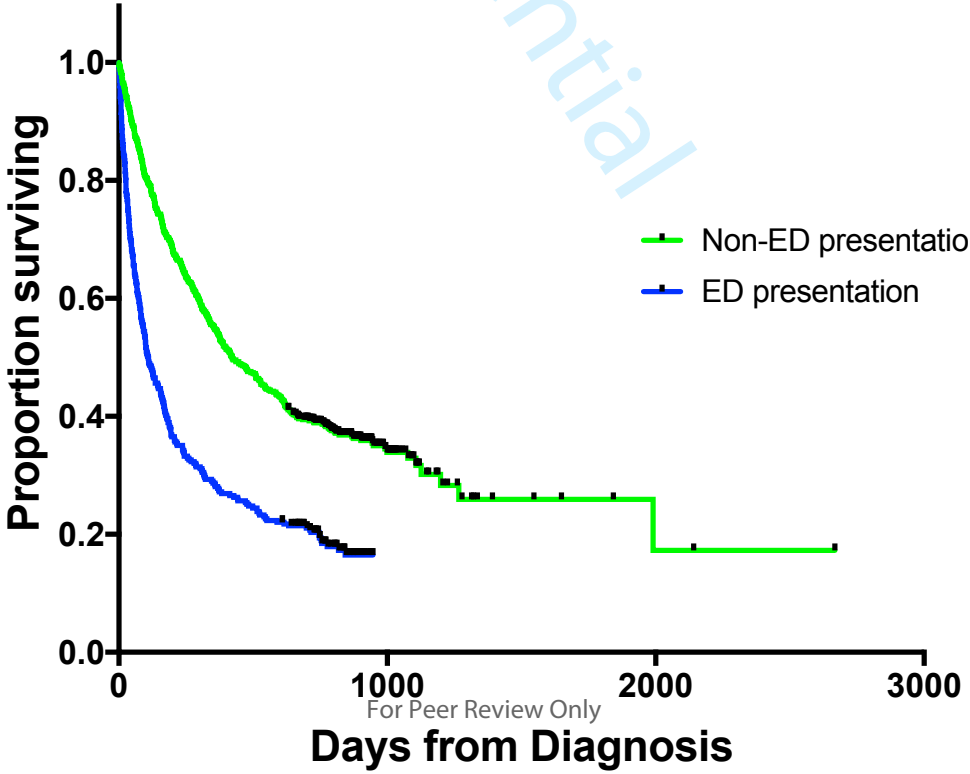

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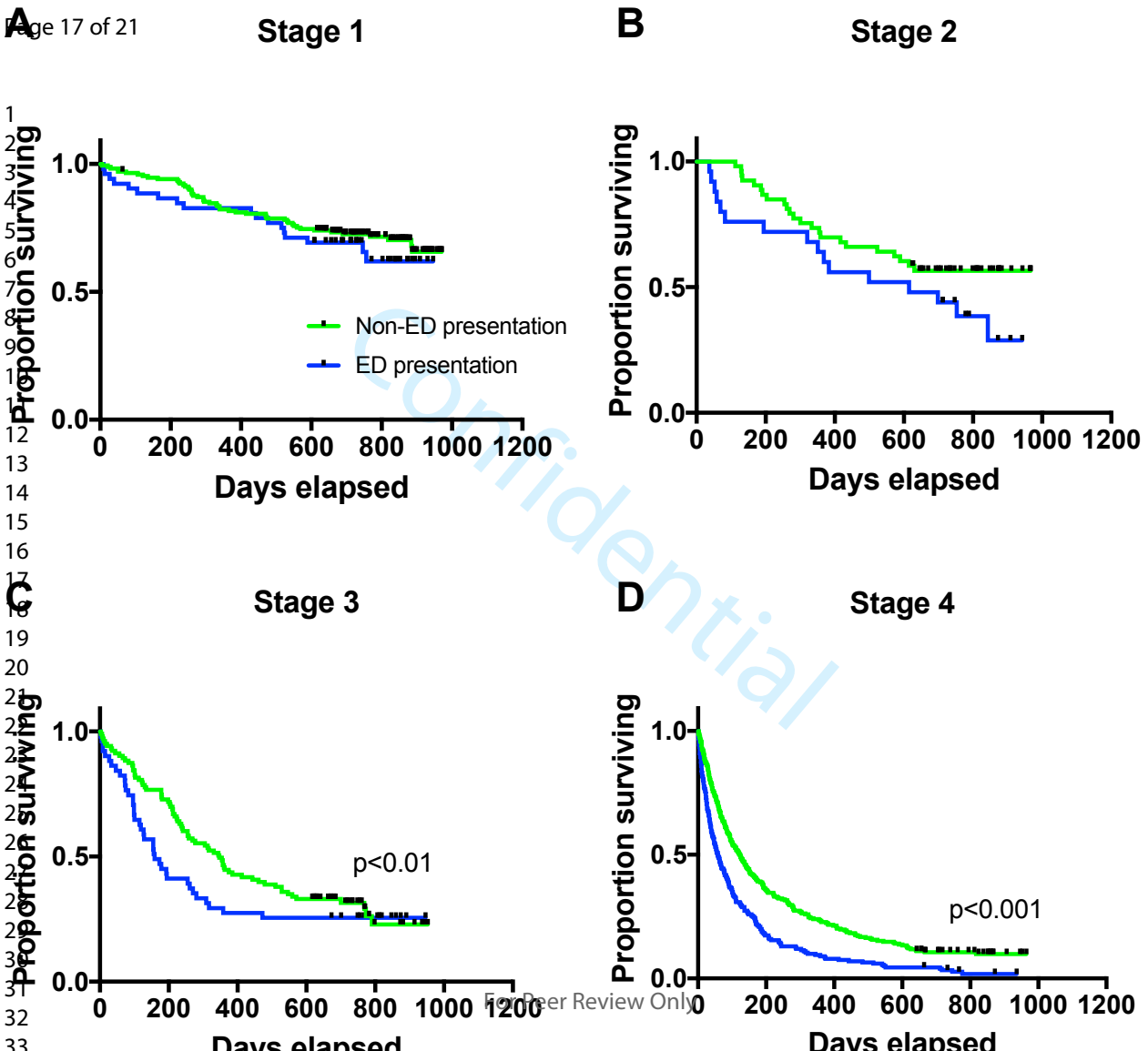

