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Thoracic Oncology- a primer

Dimensions in Oncology
Allina Health

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United Lung and Sleep Clinic
Co Chair Allina Thoracic Oncology Committee
Co Chair Allina Lung Cancer Screening Committee

November 8, 2022

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Objectives

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

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Causes of lung cancer

- Over 80% of lung cancer is related to smoking cigarette
  - Entirely preventable
- Others-
  - Radon
  - Asbestos
  - Air pollution
  - Occupational exposure
  - Somatic mutations
  - Family history of lung cancer

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2021 WHO Classification of Thoracic Malignant Epithelial Tumors and Precursors

2021 WHO classification of thoracic malignant epithelial tumors and precursors[1]

Precursor glandular lesions	Sarcomatoid carcinomas
▪ Atypical adenomatous hyperplasia ▪ Adenocarcinoma in situ • Adenocarcinoma in situ, non-mucinous • Adenocarcinoma in situ, mucinous	▪ Pleomorphic carcinoma • Giant cell carcinoma • Spindle cell carcinoma ▪ Pulmonary blastoma ▪ Carcinosarcoma
Adenocarcinomas	**Other epithelial tumors**
▪ Minimally invasive adenocarcinoma • Minimally invasive adenocarcinoma, non-mucinous • Minimally invasive adenocarcinoma, mucinous ▪ Invasive non-mucinous adenocarcinoma • Lepidic adenocarcinoma • Acinar adenocarcinoma • Papillary adenocarcinoma • Micropapillary adenocarcinoma • Solid adenocarcinoma ▪ Invasive mucinous adenocarcinoma • Mixed invasive mucinous and non-mucinous adenocarcinoma ▪ Colloid adenocarcinoma ▪ Fetal adenocarcinoma ▪ Adenocarcinoma, enteric-type ▪ Adenocarcinoma, NOS	▪ NUT carcinoma ▪ Thoracic SMARCA4-deficient undifferentiated tumor

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2021 WHO Classification of Thoracic Malignant Epithelial Tumors and Precursors

Squamous precursor lesions	Salivary gland-type tumors
▪ Squamous cell carcinoma in situ ▪ Mild squamous dysplasia ▪ Moderate squamous dysplasia ▪ Severe squamous dysplasia	▪ Adenoid cystic carcinoma ▪ Epithelial-myoepithelial carcinoma ▪ Mucoepidermoid carcinoma ▪ Hyalinizing clear cell carcinoma ▪ Myoepithelial carcinoma
Squamous cell carcinomas	**Lung neuroendocrine neoplasms**
▪ Squamous cell carcinoma, NOS • Squamous cell carcinoma, keratinizing • Squamous cell carcinoma, non-keratinizing • Basaloid squamous cell carcinoma ▪ Lymphoepithelial carcinoma	▪ Precursor lesion • Diffuse idiopathic neuroendocrine cell hyperplasia
Large cell carcinomas	**Neuroendocrine tumors**
▪ Large cell carcinoma	▪ Carcinoid tumor, NOS/neuroendocrine tumor, NOS • Typical carcinoid/neuroendocrine tumor, grade 1 • Atypical carcinoid/neuroendocrine tumor, grade 2
Adenosquamous carcinomas	**Neuroendocrine carcinomas**
▪ Adenosquamous carcinoma	▪ Small cell carcinoma • Combined small cell carcinoma ▪ Large cell neuroendocrine carcinoma • Combined large cell neuroendocrine carcinoma

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IASLC Lung Cancer Staging Project 2016 TNM 8th edition 2018

