I Curso

Multidisciplinar de investigación clínica en cáncer de pulmón

23 de enero de 2024

Breve revisión del cáncer de pulmón

Dr. Diego Márquez Medina. H. U. Miguel Servet de Zaragoza - Reina Sofía de Córdoba.

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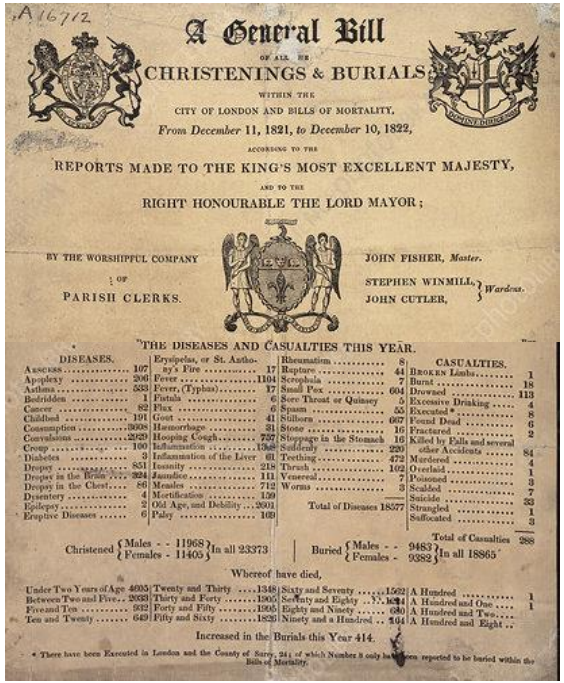
The great pretender

Dr. Diego Márquez

- **Lectures and educational activities:** Amgen, AstraZeneca, Bayer, Boehringer, BMS, Celgene, Lilly, Merck, Novartis, Pfizer, Pharmamar, Roche, Sanofi, Takeda.
- **Consulting, advisory role:** Amgen, AstraZeneca, Bayer, Boehringer, BMS, Celgene, Lilly, Merck, Novartis, Pfizer, Roche, Sanofi, Takeda.



A General Bill
OF ALL THE
CHRISTENINGS & BURIALS
WITHIN THE
CITY OF LONDON AND BILLS OF MORTALITY,
From December 11, 1821, to December 10, 1822,
ACCORDING TO THE
REPORTS MADE TO THE KING'S MOST EXCELLENT MAJESTY,
AND TO THE
RIGHT HONOURABLE THE LORD MAYOR;

BY THE WORSHIPFUL COMPANY OF PARISH CLERKS.

JOHN FISHER, *Master.*
STEPHEN WINMILL, JOHN CUTLER, *Wardens.*

"THE DISEASES AND CASUALTIES THIS YEAR.

DISEASES.						CASUALTIES.	
Abscess	107	Erysipelas, or St. Antho-ny's Fire	17	Rheumatism	8	Broken Limbs	1
Apoplexy	206	Fever	1104	Rupture	44	Burnt	18
Asthma	338	Fever, (Typhus)	17	Scrophula	7	Drowned	113
Bedridden	1	Fistula	6	Small Pox	604	Excessive Drinking	4
Cancer	82	Flux	6	Sore Throat or Quinsey	5	Executed *	8
Childbed	191	Gout	41	Spasm	55	Found Dead	6
Consumption	4808	Hæmorrhage	31	Stillborn	667	Fractured	2
Convulsions	2269	Hooping Cough	757	Stone	16	Killed by Falls and several other Accidents	84
Croup	100	Inflammation	1348	Stoppage in the Stomach	16	Murdered	4
Diabetes	3	Inflammation of the Liver	61	Suddenly	220	Overlaid	1
Dropsy	851	Insanity	218	Teething	472	Poisoned	3
Dropsy in the Brain	324	Jaundice	111	Thrush	102	Scalded	7
Dropsy in the Chest	26	Measles	712	Venereal	7	Suicide	33
Dysentery	4	Mortification	139	Worms	3	Strangled	1
Epilepsy	2	Old Age, and Debility	2801			Suffocated	3
Eruptive Diseases	6	Palsy	103	Total of Diseases	18577	Total of Casualties	288

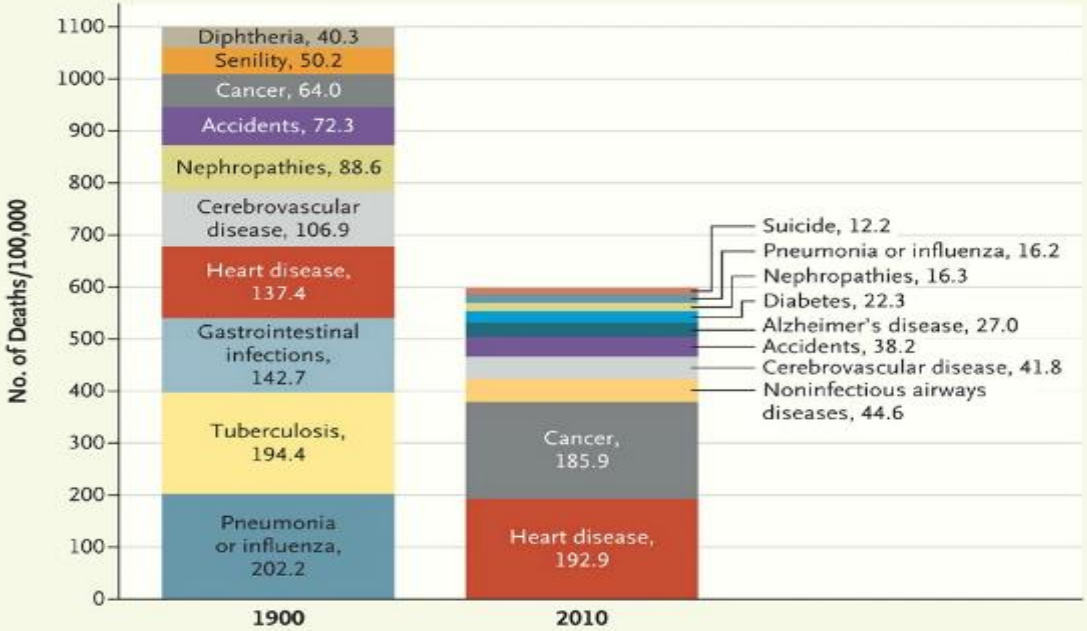
Christened { Males - - 11968 / Females - 11405 } In all 23373 | Buried { Males - - 9483 / Females - 9382 } In all 18865

Whereof have died,

Under Two Years of Age	4035	Twenty and Thirty	1348	Sixty and Seventy	1502	A Hundred	1
Between Two and Five	2033	Thirty and Forty	1905	Seventy and Eighty	1114	A Hundred and One	1
Five and Ten	932	Forty and Fifty	1905	Eighty and Ninety	680	A Hundred and Two	
Ten and Twenty	649	Fifty and Sixty	1825	Ninety and a Hundred	104	A Hundred and Eight	

Increased in the Burials this Year 414.

* There have been Executed in London and the County of Surry, 24; of which Number 8 only have been reported to be buried within the Bills of Mortality.



