Allina Health

Thoracic Oncology- a primer

Dimensions in Oncology
Allina Health

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Allina Lung Cancer Screening Physician Lead

November 9, 2021

Objectives

- Understand causes of and prevention of lung cancer
- Understand State of Lung Cancer
- Understand Models of Care
- Understand above in context of care delivered at Allina

Causes of lung cancer

- Over 80% of lung cancer is related to smoking cigarette
  - Entirely preventable
- Others- radon, asbestos, air pollution, occupational exposure to chemicals, family history of lung cancer

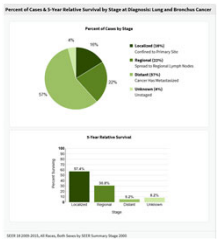
History…

- In 1900 there were less than 80 cases of primary lung cancer recorded in the medical literature.
- In 1912 Adler wrote monograph on lung cancer and apologized for writing a book on such a rare disease

Lung Cancer at a glance

National Cancer Institute

Stages and Survival



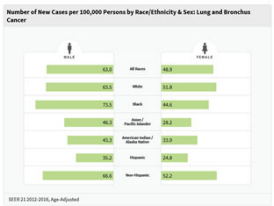
How common?

	Common Types of Cancer	Estimated New Cases 2019	Estimated Deaths 2019
1.	Breast Cancer (Female)	268,600	41,760
2.	Lung and Bronchus Cancer	228,150	142,670
3.	Prostate Cancer	174,650	31,620
4.	Colorectal Cancer	145,600	51,020
5.	Melanoma of the Skin	96,480	7,230
6.	Bladder Cancer	80,470	17,670
7.	Non-Hodgkin Lymphoma	74,200	19,970
8.	Kidney and Renal Pelvis Cancer	73,820	14,770
9.	Uterine Cancer	61,880	12,160
10.	Leukemia	61,780	22,840

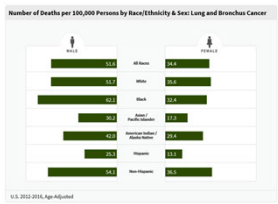
Lung Cancer at a glance

National Cancer Institute

In incidence

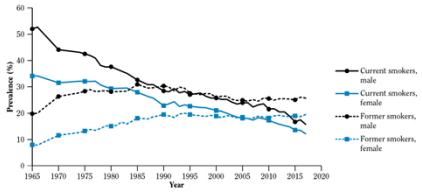


In deaths



2020 Report

Figure ES.1 Trends in prevalence (%) of current and former cigarette smoking among adults 18 years of age and older, by sex; National Health Interview Survey (NHIS) 1965–2017; United States



Source: NHIS, National Center for Health Statistics, public use data, 1965–2017.
Note: From 1965 to 2017, data were reported for the following years: 1965, 1966, 1970, 1974, 1976–1980, 1983, 1985, 1987, 1988, 1990–1995, and 1997–2017.

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Lung Cancer at a glance
National Cancer Institute

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The Effect of Advances in Lung-Cancer Treatment on Population Mortality.
Howlander et al. NEJM 2020;383:640-9

- Describe trends in mortality amongst patients with different subtypes of lung cancer in the context of changing incidence and survival patterns in the US general population
  - NSCLC-
    - Mortality decreased faster than incidence
    - Decrease associated with improvement in survival over time that corresponded to the timing of approval of targeted therapy
    - Noted both amongst men and women, across all races and ethnic groups
  - SCLC-
    - Mortality decrease related almost entirely to declining incidence with no improvement in survival
    - Correlates with limited advances in the time frame examined

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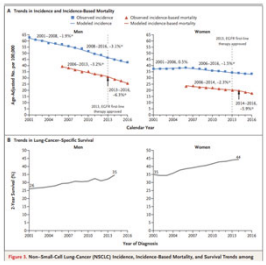
NSCLC-
Trends in Incidence and Incidence-Based Mortality



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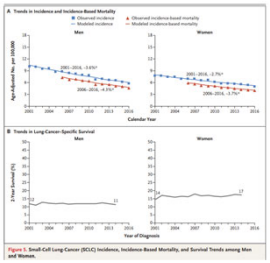
SCLC-
Trends in Incidence and Incidence-Based Mortality



