

Cribado de cáncer de pulmón en el trasplante de órgano sólido

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Declaración: Chiesi, Astellas, Nordicpharma (Viajes a Congresos, Ponencias, Becas)

No conflictos de interés respecto a esta charla.

Esta presentación no incluye presentación ni discusión de uso de fármacos
no aprobados o en investigación

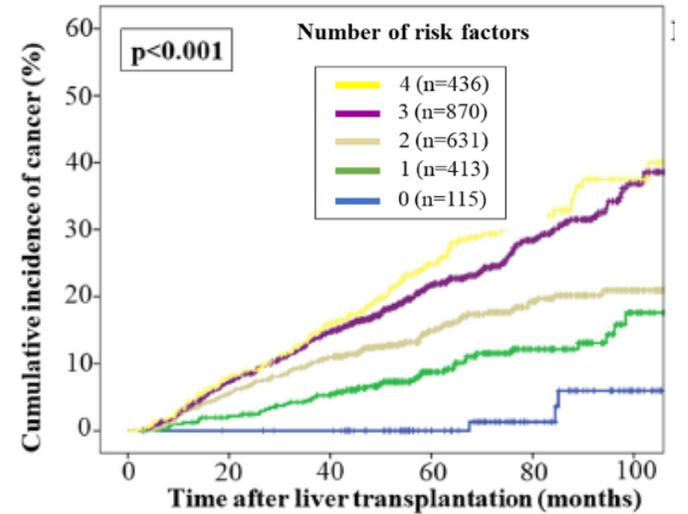
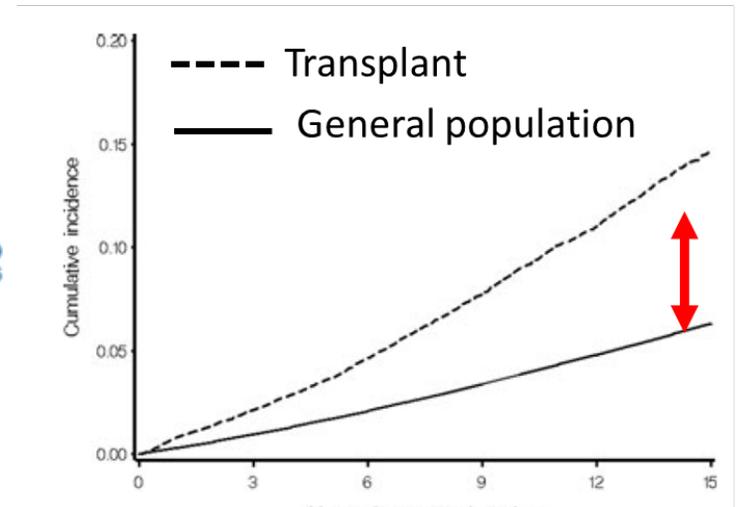
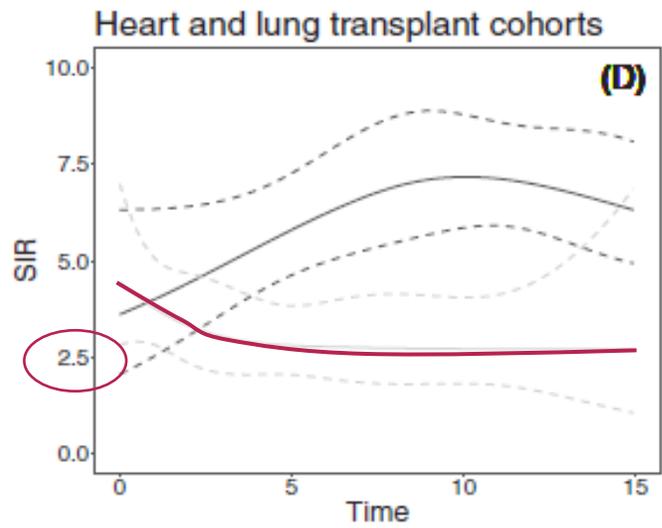
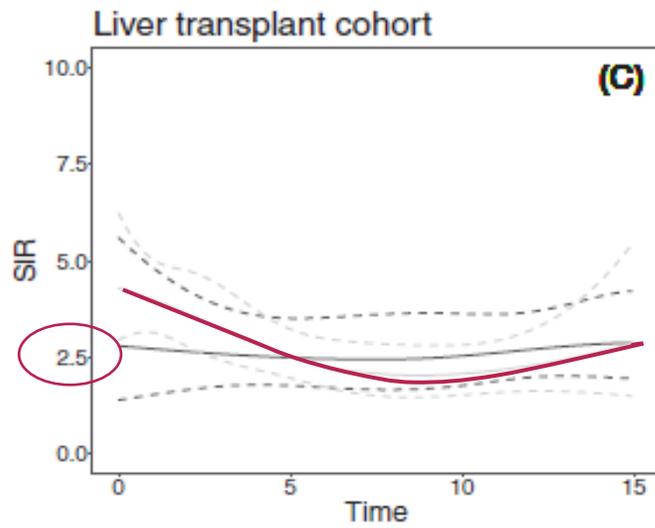
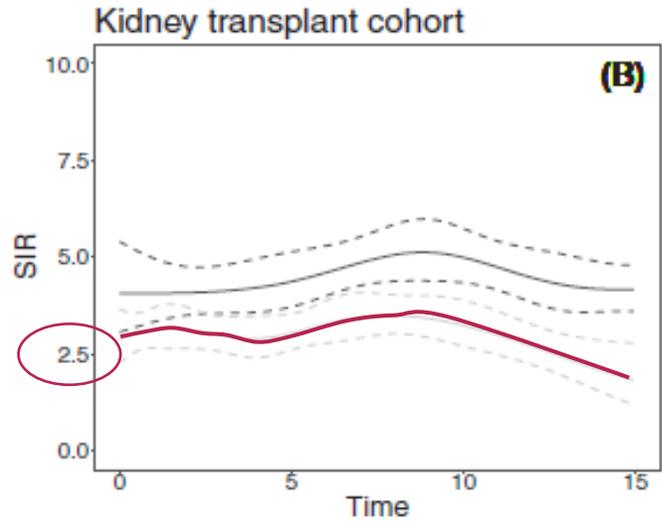
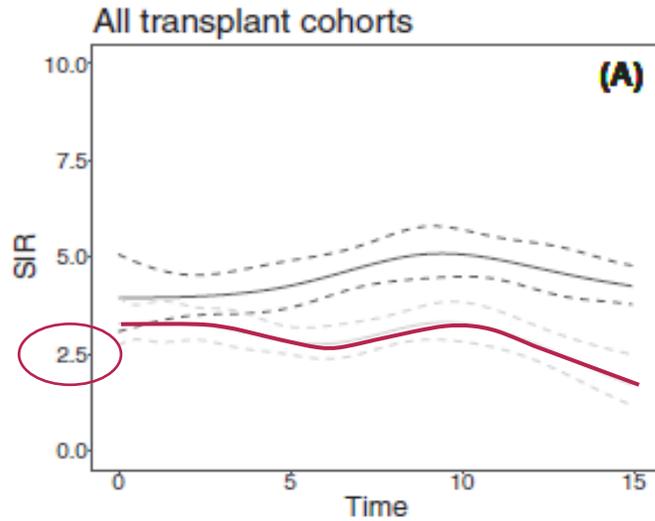
Outline