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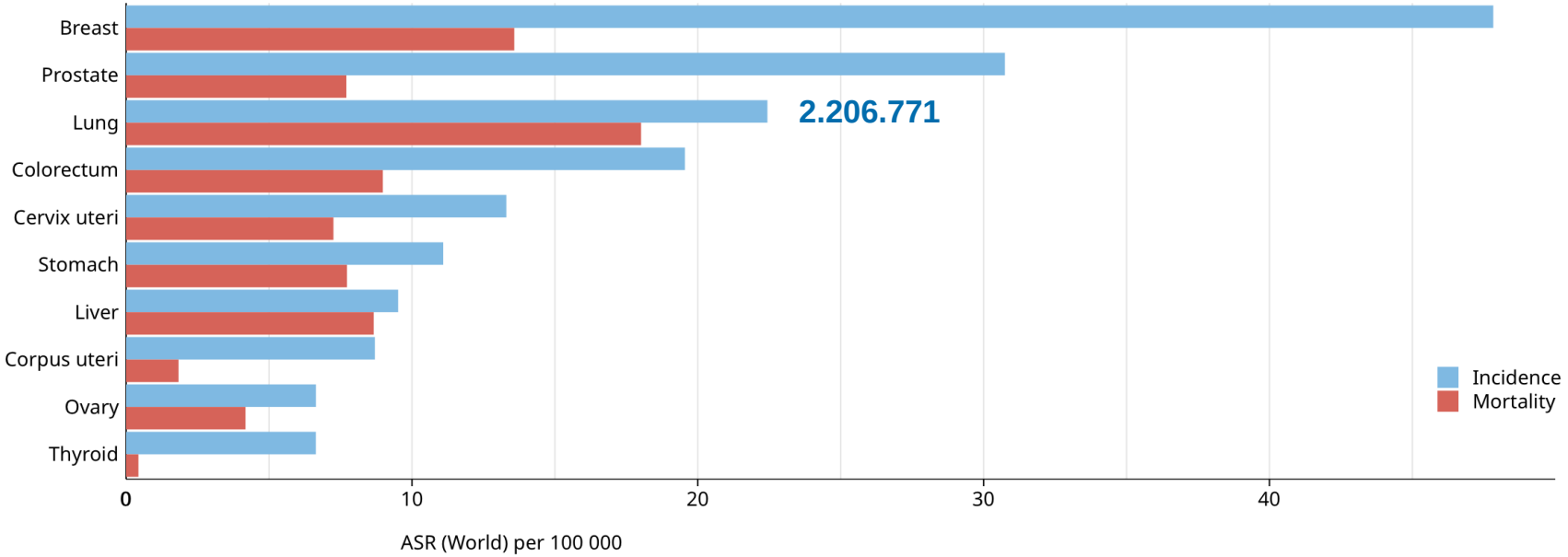
Worldwide 2020

Estimated age-standardized incidence and mortality rates (World) in 2020, World, both sexes, all ages (excl. NMSC)



Globocan, 2020

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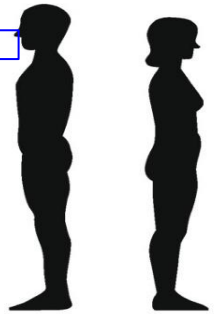
Cancer Statistics 2024, EEUU

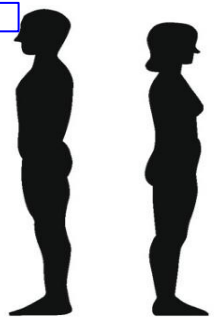
Estimated New Cases

Male			Female		
Prostate	299,010	29%	Breast	310,720	32%
Lung & bronchus	116,310	11%	Lung & bronchus	118,270	12%
Colon & rectum	81,540	8%	Colon & rectum	71,270	7%
Urinary bladder	63,070	6%	Uterine corpus	67,880	7%
Melanoma of the skin	59,170	6%	Melanoma of the skin	41,470	4%
Kidney & renal pelvis	52,380	5%	Non-Hodgkin lymphoma	36,030	4%
Non-Hodgkin lymphoma	44,590	4%	Pancreas	31,910	3%
Oral cavity & pharynx	41,510	4%	Thyroid	31,520	3%
Leukemia	36,450	4%	Kidney & renal pelvis	29,230	3%
Pancreas	34,530	3%	Leukemia	26,320	3%
All sites	**1,029,080**		**All sites**	**972,060**	



Estimated Deaths

Male			Female		
Lung & bronchus	65,790	20%	Lung & bronchus	59,280	21%
Prostate	35,250	11%	Breast	42,250	15%
Colon & rectum	28,700	9%	Pancreas	24,480	8%
Pancreas	27,270	8%	Colon & rectum	24,310	8%
Liver & intrahepatic bile duct	19,120	6%	Uterine corpus	13,250	5%
Leukemia	13,640	4%	Ovary	12,740	4%
Esophagus	12,880	4%	Liver & intrahepatic bile duct	10,720	4%
Urinary bladder	12,290	4%	Leukemia	10,030	3%
Non-Hodgkin lymphoma	11,780	4%	Non-Hodgkin lymphoma	8,360	3%
Brain & other nervous system	10,690	3%	Brain & other nervous system	8,070	3%
All sites	**322,800**		**All sites**	**288,920**	



Estimates are rounded to the nearest 10, and cases exclude basal cell and squamous cell skin cancers and in situ carcinoma except urinary bladder. Estimates do not include Puerto Rico or other US territories. Ranking is based on modeled projections and may differ from the most recent observed data.

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ACS, 2024

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Cancer in Spain, 2023

Estimación de incidencia en hombres y mujeres

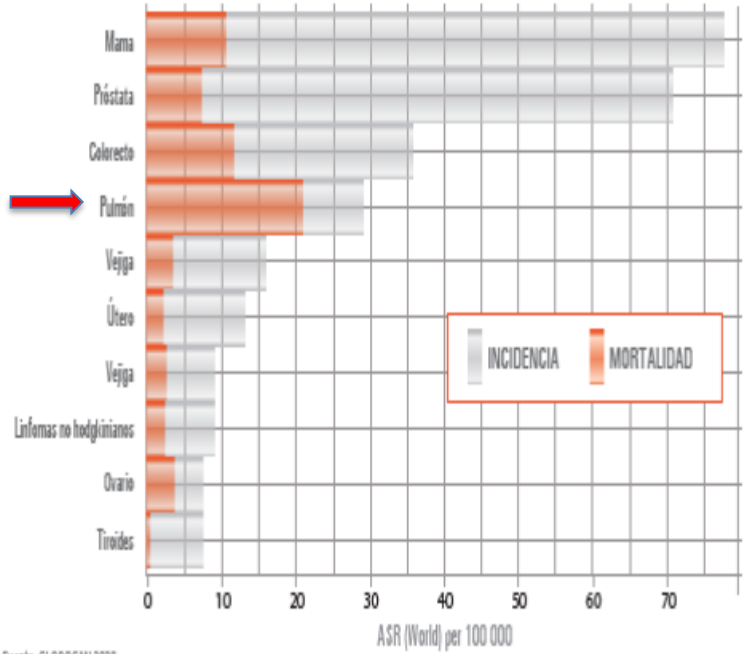
TIPO TUMORAL	N
Cavidad oral y faringe	5.644
Esófago	1.899
Estómago	4.231
Colon	17.340
Recto	9.017
Hígado	5.164
Vesícula biliar	1.384
Páncreas	4.770
Laringe	2.983
Pulmón	22.266
Melanoma de piel	3.786
Próstata	29.002
Testículo	1.510
Riñón (sin pelvis)	5.924
Vejiga urinaria	17.731
Encéfalo y sistema nervioso	2.271
Tiroides	1.433
Linfoma de Hodgkin	844
Linfomas no hodgkinianos	5.491
Mieloma	1.757
Leucemias	3.430
Otros	10.669
Todos excepto piel no melanoma	158.544

Fuente: Red Española de Registros de Cáncer (REDECAN).

TIPO TUMORAL	N
Cavidad oral y faringe	2.238
Esófago	403
Estómago	2.701
Colon	11.125
Recto	5.239
Hígado	1.531
Vesícula biliar	1.264
Páncreas	4.510
Laringe	395
Pulmón	9.016
Melanoma de piel	4.263
Mama	35.001
Cérvix uterino	2.326
Cuerpo uterino	7.171
Ovario	3.584
Riñón (sin pelvis)	2.702
Vejiga urinaria	3.963
Encéfalo y sistema nervioso	1.801
Tiroides	4.651
Linfoma de Hodgkin	696
Linfomas no hodgkinianos	4.452
Mieloma	1.325
Leucemias	2.981
Otros	7.377
Todos excepto piel no melanoma	120.715

Fuente: Red Española de Registros de Cáncer (REDECAN).