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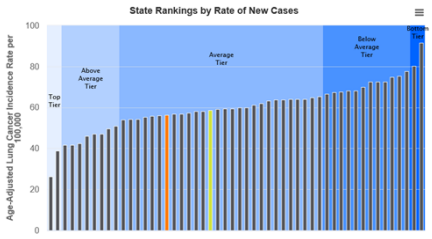
State of Lung Cancer Report: 2020
-Explores how lung cancer varies by state



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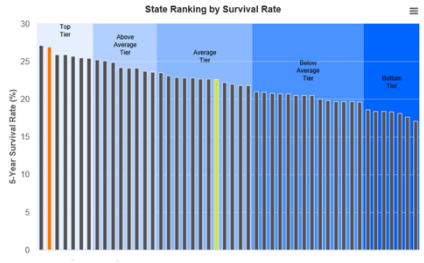

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Thoracic Oncology Program Committee 2020

- COVID 19 pandemic and patient care
- Creation of Allina Health Cancer Institute
- Communication
- In house NGS with ongoing iterations (TAT, panel size, ADAURA)
- Guidelines for Mediastinal Staging
- Management of pulmonary nodules- risk stratification and Nodify XL (ongoing)
- Lung Cancer Screening (ongoing)
- STS Harvest summary
- Curt Anderson published in Lancet- "Patient perspectives- Reducing stigma around smoking would encourage more early lung cancer screening"
- Guidelines for CNS Imaging Guidelines updated
- Guidelines re Adequacy of Specimen reviewed and update deferred
- Discussion of Research Trials
- Discussion re surgical approaches
- Discussion re role of liquid biopsy
- Review of quality data Stage 3/N2 disease
- Care coordinators transitioned to Nurse navigators
- Administrative- Sharepoint, Microsoft Teams

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Lung Cancer Screening

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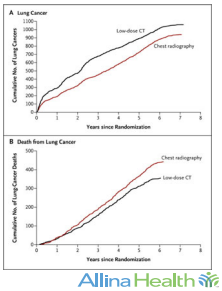
Reduced Lung-Cancer Mortality with Low-Dose Computed Tomographic Screening (NLST)
Aberle et al. NEJM 2011;365:395-409

- Prospective randomized trial
- 53,454 individuals at high risk
- 1:1 randomization LDCT and CXR – detection of pulmonary nodules
- 3 annual screens
- Criteria-
  - 55-74 yo,
  - >=30 pack year history of smoking
  - active smokers or quit within 15 years
- Screening adherence 90%
- Primary endpoint- lung cancer mortality
  - Relative reduction in mortality from lung cancer with LDCT 20%
  - Rate of death from any cause was reduced by 6.7%
- NNS 1:320



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IASLC 19th World Conference on Lung Cancer
September 23–26, 2018 Toronto, Canada
WCLC2018.IASLC.ORG #WCLC2018

NELSON - trial ISRCTN 63545820

- **Randomized Controlled Trial**
- **Recruitment through population-based registries**
- **CT screening vs. no screening**
- **Different screening intervals**
- **Volume & Volume Doubling Time of nodules**
- **Central reading of CT images**
- **Expert causes of death committee &**
- **Follow up through national registries**

Trial, initially powered (80%) for high risk **males**, to detect a lung cancer mortality reduction of ≥ 25% at 10 years after randomization (individual FU)

And includes a small subgroup of women (16%)

Harry J. de Koning, Erasmus MC, Public Health Rotterdam

IASLC 19th World Conference on Lung Cancer
September 23–26, 2018 Toronto, Canada
WCLC2018.IASLC.ORG #WCLC2018

NLST & NELSON: Lung cancer CT screening Mortality data

Male v Female ratio	
NLST+	41/59
NELSON	16/84

Percent LC Mortality Decrease			
Trial	Men	Women	50:50 M/F
NLST*	8%	27%	**18%**
NELSON**	26%	39-61%	**33 – 44%**

Pinsky et al. The National Lung Screening Trial: *Cancer* 2013; **119**(22): 3976-83. *Aberle, et al. The National Lung Screening Trial: overview and study design. *Radiology* 2011; **258**(1): 243
**Effects of Volume CT Lung Cancer Screening: Mortality Results of the NELSON Randomised-Controlled Population Based Trial De Koning et al 2018

UNIVERSITY OF LIVERPOOL

USPSTF Recommendation Statement

JAMA. 2021;325(10):962-970. doi:10.1001/jama.2021.1117

- Age 50-80 years and
- 20 pack year history of smoking and
- Currently smoke or have quit within the past 15 years
- To be discontinued if once a person has not smoked for 15 years or develops a health problem that substantially limits life expectancy or the ability or willingness to have curative lung surgery