- 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 *≤1*	IA1	IIB	IIIA	IIIB
	T1b *>1-2*	IA2	IIB	IIIA	IIIB
	T1c *>2-3*	IA3	IIB	IIIA	IIIB
T2	T2a *Cent, Visc Pl*	IB	IIB	IIIA	IIIB
	T2a *>3-4*	IB	IIB	IIIA	IIIB
	T2b *>4-5*	IIA	IIB	IIIA	IIIB
T3	T3 *>5-7*	IIB	IIIA	IIIB	IIIC
	T3 *Inv*	IIB	IIIA	IIIB	IIIC
	T3 *Satell*	IIB	IIIA	IIIB	IIIC
T4	T4 *>7*	IIIA	IIIA	IIIB	IIIC
	T4 *Inv*	IIIA	IIIA	IIIB	IIIC
	T4 *Ipsi Nod*	IIIA	IIIA	IIIB	IIIC
M1	M1a *Contr Nod*	IVA	IVA	IVA	IVA
	M1a *Pl Dissem*	IVA	IVA	IVA	IVA
	M1b *Single*	IVA	IVA	IVA	IVA
	M1c *Multi*	IVB	IVB	IVB	IVB

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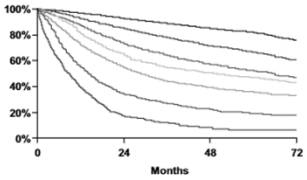
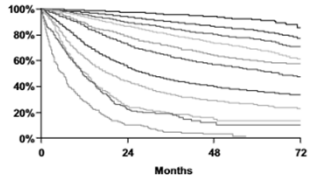
The IASLC Lung Cancer Staging Project: Proposals for Revision of the TNM Stage Groupings in the Forthcoming (Eighth) Edition of the TNM Classification for Lung Cancer

A



7th Ed.	Events / N	MST	24 Month	60 Month
IA	1119 / 6303	NR	93%	82%
IB	768 / 2492	NR	85%	66%
IIA	424 / 1008	66.0	74%	52%
IIB	382 / 824	49.0	64%	47%
IIIA	2139 / 3344	29.0	55%	36%
IIIB	2101 / 2624	14.1	34%	19%
IV	664 / 882	8.8	17%	6%

B



Proposed	Events / N	MST	24 Month	60 Month
IA1	68 / 781	NR	97%	92%
IA2	505 / 3105	NR	94%	83%
IA3	546 / 2417	NR	90%	77%
IB	560 / 1928	NR	87%	68%
IIA	215 / 585	NR	79%	60%
IIB	605 / 1453	66.0	72%	53%
IIIA	2052 / 3200	29.3	55%	36%
IIIB	1551 / 2140	19.0	44%	26%
IIIC	831 / 986	12.6	24%	13%
IVA	336 / 484	11.5	23%	10%
IVB	328 / 398	6.0	10%	0%

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Lung Cancer at a glance

National Cancer Institute

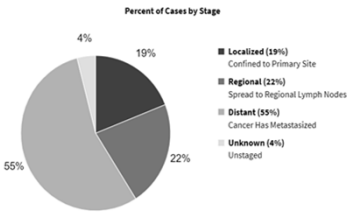
How Common Is This Cancer?

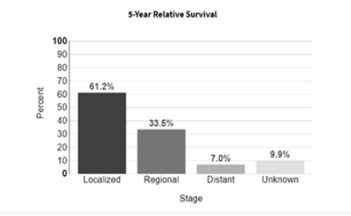
Compared to other cancers, lung and bronchus cancer is fairly common.

Common Types of Cancer	Estimated New Cases 2022	Estimated Deaths 2022
1. Breast Cancer (Female)	287,850	43,250
2. Prostate Cancer	268,490	34,500
3. Lung and Bronchus Cancer	**236,740**	**130,180**
4. Colorectal Cancer	151,030	52,580
5. Melanoma of the Skin	99,780	7,650
6. Bladder Cancer	81,180	17,100
7. Non-Hodgkin Lymphoma	80,470	20,250
8. Kidney and Renal Pelvis Cancer	79,000	13,920
9. Uterine Cancer	65,950	12,550
10. Pancreatic Cancer	62,210	49,830

Lung and bronchus cancer represents 12.3% of all new cancer cases in the U.S.

In 2022, it is estimated that there will be 236,740 new cases of lung and bronchus cancer and an estimated 130,180 people will die of this disease.