Figura 15. Tasas de incidencia y mortalidad estimadas por cáncer en España para ambos sexos (excluidos los tumores cutáneos no-melanoma).

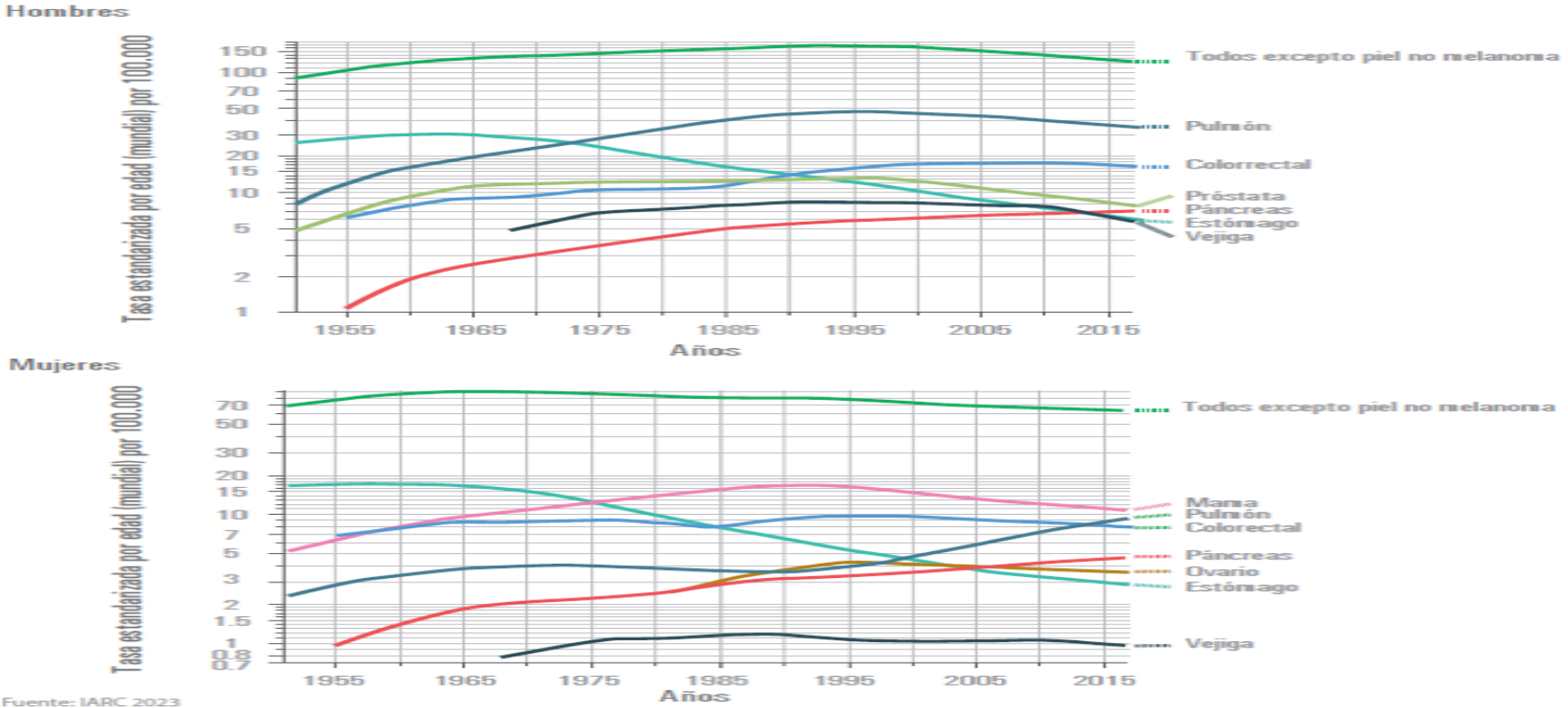


Fuente: GLOBOCAN 2020
Gráfico: Global Cancer Observatory (http://gco.iarc.fr/)
© International Agency for Research on Cancer 2023

www.seom.org/Las_cifras_del_cancer_en_Esp_2023.pdf

Incidence

Figuras 19. Evolución temporal de la mortalidad estandarizada por distintos tumores en España, por sexos.



Fuente: IARC 2023

www.seom.org/Las_cifras_del_cancer_en_Esp_2023.pdf

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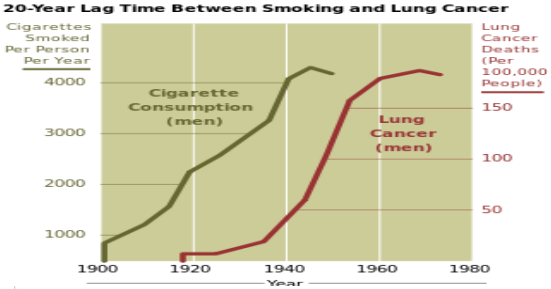
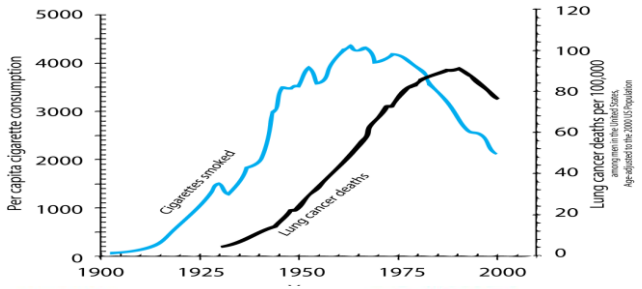
Risk factors

Carcinogens, Group 1, WHO

- Smoking
- Radon gas
- Asbestos
- Second-hand smoking
- Genetics
- Radiation
- Occupational
- Arsenic (H_20), diesel...





- **Media:** 90 Bq/m3
- **6% casas:** > 200 Bq/m3

Muy ALTO
10% viviendas: ***> 400 Bq/m3***

BASTANTE ALTO
10% viviendas: ***301-400 Bq/m3***

The omission of **sex** as a factor in developing clinical management of patients is likely to be to the detriment of more efficient health care. Personalized medicine **cannot** be performed without taking **sex** into consideration as a fundamental prognostic factor.

Siegel. CA Cancer J Clin, 2023.
Paz-Ares. ICAPEM, 2023
Nakamura . Ann Thorac Cardiovasc Surg, 2011