- It is a Grade B recommendation- moderate certainty of moderate benefit in high risk patients
  - High quality screen

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Important considerations

- Concept of efficacy and effectiveness of clinical trials
- Goal to screen maximum number of people
- LCS likely to evolve over time with incorporation of volumetrics, gender based screening, risk stratification models, proteomics, genomics
- Shared Decision Making Visit
  - False positives
  - False negatives
  - Detection of indolent cancers
  - False reassurance, real anxiety
  - Incidental findings
  - Tobacco cessation efforts
- Retention rate
- Nodule management protocols

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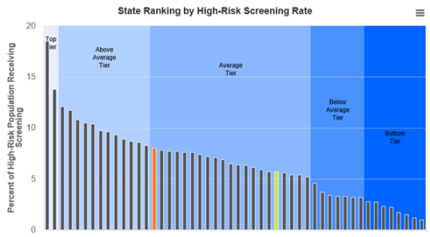

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At Allina

Schedule Status: Green

Milestone	Completion Date	Revised Date	Actual Finish Date	Milestone Status
Initiation	5/31/15		5/31/15	Complete
Planning	8/31/15		8/31/15	Complete
Phase I Metro Hospital Go Live	10/31/15		12/31/15	Complete
Epic Lung Module ANW	6/19/17		6/19/17	Complete
Epic Lung Module New Ulm	7/18/17	8/10/17	9/6/17	Complete
SI Interface Mercy Hospital	12/11/17		12/11/17	Complete
SPR Interface United Hospital	11/5/18		11/5/18	Complete
Epic Lung Module Cambridge	1/8/19		1/8/19	Complete
Epic Lung Module Faribault/DOH	TBD			
Epic Lung Module Buffalo	8/12/19		8/12/19	Complete
Epic Lung Module River Falls	8/12/19		8/12/19	Complete
Affiliates	TBD			

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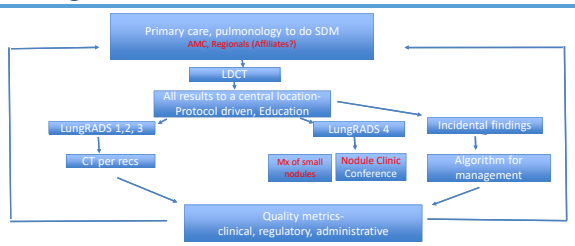
Future state...single hybrid integrated Allina Program



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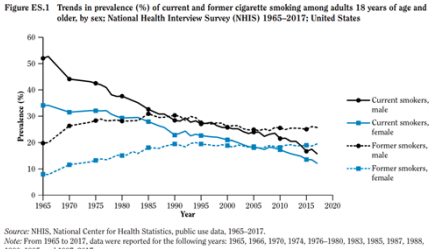
2020 Report



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Smoking Cessation

- Potential Impact of Cessation Interventions at the Point of Lung Cancer Screening on Lung Cancer and Overall Mortality in the United States. Cao et al. JTO 2020;15(7):1160-69
  - 50% who are current smokers should be offered cessation interventions
  - Impact of adding smoking cessation is unclear
  - Lung cancer simulation model- hypothetical one time cessation intervention vs none, screen eligible born between 1950-60, multiple model inputs
  - Smoking cessation reduces lung cancer mortality and delays overall deaths vs screening alone across all assumptions
- Smoking Cessation After a Cancer Diagnosis Is Associated With Improved Survival. JTO 2020;15(5):705-708
  - All patients with cancer should have access to evidence based smoking cessation support as a standard part of cancer care
  - Smoking cessation should be viewed as an effect modifier for improving cancer treatment outcomes
  - Smoking assessment and support should be incorporated into clinical trial designs
  - Research to identify best methods to help patient quit
  - Financial resources are needed to support smoking cessation

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Smoking Cessation

- In association with LCS
- In those diagnosed and treated for lung cancer
- In those newly diagnosed with lung cancer
- Ideally- should be part of cancer care for all patients

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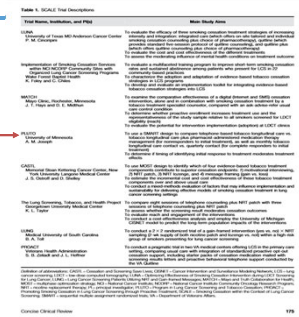
SCALE Collaboration