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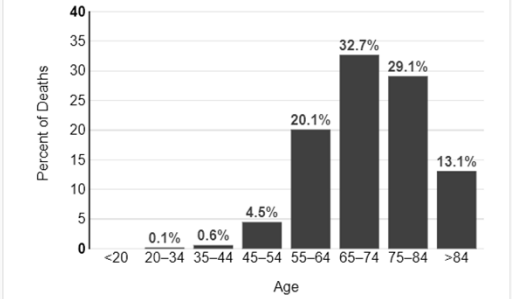
Lung Cancer at a glance

National Cancer Institute

Percent of Deaths by Age Group: Lung and Bronchus Cancer



The percent of lung and bronchus cancer deaths is highest among people aged 65–74.

Median Age At Death
72

U.S. 2016–2020, All Races, Both Sexes

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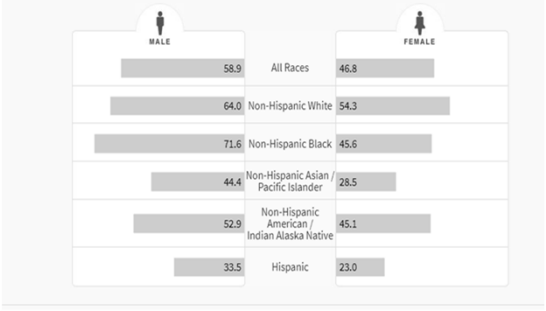
Lung Cancer at a glance

National Cancer Institute

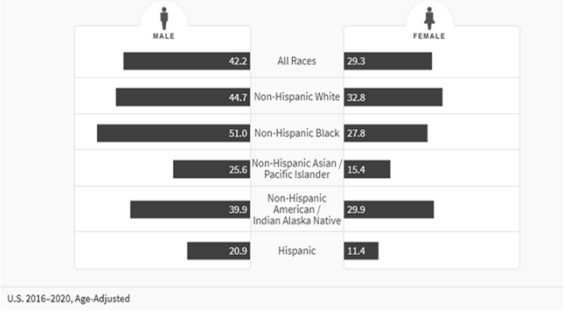
In incidence

Rate of New Cases per 100,000 Persons by Race/Ethnicity & Sex: Lung and Bronchus Cancer



In deaths

Death Rate per 100,000 Persons by Race/Ethnicity & Sex: Lung and Bronchus Cancer



U.S. 2016–2020, Age-Adjusted

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Lung Cancer at a glance

National Cancer Institute

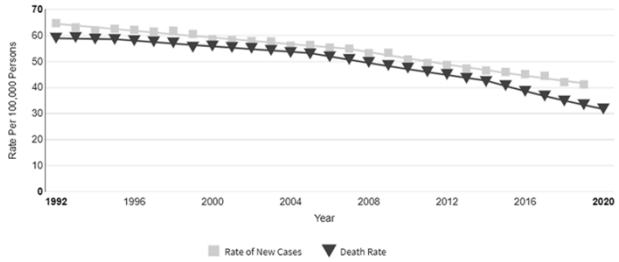
At a Glance

Estimated New Cases in 2022	236,740
% of All New Cancer Cases	12.3%
Estimated Deaths in 2022	130,180
% of All Cancer Deaths	21.4%