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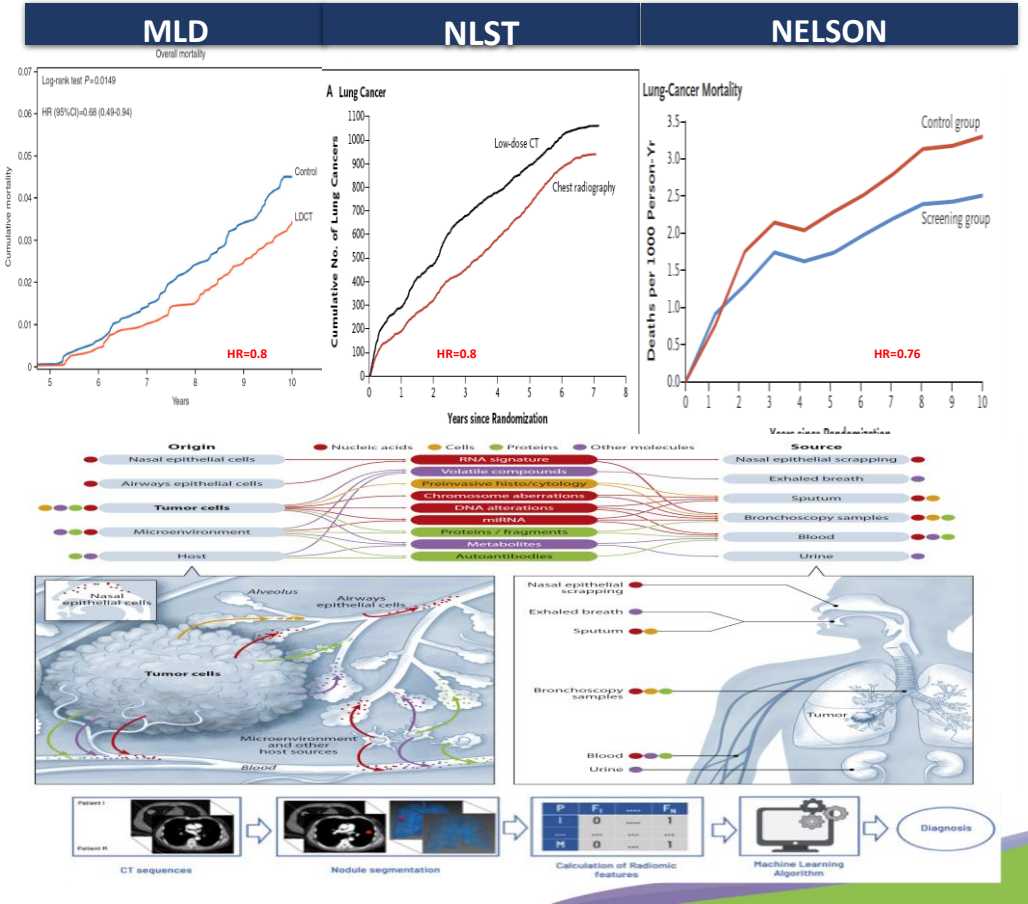
Prevention



Konig. N Engl J Med, 2020
Pastorino. Ann Oncol, 2019
Aberle. N Engl J Med, 2011
Won. Nat Med, 2020

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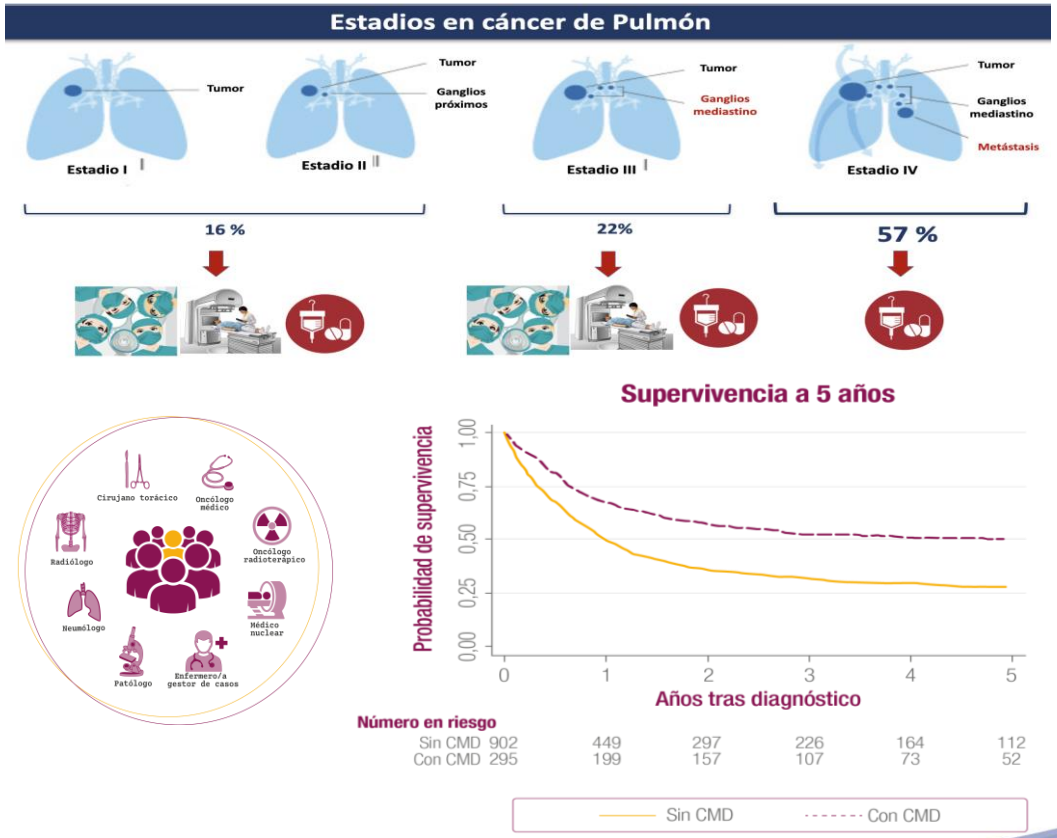
The sooner, the better

	Age group (years)					
	30–39	40–49	50–59	60–69	70–79	≥80
Bladder	15·79%	14·95%	14·29%	15·48%	17·15%	17·03%
Brain	11·75%	14·15%	17·82%	18·24%	16·64%	16·70%
Breast	4·88%	3·27%	2·49%	2·14%	3·71%	7·70%
Cervix	5·59%	9·03%	12·20%	15·73%	17·98%	15·52%
Colorectal	10·22%	11·38%	10·82%	10·59%	13·10%	16·36%
Kidney	5·01%	6·50%	8·53%	10·53%	13·10%	17·41%
Larynx	11·07%	14·29%	13·45%	14·94%	15·86%	16·79%
Liver	16·68%	17·29%	16·17%	14·67%	11·89%	14·78%
Lung	16·87%	18·26%	16·80%	15·37%	11·78%	6·70%
Melanoma of skin	3·13%	3·96%	4·89%	5·66%	7·32%	12·56%
Oesophagus	16·85%	16·21%	16·12%	15·18%	12·28%	4·59%
Oral cavity	12·83%	16·98%	18·27%	18·28%	17·88%	16·62%
Oropharynx	11·79%	14·48%	16·77%	18·31%	17·08%	13·73%
Ovary	7·24%	13·87%	17·38%	18·28%	17·08%	15·86%
Pancreas	12·86%	11·76%	12·11%	9·00%	7·18%	10·74%
Prostate	0·68%	0·67%	0·32%	0%	0%	3·69%
Stomach	18·58%	18·54%	18·03%	17·34%	16·11%	8·85%
Testis	0·58%	0·36%	0·76%	0·35%	0·63%	1·62%
Thyroid	0·11%	0·63%	1·33%	0·22%	2·57%	0%
Uterus	2·43%	5·27%	6·04%	8·68%	11·83%	14·43%

Figure 1: **Reduction in 10-year net survival incurred from a 3-month delay for the 20 most common tumour types, by age group**
Red indicates the highest decile of survival decrement, scaling down through orange and yellow to pale green, which indicates the lowest decile of survival decrement.