1. Risk of all-cancer and lung cancer in SOT
2. Cancer and mortality in SOT
3. Screening of lung cancer: methods and results
4. Current recommendations in SOT
5. Implementation of a Lung Cancer Screening Program

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Standardized Risk of Cancer in SOT



Standardized Risk of Lung Cancer in SOT

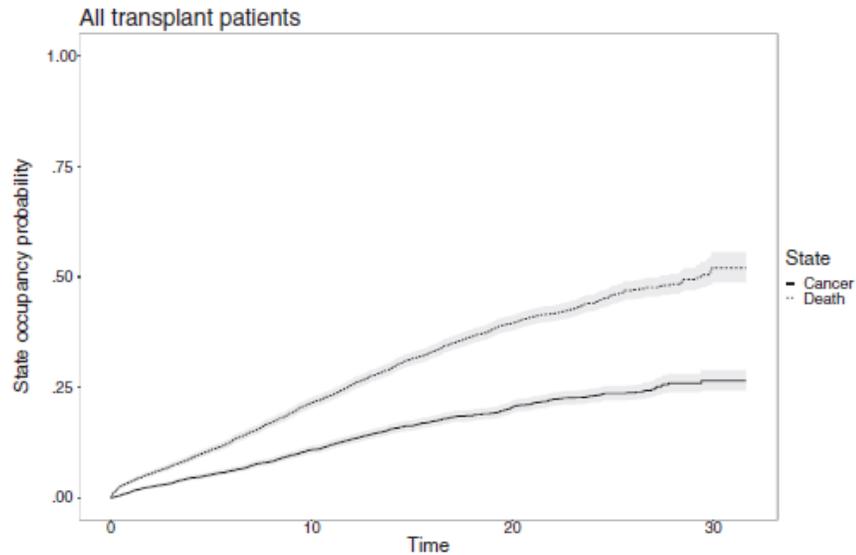
Transplant type	Standardized Incidence Ratio (SIR)	95% Confidence Interval
All	1.97 ¹	1.97-2.08
	2.00 ²	1.60-2.05
	3.90 ⁴	2.30-6.30
Kidney	1.46 ¹	1.34–1.59
	1.57 ⁵	1.15-2.02
	1.90 ²	1.50-2.50
Liver	1.50 ²	1.50-2.50
	1.95 ¹	1.74–2.19
	2.06 ³	1.73-2.46*
Heart	2.67 ¹	2.40–2.95
	3.00 ²	1.70-4.90
Lung	6.13 ¹	5.18–7.21
	3.0 ²	1.70-4.90

Engels et al. JAMA 2011¹; Friman et al. Int. J. Cancer 2022 ²; *Fu et al, Cancer Medicine 2023 ³;
 Jäämaa-Holmberg et al Acta Oncol 2019⁴; Taborelli et al, Int J Cancer 2024 ⁵

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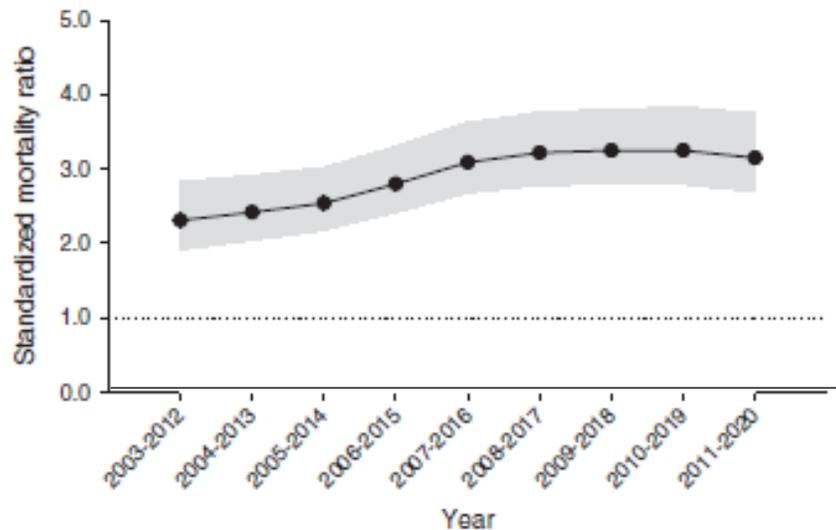
Increased Mortality of All-Cancer and Lung-Cancer After SOT



Standardized mortality ratios (SMR) for all cancers

SOT	=> 2.50 (2.2-2.7)
Kidney transplantation	=> 1.83 (1.6-2.1)
Heart transplantation	=> 3.10 (2.4-4.1)
Liver transplantation	=> 3.07 (1.8-5.2)
Males	=> 2.70 (2.4-3.0)
Females	=> 2.10 (1.7-2.5)