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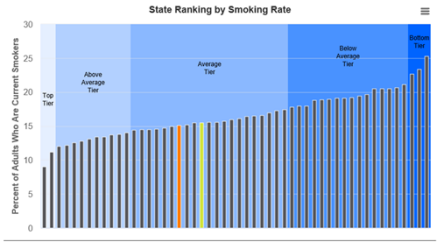

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Allina Hospitals in Minnesota and Wisconsin
(13 total; only 3 have tobacco treatment specialists (TTS) currently)

City	Hospital
Buffalo	Buffalo Hospital
Cambridge	Cambridge Medical Center
Coon Rapids	Mercy Hospital
Northfield and Faribault	District One Hospital
Fridley	Mercy Hospital - Unity Campus*
Hastings	Regina Hospital
Minneapolis	Abbott Northwestern Hospital*
New Ulm	New Ulm Medical Center
Owatonna	Owatonna Hospital
Plymouth	Abbott Northwestern - WestHealth
St. Paul (East Metro)	United Hospital
Shakopee	St. Francis Regional Medical Center
River Falls	River Falls Area Hospital in Wisconsin*

Tobacco Resources – Compared

Mayo Clinic	Fairview	Allina
TTS provider at every hospital	TTS at most hospitals	TTS at THREE locations
Outpatient counselors available at (all) clinics	TTS at most clinics	TTS at THREE clinics
Nicotine Protocols and Best Practices System Wide	YES	SOME
Eight Day Inpatient Quit Program	NO	NO
Nicotine Dependence Center	NO	NO
Support Groups	NO	NO
Quit line / Tele visits	NO	NO

Care of a lung cancer patient- fully integrated cancer care with creation of AHCI

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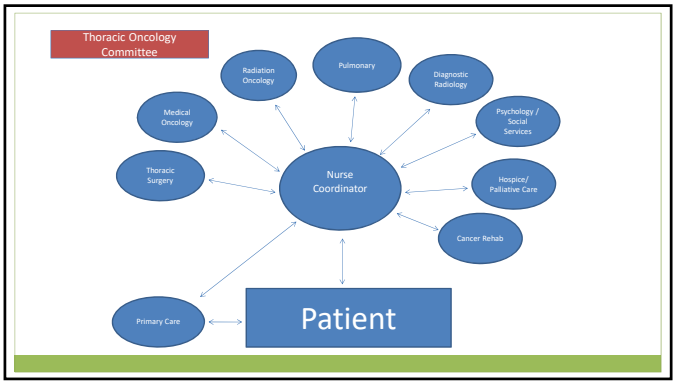

IASLC Lung Cancer Staging Project 2016

- Retrospective database of IASLC
  - 94,708 evaluable patients diagnosed with lung cancer 1990-2010
  - 77,106 included in analysis
  - 35 sources, 16 countries
  - Europe 49%, Asia 44%, North America 5%
  - 8th edition published 2016, implemented in 2018
  - Descriptors T, N, M
  - Taxonomic refinement, therapy based on clinical trials
- More stages for better prognostic stratification
- Staging modalities-
  - CT chest and FDG PET
  - Bronchoscopy with EBUS FNA of mediastinal lymph nodes
  - CT or US guided biopsy of thoracic or extra thoracic abn
  - CNS imaging (CT or MRI brain)
- Goal- diagnose, stage and obtain enough tissue for molecular markers

T/M	Label	N0	N1	N2	N3
T1	T1a	IA1	IIB	IIIA	IIIB
	T1b	IA2	IIB	IIIA	IIIB
	T1c	IA3	IIB	IIIA	IIIB
T2	T2a	IB	IIB	IIIA	IIIB
	T2a	IB	IIB	IIIA	IIIB
	T2b	IIA	IIB	IIIA	IIIB
T3	T3	IIB	IIIA	IIIB	IIIC
	T3	IIB	IIIA	IIIB	IIIC
	T3	IIB	IIIA	IIIB	IIIC
T4	T4	IIIA	IIIA	IIIB	IIIC
	T4	IIIA	IIIA	IIIB	IIIC
	T4	IIIA	IIIA	IIIB	IIIC
M1	M1a	IVA	IVA	IVA	IVA
	M1a	IVA	IVA	IVA	IVA
	M1b	IVA	IVA	IVA	IVA
	M1c	IVB	IVB	IVB	IVB