Sud. Lancet, 2020
Stone. Lung Cancer 2018

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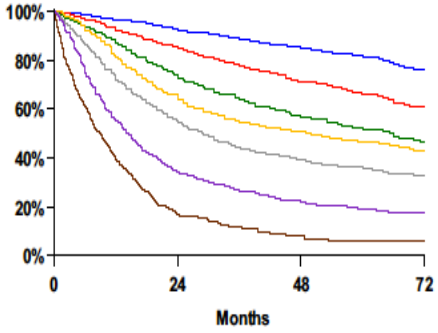
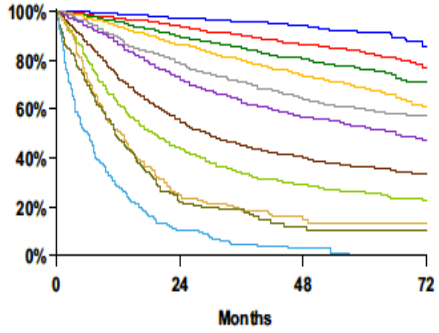
The slow train

A



B



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%

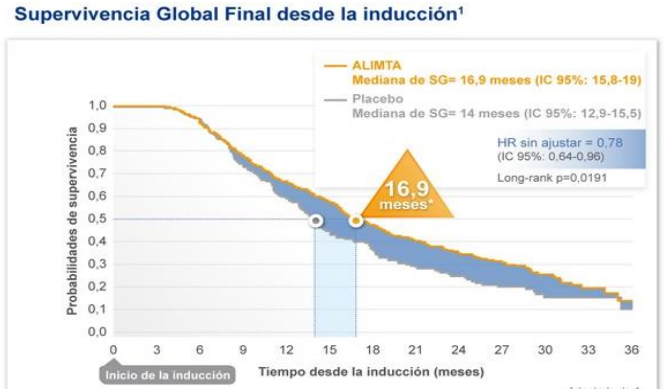
Proposed	Events / N	MST	24 Month	60 Month
IA1	68 / 781	NR	97%	92%
IA2	505 / 3105	NR	94%	83%
IA3	546 / 2417	NR	90%	77%
IB	560 / 1928	NR	87%	68%
IIA	215 / 585	NR	79%	60%
IIB	605 / 1453	66.0	72%	53%
IIIA	2052 / 3200	29.3	55%	36%
IIIB	1551 / 2140	19.0	44%	26%
IIIC	831 / 986	12.6	24%	13%
IVA	336 / 484	11.5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

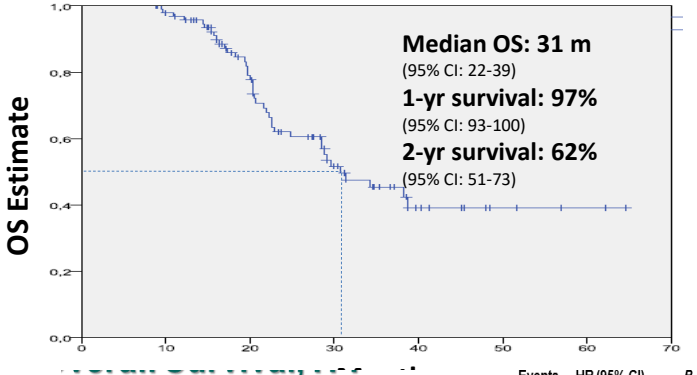
Goldstraw. J Thorac Oncol, 2015
Labadebe. Oncologist, 2018

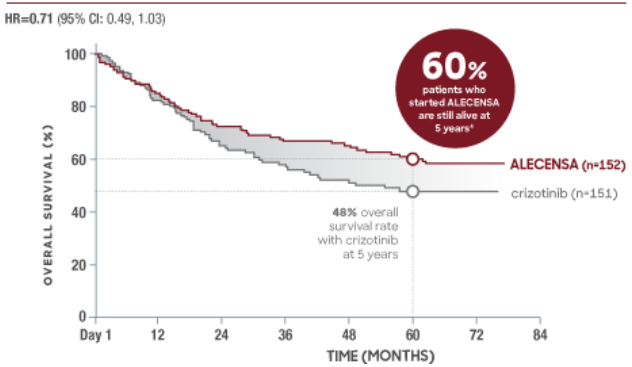
TABLE **TNM stage grouping according to the proposed 9th edition of the TNM classification of lung cancers**

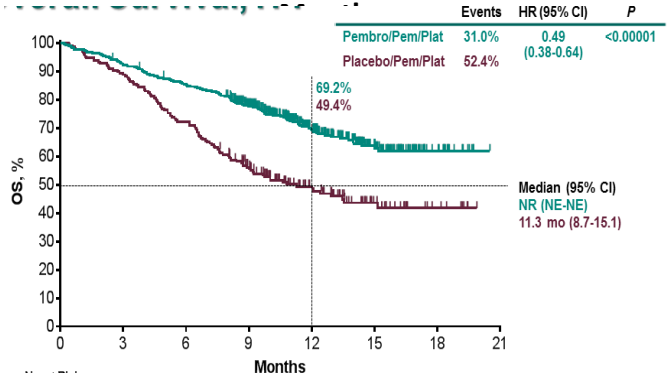
T/M	Label	N0	N1	N2		N3
				N2a	N2b	
T1	T1a ≤ 1 cm	IA1	IIA	IIB	IIIA	IIIB
	T1b > 1 to ≤ 2 cm	IA2	IIA	IIB	IIIA	IIIB
	T1c > 2 to ≤ 3 cm	IA3	IIA	IIB	IIIA	IIIB
T2	T2a	IB	IIB	IIIA	IIIB	IIIB
	T2a > 3 to ≤ 4 cm	IB	IIB	IIIA	IIIB	IIIB
	T2b > 4 to ≤ 5 cm	IIA	IIB	IIIA	IIIB	IIIB
T3	T3 > 5 to ≤ 7 cm	IIB	IIIA	IIIA	IIIB	IIIC
	T3 Invasion	IIB	IIIA	IIIA	IIIB	IIIC
	T3 Satellite nodules	IIB	IIIA	IIIA	IIIB	IIIC
T4	T4 > 7 cm	IIIA	IIIA	IIIB	IIIB	IIIC
	T4 Invasion	IIIA	IIIA	IIIB	IIIB	IIIC
	T4 Ipsilateral nodules	IIIA	IIIA	IIIB	IIIB	IIIC
M1	M1a Contralateral nodules	IVA	IVA	IVA	IVA	IVA
	M1a Pleural, pericardial effusion	IVA	IVA	IVA	IVA	IVA
	M1b Single extra-thoracic lesion	IVA	IVA	IVA	IVA	IVA
	M1c1 Multiple extra-thoracic lesions in a single organ system	IVB	IVB	IVB	IVB	IVB
	M1c2 Multiple extra-thoracic lesions in multiple organ systems	IVB	IVB	IVB	IVB	IVB