(B) Adjusted^a



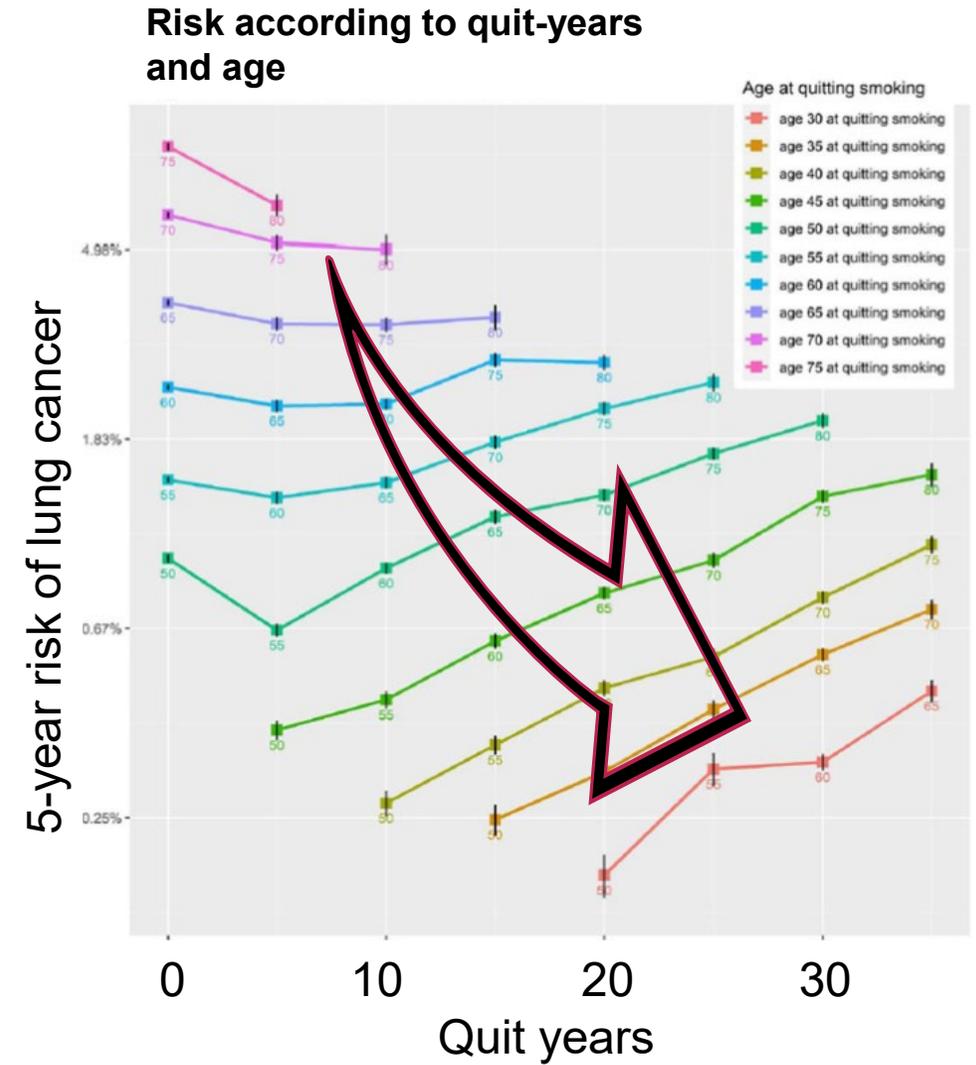