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Treatment

- NSCCA
  - Surgery, chemotherapy, radiotherapy, immunotherapy
  - In general-
    - Stage I - surgical resection with mediastinal lymph node dissection (vs local ablative therapy)
    - Stage II- surgical resection with mediastinal lymph node dissection and adjuvant chemotherapy
    - Stage III- concurrent chemo radiation therapy
      - Followed by surgical resection in selected cases only
      - Or followed by immunotherapy in unresectable disease (PACIFIC TRIAL_
    - Stage III- immunotherapy only
    - Stage IV- chemotherapy vs chemotherapy + immunotherapy vs targeted therapy
  - Era of precision medicine
  - Era of minimally invasive and lung sparing surgeries
- Small cell cancer-
  - Chemo, radiation, immunotherapy

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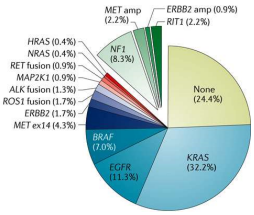
Approaching the Target… Copy That!!



Breakthrough treatments for lung cancer and melanoma have driven down cancer mortality overall from 2016 to 2017, the largest ever decline : 2.2 percent; *The New York Times*

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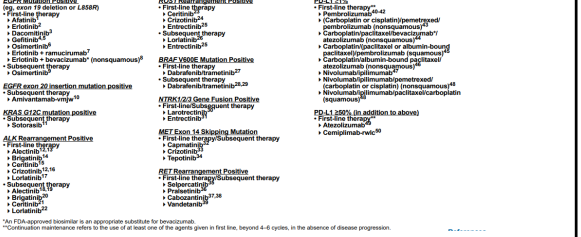

NCCN Cancer Network® **Non-Small Cell Lung Cancer**

Discussion

TARGETED THERAPY OR IMMUNOTHERAPY FOR ADVANCED OR METASTATIC DISEASE

Monitoring During Initial Therapy
- Response assessment after 2 cycles, then every 2–4 cycles with CT of known sites of disease with or without contrast or when clinically indicated.

Monitoring During Subsequent Therapy
- Response assessment with CT of known sites of disease with or without contrast every 6–12 weeks. Timing of CT scans within Guidelines parameters is a clinical decision.

***EGFR* Mutation Positive**
(eg, exon 19 deletion or *L858R*)
- First-line therapy
  - Afatinib[1]
  - Erlotinib[2]
  - Dacomitinib[3]
  - Gefitinib[4,5]
  - Osimertinib[6]
  - Erlotinib + ramucirumab[7]
  - Erlotinib + bevacizumab* (nonsquamous)[8]
- Subsequent therapy
  - Osimertinib[9]

***EGFR* exon 20 insertion mutation positive**
- Subsequent therapy
  - Amivantamab-vmjw[10]

***KRAS G12C* mutation positive**
- Subsequent therapy
  - Sotorasib[11]

***ALK* Rearrangement Positive**
- First-line therapy
  - Alectinib[12,13]
  - Brigatinib[14]
  - Ceritinib[15]
  - Crizotinib[12,16]
  - Lorlatinib[17]
- Subsequent therapy
  - Alectinib[18]
  - Brigatinib[19]
  - Ceritinib[20]
  - Lorlatinib[21]

***ROS1* Rearrangement Positive**
- First-line therapy
  - Ceritinib[24]
  - Entrectinib[25]
- Subsequent therapy
  - Lorlatinib[26]
  - Entrectinib[25]

***BRAF V600E* Mutation Positive**
- First-line therapy
  - Dabrafenib/trametinib[27]
- Subsequent therapy
  - Dabrafenib/trametinib[28,29]

***NTRK1/2/3* Gene Fusion Positive**
- First-line/Subsequent therapy
  - Larotrectinib[30]
  - Entrectinib[31]

***MET* Exon 14 Skipping Mutation**
- First-line therapy/Subsequent therapy
  - Capmatinib[32]
  - Crizotinib[33]
  - Tepotinib[34]

***RET* Rearrangement Positive**
- First-line therapy/Subsequent therapy
  - Selpercatinib[35]
  - Pralsetinib[36,37,38]
  - Cabozantinib[39]
  - Vandetanib[39]