5-Year Relative Survival

22.9%

2012–2018



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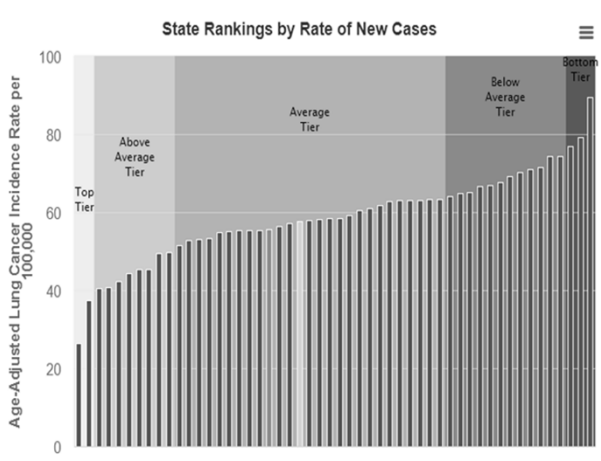
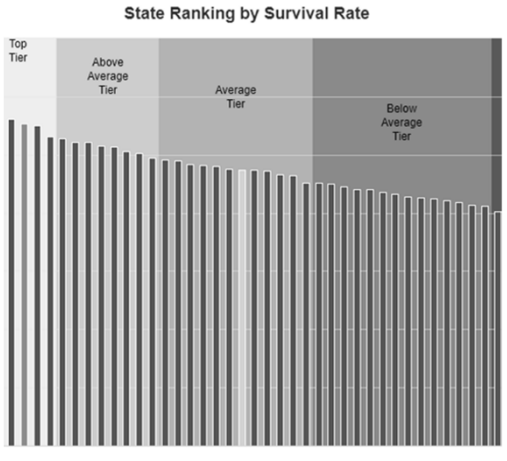
ALA State Rankings 2021

MN- red bar





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Allina Data wrt numbers

	Mercy	UTD	ANW	Total
2019	211	148	236	595
2020	163	144	214	521
2021	135	127	127	433
Total	509	419	591	

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Allina Data wrt Stage at Diagnosis

1		2019					
2		Stg 1	Stg 2	Stg 3	Stg 4	Unknown	Totals
3	Mercy	82	13	29	71	16	211
4	UTD	67	15	14	36	16	148
5	ANW	105	14	28	74	15	236
6	Totals	254	42	71	181	47	595
7							
8		2020					
9		Stg 1	Stg 2	Stg 3	Stg 4	Unknown	Totals
10	Mercy	52	15	17	64	15	163
11	UTD	57	12	18	27	30	144
12	ANW	88	9	26	71	20	214
13	Totals	197	36	61	162	65	521
14							
15		2021					
16		Stg 1	Stg 2	Stg 3	Stg 4	Unknown	Totals
17	Mercy	48	5	21	45	16	135
18	UTD	57	8	10	31	21	127
19	ANW	56	7	27	36	15	141
20	Totals	161	20	58	112	52	403

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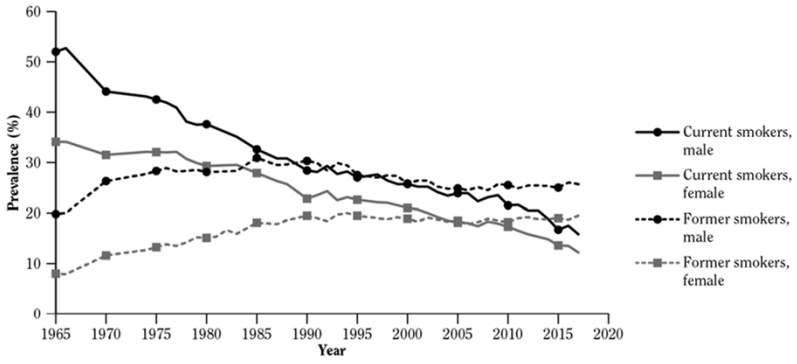
2020 Report

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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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

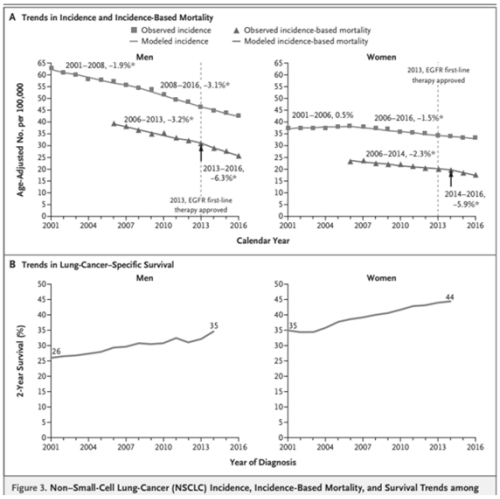

Figure 3. Non–Small-Cell Lung-Cancer (NSCLC) Incidence, Incidence-Based Mortality, and Survival Trends among