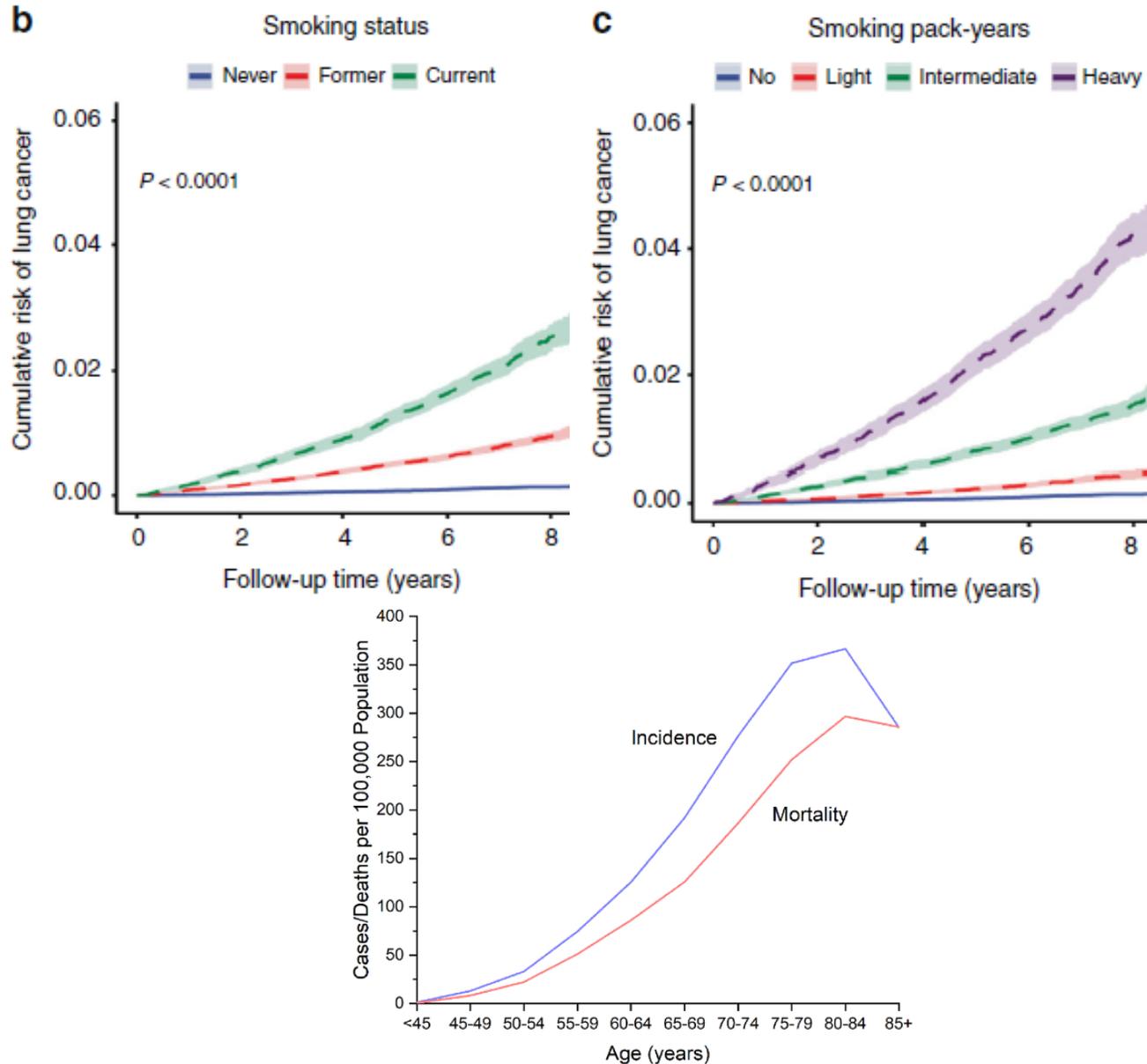
SMR for lung cancers