PD-L1 ≥1%
- First-line therapy**
  - Pembrolizumab[40-42]
  - (Carboplatin or cisplatin/pemetrexed/pembrolizumab (nonsquamous)[43]
  - Carboplatin/paclitaxel/bevacizumab†/atezolizumab (nonsquamous)[44]
  - Carboplatin/(paclitaxel or albumin-bound paclitaxel)/pembrolizumab (squamous)[43]
  - Carboplatin/albumin-bound paclitaxel/atezolizumab (nonsquamous)[45]
  - Nivolumab/ipilimumab[46]
  - Nivolumab/ipilimumab/pemetrexed/(carboplatin or cisplatin) (nonsequamous)[45]
  - Nivolumab/ipilimumab/paclitaxel/carboplatin (squamous)[46]

PD-L1 ≥50% (in addition to above)
- First-line therapy**
  - Atezolizumab[45]
  - Cemiplimab-rwlc[30]

*An FDA-approved biosimilar is an appropriate substitute for bevacizumab.
**Continuation maintenance refers to the use of at least one of the agents given in first line, beyond 4–6 cycles, in the absence of disease progression.

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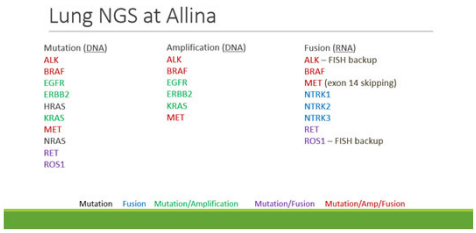
Sarah Kerr, MD



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Malignant Pleural Effusions (MPE)

- Second leading cause of exudative pleural effusions
  - lung, breast, gynecologic and lymphoma
- 125,000 hospital admission per year
- Average survival 4-7 months
- Treatment to relieve dyspnea in a minimally invasive manner, minimize number of procedures and interaction with healthcare system
- Guidelines 2000 and 2010- followed less than 50% of the time
- Most recent guidelines AJRCC 2018

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Management of Malignant Pleural Effusions

An Official ATS/STS/STR Clinical Practice Guideline
Feller-Kopman DJ et al. AJRCC 196:7:839-849

- US guidance regarding pleural interventions
- Not performing pleural interventions in asymptomatic patients
- Performing large volume thoracentesis to assess symptomatic response and lung expansion
- Interventions-
  - Role of repeat thoracentesis
  - Using either IPC or chemical pleurodesis in symptomatic patient with MPE and suspected expandable lung
  - Using IPC instead of chemical pleurodesis in patients with non expandable lung or failed pleurodesis

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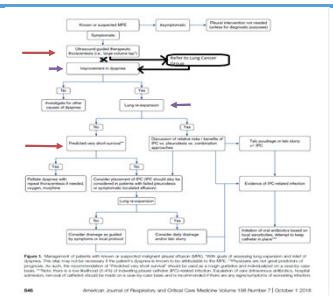
At Allina



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In summary

- The vast majority of lung cancer is caused by smoking cigarettes and is entirely preventable
- LCS using LDCT is a USPSTF 2021 Grade B recommendation and wil continue to evolve with time
- Tobacco cessation in context of LCS provides an additive benefit
- Evaluation and management of lung cancer requires a comprehensive multidisciplinary approach with attention to detail along the continuum
- The 5 year survival remains dismal at 21%

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MN has a lot of work to do

- Lung Cancer Screening
  - This will lead to increase in surgical treatments
- Tobacco control by supporting comprehensive and strong tobacco control policies-
  - Higher tobacco taxes, which both encourage people to quit and prevent children and others from starting to smoke.
  - Adequate funding of tobacco control programs, which are an important part of helping people quit and keeping potential new smokers from starting.
  - Comprehensive coverage of all FDA-approved smoking cessation medication and counseling, with no barriers to accessing them, which leads to more successful quit attempts.
- Test your house for radon and take steps to reduce your risk if levels are too high.
- Reduce your exposure to unhealthy outdoor air:
  - Stay indoors on unhealthy air days.
  - Support clean air policies, including emissions limits and no vehicle idling zones
- Minnesota falls into the above average tier for percent of patients receiving no treatment
  - Address stigma and nihilism

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References

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- The Effect of Advances in Lung-Cancer Treatment on Population Mortality. Howlander et al. NEJM 2020;383:640-9
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- Reduced Lung-Cancer Mortality with Low-Dose Computed Tomographic Screening (NLST) Aberle et al. NEJM 2011;365:395-409
- Reduced Lung-Cancer Mortality with Volume CT Screening in a Randomized Trial. Koenig et al. NEJM 2020; 382:503-513
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