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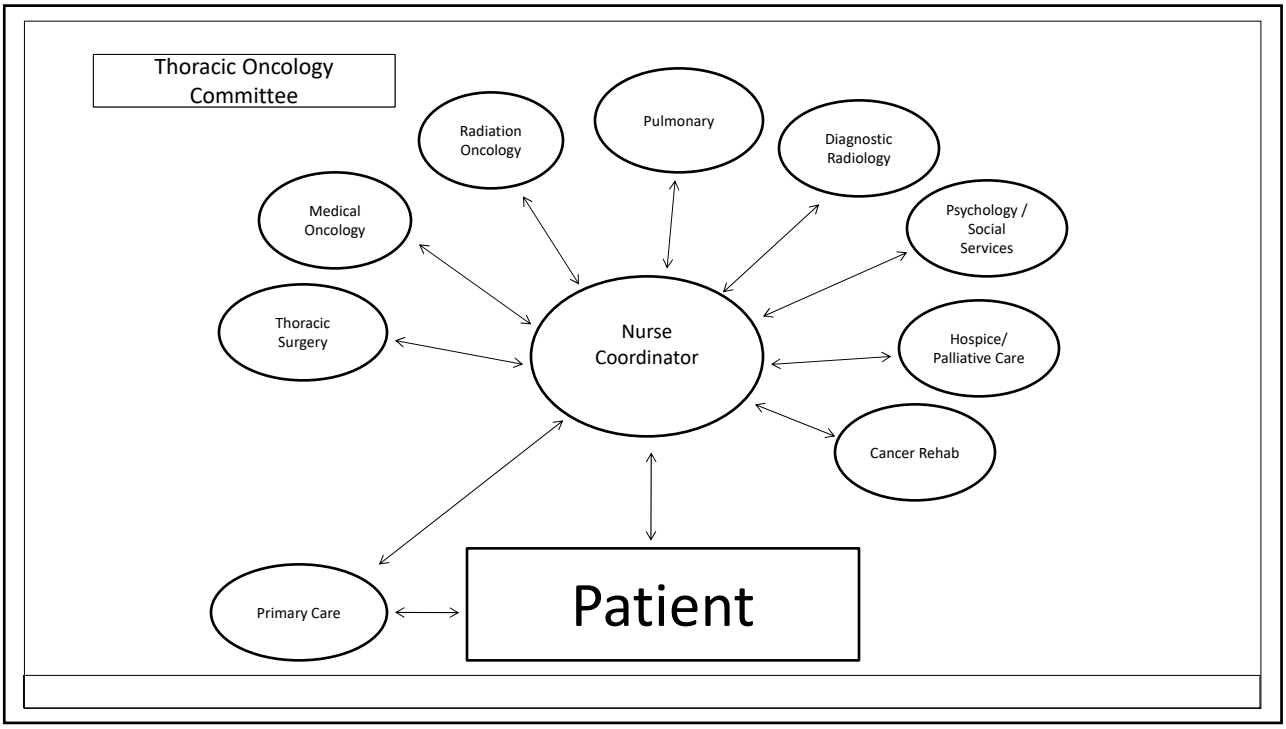

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Thoracic Oncology Program Committee 2020 -reports to Allina Safety, Quality and Accreditation Committee

- 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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Thoracic Oncology Program Committee 2020 -reports to Allina Safety, Quality and Accreditation Committee

- Incorporation of HRO training
- State of Lung Cancer Report 2020
- Lung Cancer Screening and Tobacco Cessation
- Management of pleural catheters
- Evaluation of pulm nodules- risk calculators, proteomics, robotic biopsy platforms
- Pathology- NGS update and follow of MPE volumes, in house PDL1 testing, role of Liquid biopsy, reflex testing of surgical specimens based on ADAURA and IMPOWER 010 Trials
- Lung cancer clinical trials update
- STS database
- Consensus Guideline Review – Stage 1
- PRECISION medicine
- Role of Genetics in lung cancer
- Breath of Hope