=> any SOT	- 1.91 (1.5-2.4)
=> kidney tx	- 1.57 (1.2 -2.2)
	- 1.42 (1.1 - 1.8)
=> liver tx	- 2.30 (1.8-3.2)

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Association between age, smoking status, cumulative dose and risk of lung cancer



Simplified PLCOm2012: Selection criteria for lung cancer screening

Usual threshold for screening: $\geq 1.5\%$ at 6 years



The calculated 6-year risk of lung cancer is: **1.6%**

Lung Cancer Screening with Low density Chest CT in the general population

Study	Country	Publication Year	Design	Participants	Age	Pack-years	Follow-up (mean years)	Lung cancer rate in LDCT (baseline)	Stage I lung cancer	Mortality reduction
I-ELCAP	USA and others	2006	IDCT	31,567	≥40	-	10	1.3%	85.0%	-
NLST	USA	2011	IDCT vs CXR	53,454	55-74	≥30	6.5	1.0%	63.0%	20%
DANTE	Italy	2015	IDCT vs Control	2,811	60-74	≥20	8.3	2.2%	57.0%	-
DLCST	Denmark	2016	IDCT vs Control	4,104	60-69	≥20	10	1.0%	58.8%	-
ITALUNG	Italy	2017	IDCT vs Control	3,206	55-69	≥20	9	1.0%	63.3%	-
MILD	Italy	2019	IDCT vs Control	4,099	49-70	≥15	8.3	0.8%	58.3%	-
LUSI	Germany	2020	IDCT vs CXR	4,052	50-69	≥15	8.8	1.1%	69.4%	-
NELSON	Netherlands + Belgium	2020	IDCT vs Control	15,789	50-74	≥15	10	0.9%	58.6%	24% men 33% women

LDCT: Low-dose computed tomography; CXR: Chest X-ray; Control: No screening intervention

Lung cancer rate in LDCT baseline: Percentage of detected lung cancer in the initial scan

The sensitivity of CXR for lung cancer was reported in prior studies = 25%; specificity not reported. Cost-effective.