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Table 1: Characteristics of the patient populations for both ED and non-ED route to diagnosis

Characteristics	Frequency (%)		
	Total (N=946)	ED (N= 336)	Non-ED (N= 610)
Sex			
Male	491 (51.9)	182 (54.2)	309 (50.7)
Female	455 (48.1)	154 (45.8)	301 (49.3)
Mean Age, years +/- SD	70.3 +/- 11 years	71.2 +/-11 years	69.7 +/-10 years
Age Range, years	18-98	33-98	18-97
Age group (years)			
≤60	163 (17.2)	56 (16.7)	107 (17.5)
60-69	265 (28.0)	84 (25.0)	181 (29.7)
70-79	348 (36.8)	129 (38.4)	219 (35.9)
≥80	170 (18.0)	67 (19.9)	103 (16.9)
Indication for testing			
Symptomatic	751 (79.4)	314 (93.5)	437 (71.6)
Incidental	78 (8.2)	12 (3.6)	66 (10.8)
Surveillance	104 (11.0)	10 (3.0)	94 (15.4)
Screening	13 (1.4)	0 (0.0)	13 (2.1)
Stage at diagnosis			
Unknown	14 (1.5)	4 (1.2)	10 (1.6)
Occult	3 (0.3)	3 (0.9)	0 (0.0)
0	9 (1.0)	1 (0.3)	8 (1.3)
I	218 (23.0)	49 (14.6)	169 (27.7)
II	82 (8.7)	28 (8.3)	54 (8.9)
III	155 (16.4)	51 (15.2)	104 (17.0)
IV	465 (49.2)	200 (59.5)	265 (43.4)
Deaths	592 (62.5)	247 (73.1)	345 (56.7)

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Appendix A. Signs and Symptoms of Lung Cancer Requiring Investigation (Nova Scotia Health Authority's Cancer Care Program (previously Cancer Care Nova Scotia))

Signs and symptoms of lung cancer that require immediate referral to emergency department:

Acute significant hemoptysis (e.g. 2 tbsp. in one episode, 1 cup in 24 hours).
Suspected superior vena cava obstruction.
Stridor/symptomatic central airway obstruction.
New neurological signs suggestive of brain metastasis or cord compression.
Symptoms suggestive of paraneoplastic syndrome with severe metabolic disturbance (e.g. hyponatremia hypercalcemia).

Signs and symptoms of lung cancer that require work up:

Hemoptysis.
Features suggestive of paraneoplastic syndromes.
Supraclavicular lymphadenopathy.
Unexplained/uninvestigated increase in dyspnea.
Features of metastatic lung cancer.
Unexplained cough persisting for more than 3 weeks.
Unexplained hoarseness persisting for more than 3 weeks.
Unexplained weight loss/loss of appetite persisting for more than 3 weeks.
Unexplained chest and/or shoulder pain persisting for more than 3 weeks.
Uninvestigated/unexplained abnormal chest signs persisting for more than 3 weeks.
Unexplained changes in existing symptoms in patients with underlying chronic respiratory problems persisting for more than 3 weeks.

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