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Management

- NSCCA
  - Depends on type, stage, lung function and general health/comorbidities
  - Combination of surgery, chemotherapy, radiotherapy, immunotherapy
    - neoadjuvant and adjuvant settings
  - Era of precision medicine
  - Era of minimally invasive and lung sparing surgeries
- Small cell cancer-
  - Chemo, radiation, immunotherapy
- Management of adverse effects/complications
- Management of malignant pleural effusion

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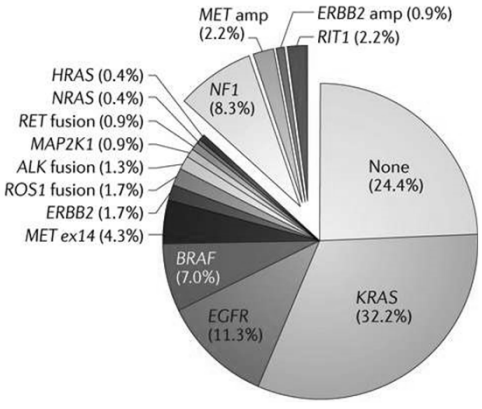
Approaching the Target… Copy That!!



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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National Comprehensive Cancer Network®

NCCN Guidelines Version 5.2022
Non-Small Cell Lung Cancer

NCCN Guidelines Index
Table of Contents
Discussion

TARGETED THERAPY OR IMMUNOTHERAPY FOR ADVANCED OR METASTATIC DISEASE[a,b]

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

EGFR S768I, L861Q,* and/or *G719X
- First-line therapy
  - Afatinib[1,10]
  - Erlotinib[2]
  - Dacomitinib[3]
  - Gefitinib[4,5]
  - Osimertinib[6,11]
- Subsequent therapy
  - Osimertinib[9]

***EGFR Exon 20* Insertion Mutation Positive**
- Subsequent therapy
  - Amivantamab-vmjw[12]
  - Mobocertinib[13]

***KRAS G12C* Mutation Positive**
- Subsequent therapy
  - Sotorasib[14]

***ALK* Rearrangement Positive**
- First-line therapy
  - Alectinib[15,16]
  - Brigatinib[17]
  - Ceritinib[18]
  - Crizotinib[15,19]
  - Lorlatinib[20]
- Subsequent therapy
  - Alectinib[21,22]
  - Brigatinib[23]
  - Ceritinib[24]
  - Lorlatinib[25]

***ROS1* Rearrangement Positive**
- First-line therapy
  - Ceritinib[24]
  - Crizotinib[27]
  - Entrectinib[28]
- Subsequent therapy
  - Lorlatinib[29]
  - Entrectinib[28]

***BRAF* V600E Mutation Positive**
- First-line therapy
  - Dabrafenib/trametinib[30,31]
  - Dabrafenib[30]
  - Vemurafenib
- Subsequent therapy
  - Dabrafenib/trametinib[31,32]

***NTRK1/2/3* Gene Fusion Positive**
- First-line/Subsequent therapy
  - Larotrectinib[33]
  - Entrectinib[34]

***MET* Exon 14 Skipping Mutation**
- First-line therapy/Subsequent therapy
  - Capmatinib[35]
  - Crizotinib[36]
  - Tepotinib[37]

***RET* Rearrangement Positive**
- First-line therapy/Subsequent therapy
  - Selpercatinib[38]
  - Pralsetinib[39]
  - Cabozantinib[40,41]

***ERBB2 (HER2)* Mutation Positive**
- Subsequent therapy
  - Fam-trastuzumab deruxtecan-nxki[42]
  - Ado-trastuzumab emtansine[43]