Risks: Advanced diagnosis effect on survival/duration of the disease; Overdiagnosis; False positive; Exposure to radiation

Effect of LDCT screening on lung cancer-related mortality (general population)

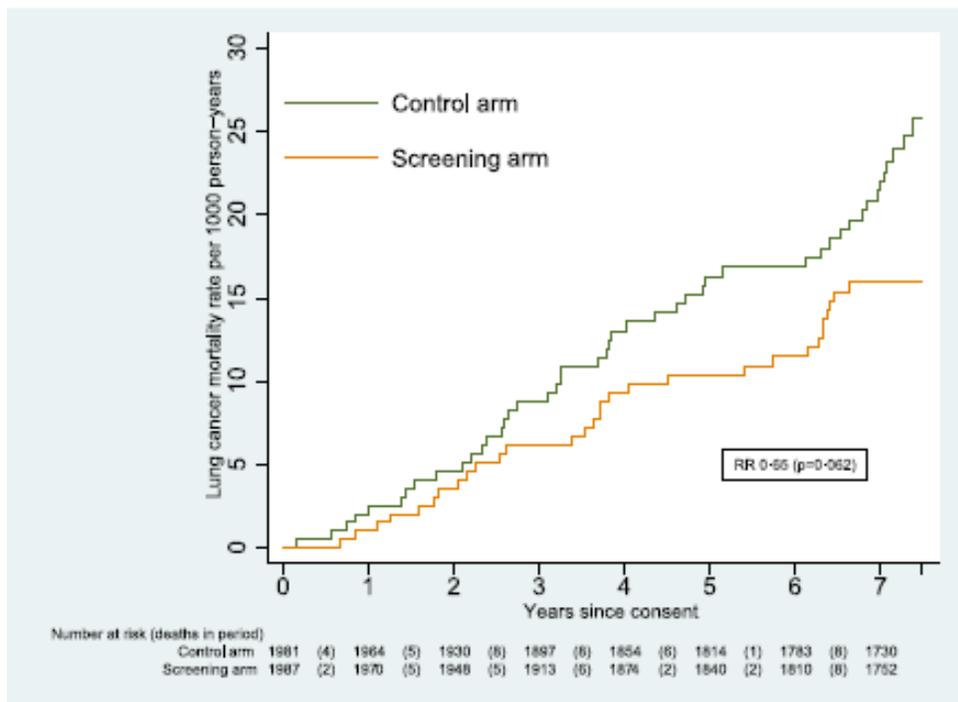
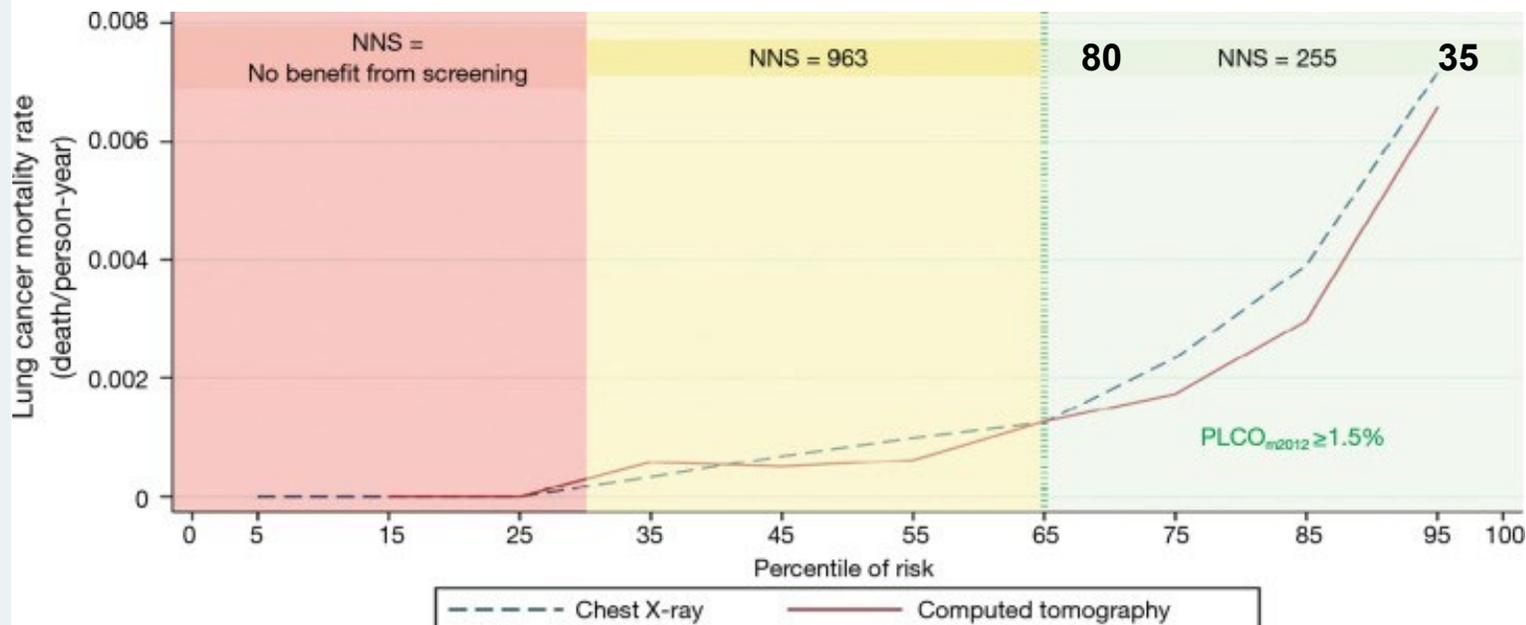