Every little thing she does is magic



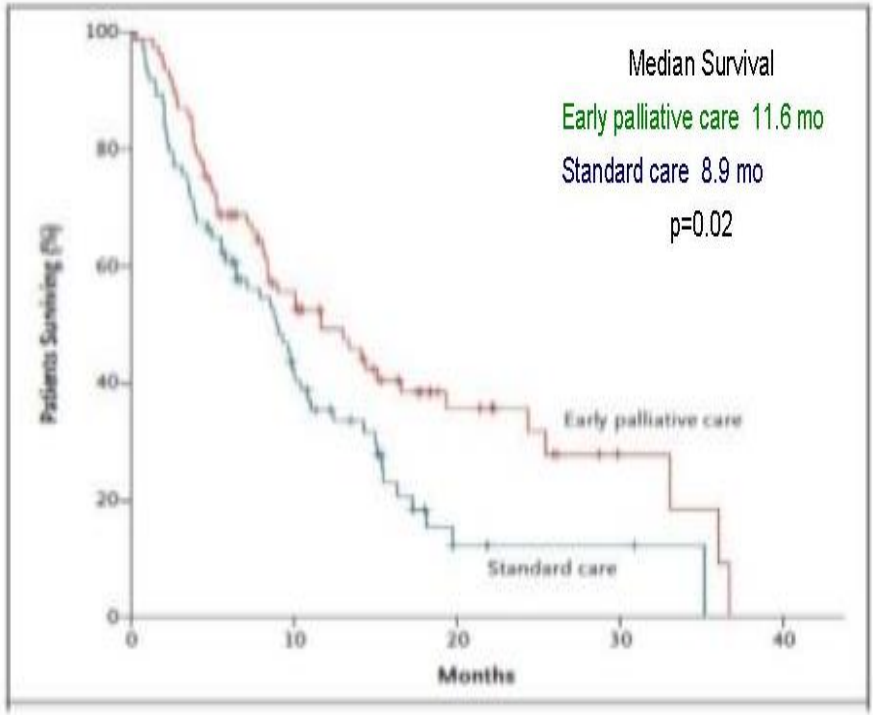


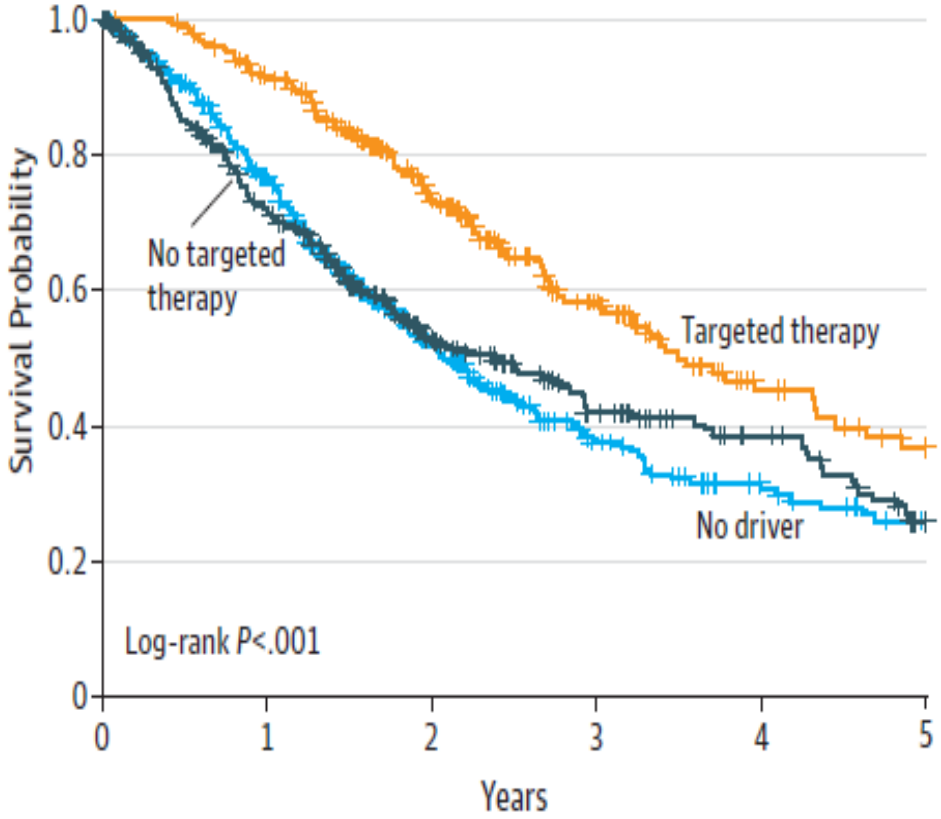




Paz-Ares. ASCO, 2013
De Castro. ELCC 2012
Hotta. J Clin Oncol, 2022
Reck. ELCC, 2022

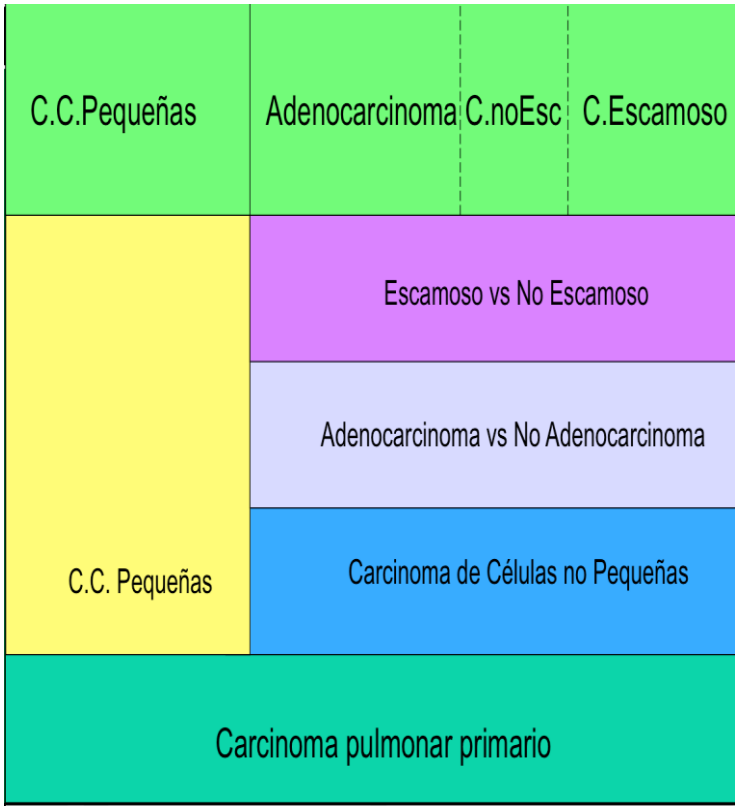
Everyone.

