Survival rates are much higher when lung cancer is diagnosed and treated at an early stage—before the disease spreads. With the advent of low-dose CT and increasing appreciation of the importance of early identification and treatment of lung cancer, lung nodule management is becoming a greater part of the practices of pulmonologists, primary care physicians, and early detection lung cancer programs. As more incidental pulmonary nodules (IPNs) are found, a regimented and strict follow-up is needed to ensure high-risk patients are captured and treated earlier rather than later.
INTRODUCTION

Lung cancer has significant mortality that is notably higher than other cancers, which has led to an increase in research that focuses on improving outcomes. Of these, early identification of suspected malignancy and improvements in therapeutics has led to gradual improvement of outcomes in recent years. This is evidenced by the overall reduction in late-stage cancer with an associated increase in early-stage cancer. Later-stage cancers have significantly worse prognosis and increased morbidity and mortality. Earlier identification of cancer leads to improved outcomes and survival. The National Lung Screening Trial (NLST), a research study sponsored by the National Cancer Institute, showed reduced lung cancer mortality by using low-dose helical CT scans, and the ability to diagnose lung cancer earlier in certain high-risk populations. An increasing use of CT scans in recent years has provided a new population of IPNs that may potentially change the way the lung cancer paradigm is viewed. The challenge becomes how best to manage and follow IPNs.
Low-risk IPNs are defined as having a less than 5% risk of malignancy, and high-risk IPNs are defined as having a greater than 60% risk of malignancy. Intermediate-risk IPNs fall in between with a 5-60% risk of malignancy, and they typically have a diameter of 7-20 mm. The nodule size plays a large part in the risk, and the greater the size, the higher the likelihood of developing malignancy. There are other variables that also increase the likelihood of malignancy, such as radiographic appearance, calcification, single vs multiple nodules, and, of course, patient history. This requires a complete and thorough approach with evidence-based risk assessment and follow-up. Combining the efficacy of CT with risk calculators based on historical cohorts can lead to optimal risk stratification for lung cancer. As prediction models improve, there is the expectation of more IPNs falling into low or high-risk categories with fewer intermediate-risk IPNs. As these models evolve, the key will undoubtedly be to shift as many individuals from intermediate risk to high risk or to low risk and thus from late-stage to early-stage lung cancer. However, IPNs will still require close monitoring and follow-up.

### PATHOLOGIC STAGE & 5-YEAR SURVIVAL RATES

<table>
<thead>
<tr>
<th>TNM Pathologic Stage</th>
<th>5-Year Survival (IASLC, 8th Edition N0, M0, R0)</th>
<th>5-Year Survival (SEER, 2020)</th>
<th>Case Distribution (SEER, 2020)</th>
</tr>
</thead>
<tbody>
<tr>
<td>T1 a,b,c (local)</td>
<td>81-92%</td>
<td>57.4%</td>
<td>16%</td>
</tr>
<tr>
<td>T2 a,b (regional)</td>
<td>65-74%</td>
<td>30.8%</td>
<td>22%</td>
</tr>
<tr>
<td>T3 (advanced)</td>
<td>57%</td>
<td>5.2%</td>
<td>57%</td>
</tr>
<tr>
<td>T4 (advanced)</td>
<td>47%</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Table:** The International Association for the Study of Lung Cancer (IASLC) 8th Edition of tumor, node, metastasis (TNM) staging expected 5-year survival rates and SEER April 2020 5-year survival by local, regional, and advance classification, and patient distribution for all pulmonary and bronchus cancers.
IMPORTANCE OF EARLY DETECTION

The wide-ranges of overall 5-year survival within the same stage are due to subgroups within each stage with differing mortality rates. The defining principle is simply that the earlier the stage when lung cancer is diagnosed, the higher the overall survival rate. Given these facts, shifting as many cancer diagnoses to earlier stages will undoubtedly decrease the rates of late-stage disease diagnosed and improve overall mortality with the same number of individuals ultimately diagnosed with lung cancer. Evidence to support this has been identified across multiple studies with increasing proportions of early-stage lung cancer noted as robust nodule management programs develop. Additionally, there are studies that have demonstrated higher stages of cancer due to delays (e.g., follow-up, diagnosis, and treatment).

Increasingly, IPNs are found incidentally on CT scans of the chest performed for other indications. In one cohort, this was ~30% of all CT scans of the chest. When you consider there are over 75 million CT scans performed in the United States every year, the occurrence of IPNs is likely even higher when factoring in nodules noted on neck, spine, and abdominal CT scans with an overlap of the lungs. Although many of these IPNs may be benign or resolve, as is also the case in lung cancer screening patients, some benign nodules may become malignant. Identification and follow-up of these IPNs have the potential to have a significant impact on outcomes. Multiple studies have demonstrated the promise of this path, but a large study such as the NLST for IPNs has yet to be performed. Data does not suggest a linear increase in lung cancer diagnoses with increasing identification of IPNs; however, given the low rates of malignancy in the NLST cohort and the limited follow-up IPNs have had historically, this may not be surprising.

The Fleischner Society guidelines, along with risk calculators (such as the Brock and Mayo calculators), offer one way to have a regimented follow-up plan for incidental pulmonary nodules.
Eon has engineered the most powerful patient management platform on the market to identify IPNs and longitudinally track patients to ensure exams and procedures are scheduled and followed according to guidelines. Using best-in-class Computational Linguistics data science models, Eon’s Essential Patient Management (EPM) solution captures patients at risk for catastrophic disease early—when it matters most—and ensures adherence so no patient falls through the cracks. EPM arms providers with predictive guideline-based intelligence that delivers an overall accuracy of 98.95% and captures nodules with 98.99% precision. And with EPM’s advanced care logic, complicated triggers for next steps are made easy—eliminating errors and opportunity for miscommunication. The Eon approach saves FTE time by cutting out the noise, allowing them to focus on patients who might actually have lung cancer. This is Eon’s mission—identify nodules, ensure follow-up, and improve outcomes.
CONCLUSION

There are multiple studies that describe worsening outcomes and increased likelihood of upstaging when there is a delay between lung cancer diagnosis and treatment. There are subtleties in terms of which stages of lung cancer are most influenced by delays, but the interpretation can become convoluted. Suffice to say that earlier identification, diagnosis, and treatment of IPNs can lead to overall improved lung cancer outcomes. This can represent improved progression-free survival, morbidity/mortality, and overall treatment outcomes. Some studies demonstrated worsening outcomes by delays of months while others were able to identify changes in outcomes and survival by delays of weeks. Coughlin et al. found for stage II patients waiting between 2 and 3 months had significantly decreased survival (hazard ratio 3.6, p = 0.036) and increased incidence of upstaging (odds ratio 2.0, p = 0.020) than those waiting 0 to 1 month. For those waiting between 1 and 2 months, there was no significant difference in survival or upstaging. This is especially important for IPNs when so many are not adequately followed.

There are many aspects of IPN management that still need to be studied, but the one consensus that can be reached in the current literature is that early identification and early treatment of the high-risk cohort of patients will lead to improved outcomes in a disease that already has unacceptably high rates of mortality.
REFERENCES

- https://www.medpagetoday.com/hematologyoncology/lungcancer/87444
Eon is a Denver-based healthtech company dedicated to revolutionizing the way healthcare data is gathered, curated, and shared among industry professionals. We are on a mission to ensure the right data reaches the right people at the right time to identify disease early and stop it in its tracks.

Together we can defy disease.