PD-L1 ≥1%
- First-line therapy[d]
  - Pembrolizumab[44-46]
  - (Carboplatin or cisplatin)/pemetrexed/pembrolizumab (nonsquamous)[47,48]
  - Carboplatin/paclitaxel/bevacizumab[c]/atezolizumab (nonsquamous)[49]
  - Carboplatin/(paclitaxel or albumin-bound paclitaxel)/pembrolizumab (squamous)[50]
  - Carboplatin/albumin-bound paclitaxel/atezolizumab (nonsquamous)[50]
  - Nivolumab/ipilimumab[51]
  - Nivolumab/ipilimumab/pemetrexed/(carboplatin or cisplatin) (nonsquamous)[52]
  - Nivolumab/ipilimumab/paclitaxel/carboplatin (squamous)[52]

PD-L1 ≥50% (in addition to above)
- First-line therapy[d]
  - Atezolizumab[53]
  - Cemiplimab-rwlc[54]

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Sarah Kerr, MD

Lung NGS at Allina

Mutation (DNA)	Amplification (DNA)	Fusion (RNA)
ALK	ALK	ALK – FISH backup
BRAF	BRAF	BRAF
EGFR	EGFR	MET (exon 14 skipping)
ERBB2	ERBB2	NTRK1
HRAS	KRAS	NTRK2
KRAS	MET	NTRK3
MET		RET
NRAS		ROS1 – FISH backup
RET		
ROS1		

Mutation Fusion Mutation/Amplification Mutation/Fusion Mutation/Amp/Fusion

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Lung Cancer Screening

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- T0, T1, T2
- Criteria-
  - 55-74 years old
  - >=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%
- Of note- no defined management algorithm
- Blacks 4.4%
- NNS 1:320

Reduced Lung-Cancer Mortality with Volume CT Screening in a Randomized Trial. NELSON TRIAL
Koning et al. DOI: 10.1056/NEJMoa1911793

- Prospective randomized trial
- 13,105 men, 2595 women at high risk
- 1:1 randomization LDCT vs no screening
- 4 screens- T0, T1, T3 and T5.5 years, follow up for 11 years
- Volume and Volume Doubling Times
- Criteria-
  - 55-74 yo
  - >10 cigs/d for 30 years, >15 cigs/d for 25 years
  - active smokers or quit within 10 years
- Screening adherence 90%
- Primary endpoint- lung cancer mortality
  - Relative reduction in mortality of 26% in men and higher yet in women
- Percentage of patients with positive tests-
  - NELSON 2.1% (PPV 43.5%)
  - NLST 24% (PPV 3.8%)
- Lower stage and mainly surgical treatment

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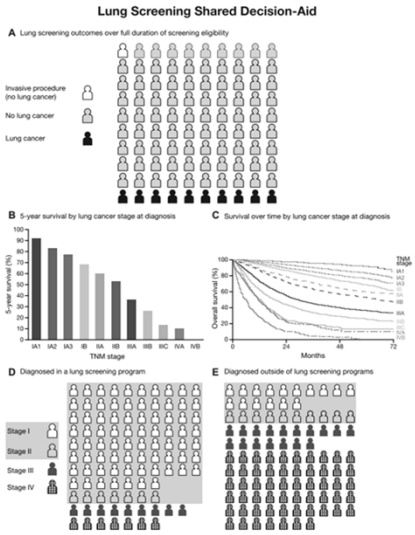
Lung Screening Benefits and Challenges: A Review of The Data and Outline for Implementation.

Sands et al. J Thorac Oncol 2021;16(1):37-53



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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
- CMS Decision Memo 2022

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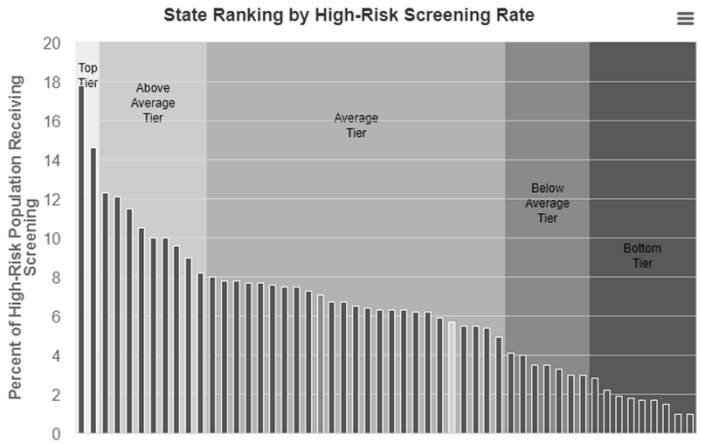
ALA State Rankings 2021