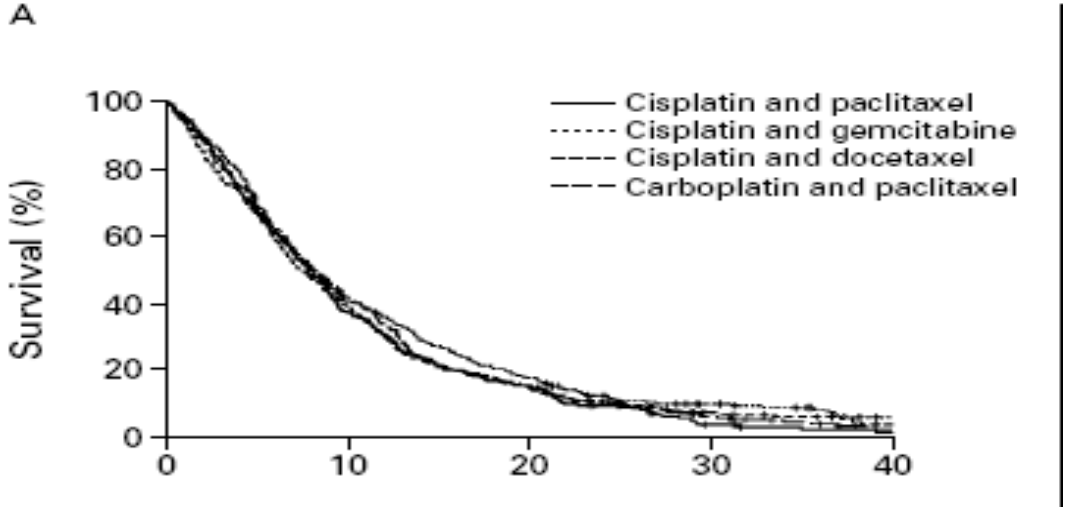




Temel. ASCO, 2010
Kris. Clin Lung Cancer, 2014

From Pathology to Biology

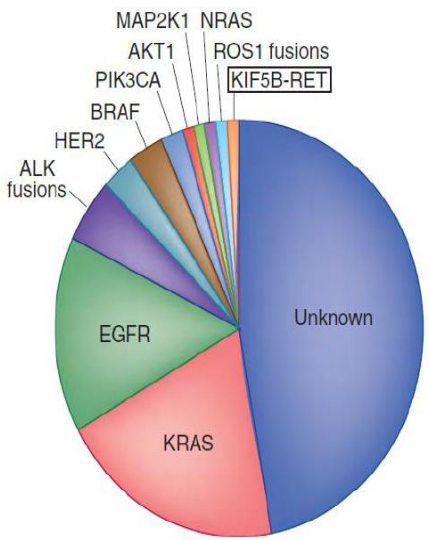




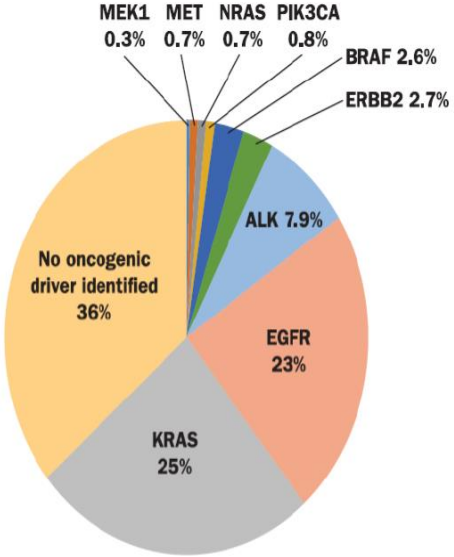
Variable	Cisplatin and Paclitaxel (N=288)	Cisplatin and Gemcitabine (N=288)	Cisplatin and Docetaxel (N=289)	Carboplatin and Paclitaxel (N=290)	Total (N=1155)
Survival					
Median (95% CI) — mo	7.8 (7.0–8.9)	8.1 (7.2–9.4)	7.4 (6.6–8.8)	8.1 (7.0–9.5)	7.9 (7.3–8.5)
1 yr (95% CI) — %	31 (26–36)	36 (31–42)	31 (26–36)	34 (29–40)	33 (30–36)
2 yr (95% CI) — %	10 (5–12)	13 (7–15)	11 (7–14)	11 (7–14)	11 (8–12)
Median time to progression (95% CI) — mo	3.4 (2.8–3.9)	4.2 (3.7–4.8)†	3.7 (2.9–4.2)	3.1 (2.8–3.9)	3.6 (3.3–3.9)

Schindler. N Engl J Med, 2002
Shepherd. N Engl J Med, 2005

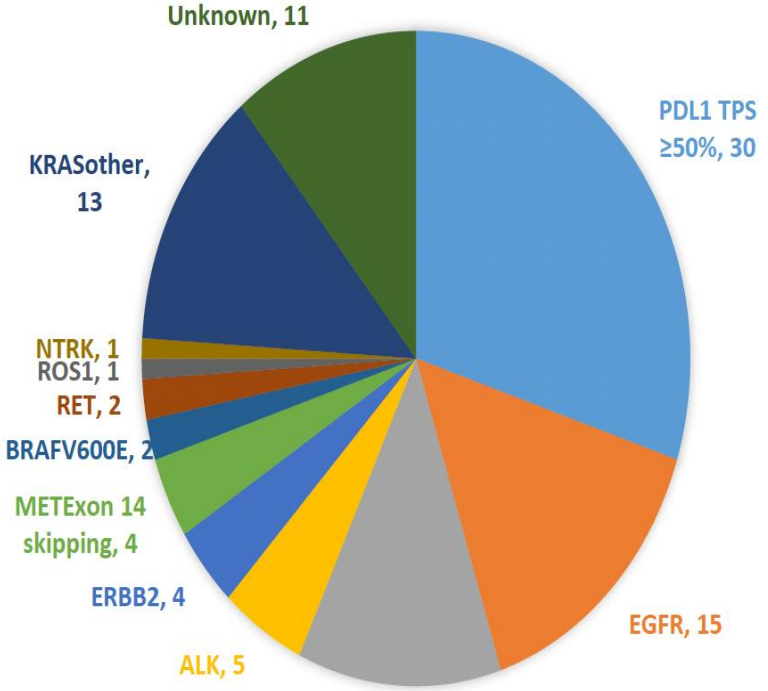
Time after time.



Pao and Hutchinson 'Chipping away at the lung cancer genome'
Nature Medicine. **March 2012**



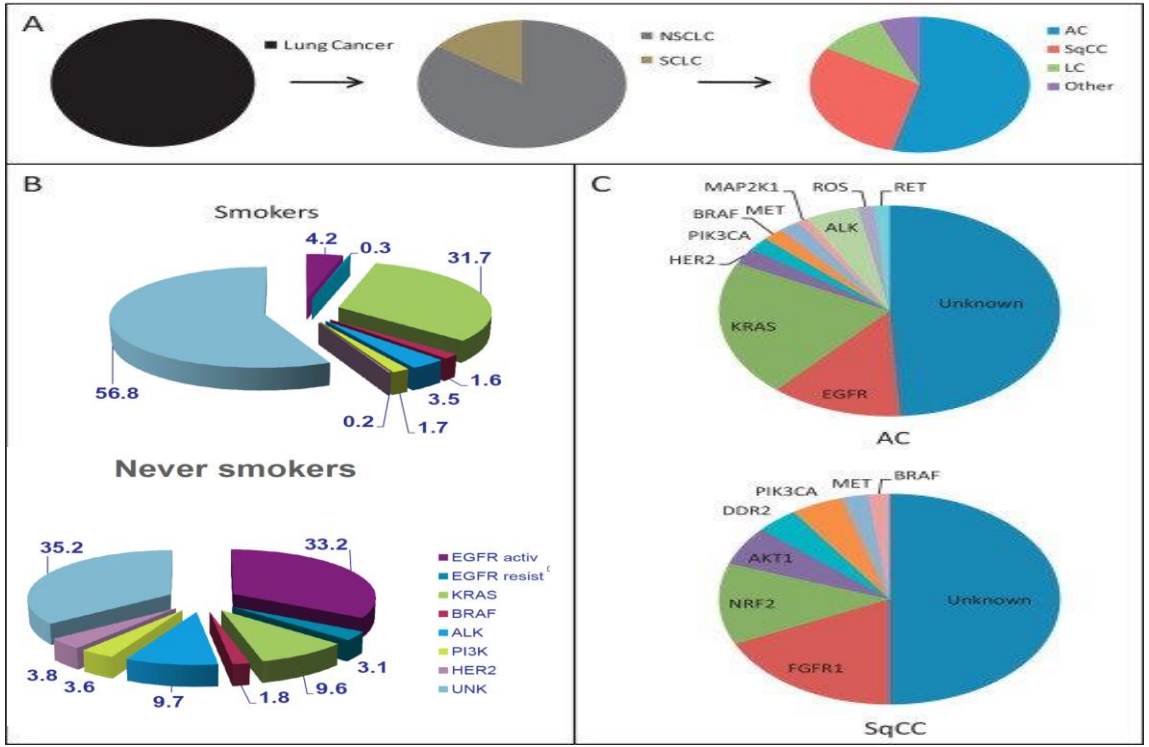
Scholl et al. Lung Cancer Mutation Consortium
J Thorac Oncol. **May 2015**



2020: biomarkers with drug targets

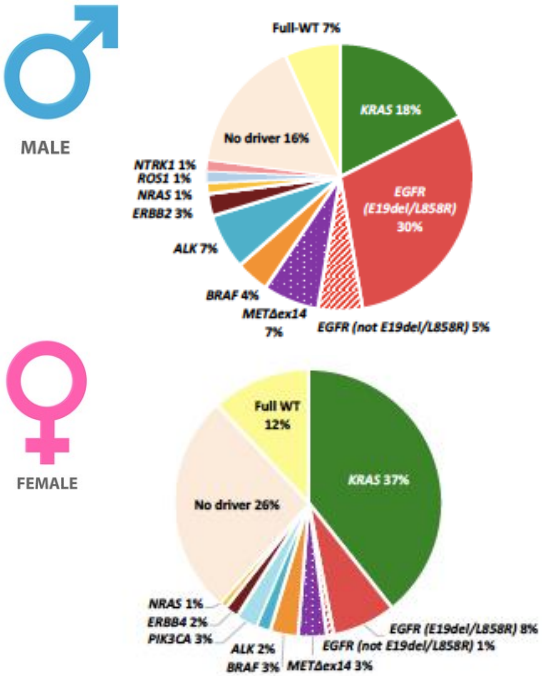
Depending on

Smoking



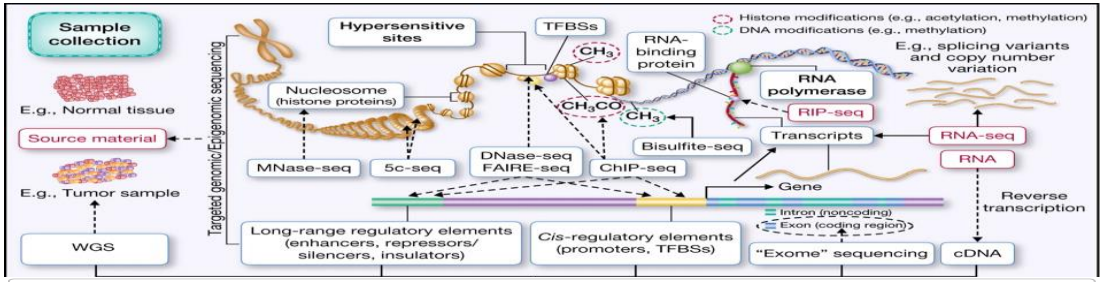
Histology

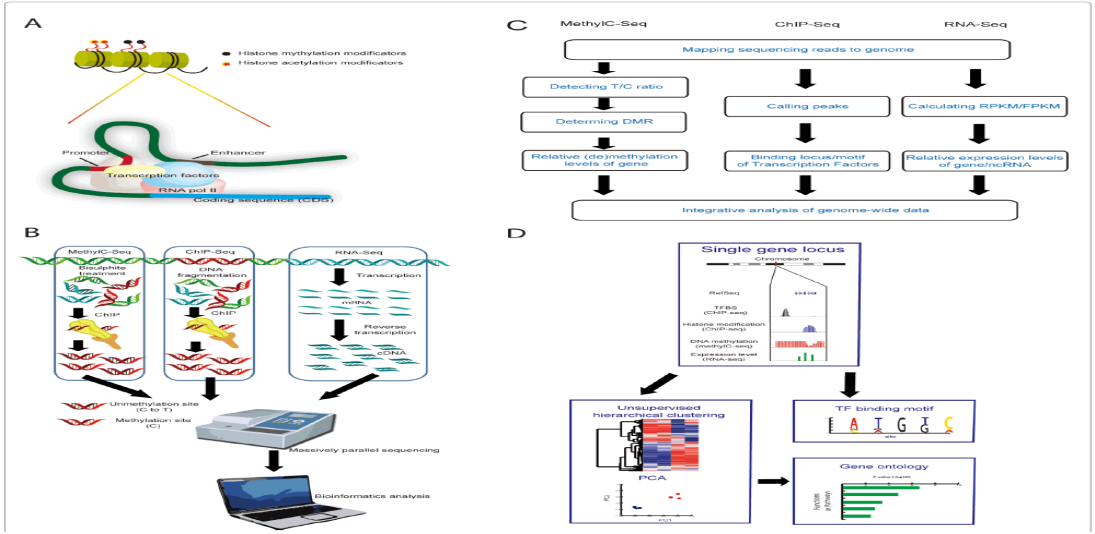
Gender



Pikor. Lung Cancer, 2013
Mederos. ESMO, 2020
Marin. Cancers, 2020
Barlesi. ASCO, 2013

Accurate diagnosis is warranted



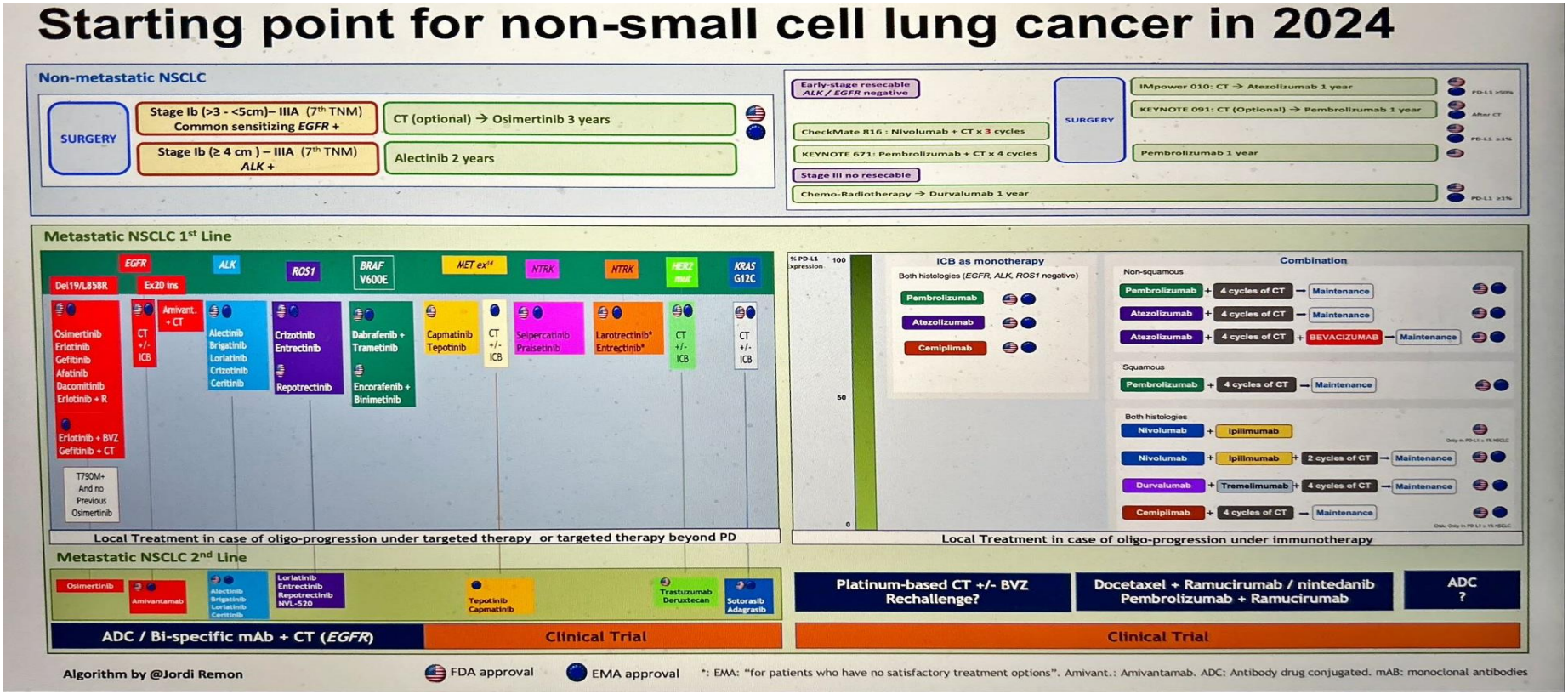


Target	Prevalence	Initial FDA Approval	Drugs
EGFR	10-15%	2003	Gefitinib, Erlotinib, Afatinib, Osimertinib,
ALK	2-7%	2011	Crizotinib, Ceritinib, Alectinib, Lorlatinib, Brigantinib,
ROS-1	1-2%	2016	Crizotinib, Entrectinib, Ceritinib, Lorlatinib
PD-L1 TPS 50%	30%	2016	Pembrolizumab, Atezolizumab
B-RAF^{V600E}	2%	2017	Dabrafenib+Trametinib, Vemurafenib
NTRK	0.2-3%	2018	Larotrectinib, Entrectinib
HER-2 (ERBB2)	2-5%	May 2020	Trastuzumab deruxtecan (Enhertu)
MET $^{exon\ 14\ skipping}$	3-4%	May 2020	Capmatinib; ?Tepotinib?, Crizotinib
RET	1-2%	September 4, 2020	Salpercatinib, Pralsetinib, Carbozantinib, Vandetanib
K-RAS ^{G12C}	12%	***December 8, 2020****	Sotorasib (AMG510)

Osarogiagbon. WCLC, 2020

I Curso
Multidisciplinar de investigación clínica en cáncer de pulmón

In order to…



Remon. The whole world, 2024

Gracias a vosotros