MN- red bar



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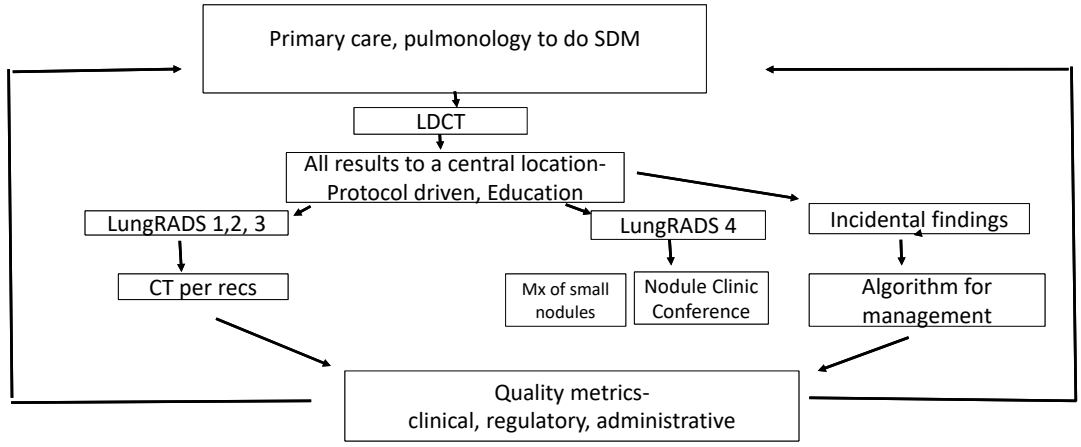
Hybrid integrated Allina Program – live since 10/18/2022



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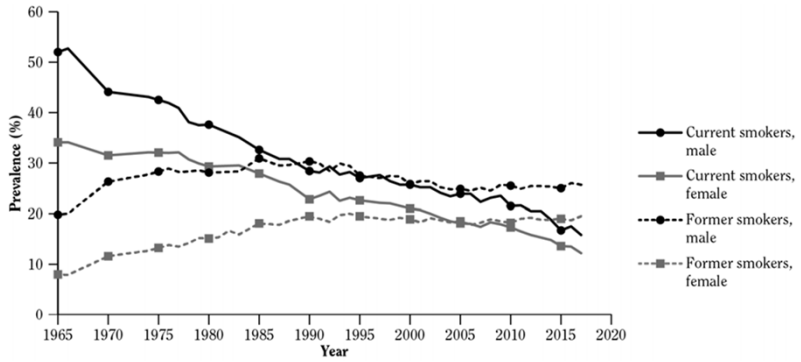
2020 Report

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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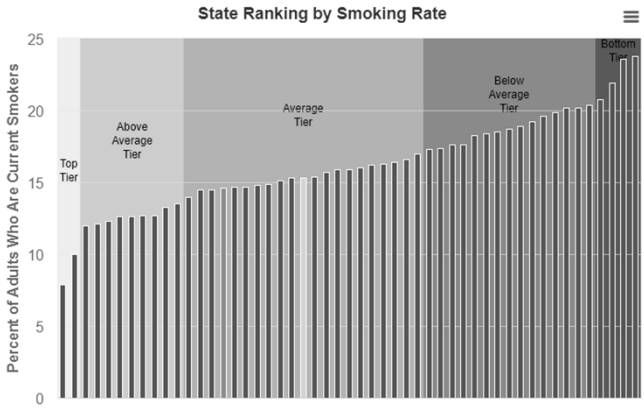
ALA State Rankings 2021

MN- red bar



- Within Allina-
  - 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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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 will 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 22%

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But there is great optimism…

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