Fig. 2. Cumulative mortality from lung cancer.



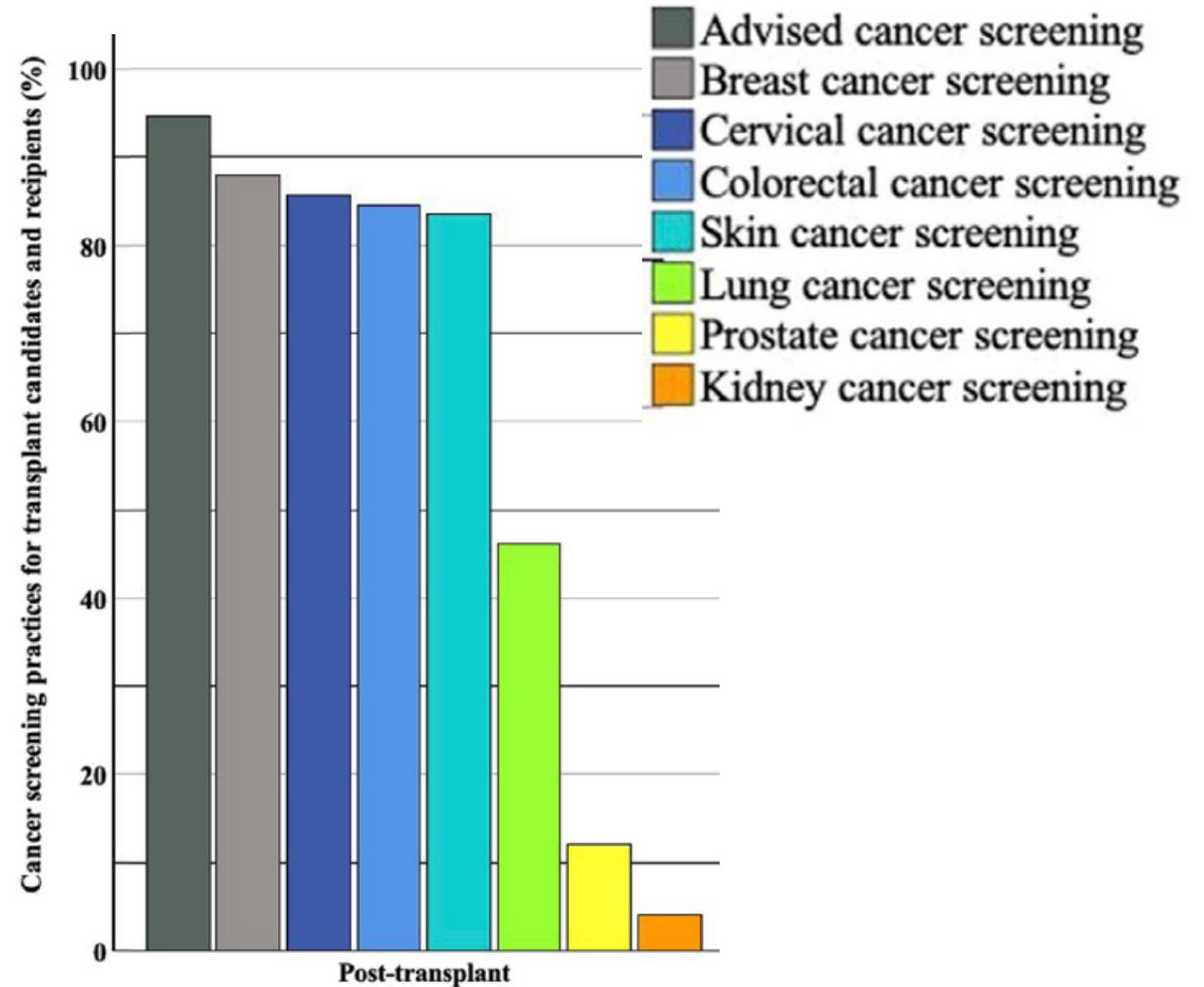
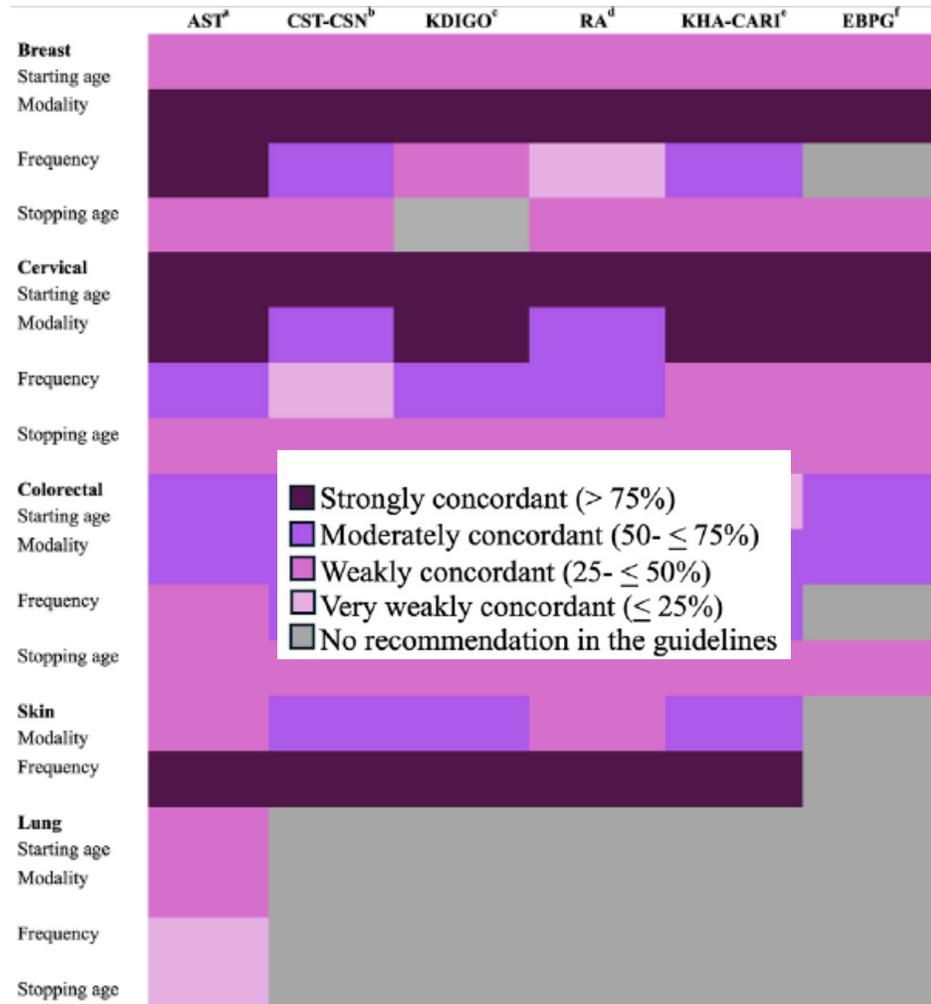
***High risk US TASK FORCE** : 50-80 y-o individuals with cumulative smoking history > 20 pack/year (active smokers / past history 15y)

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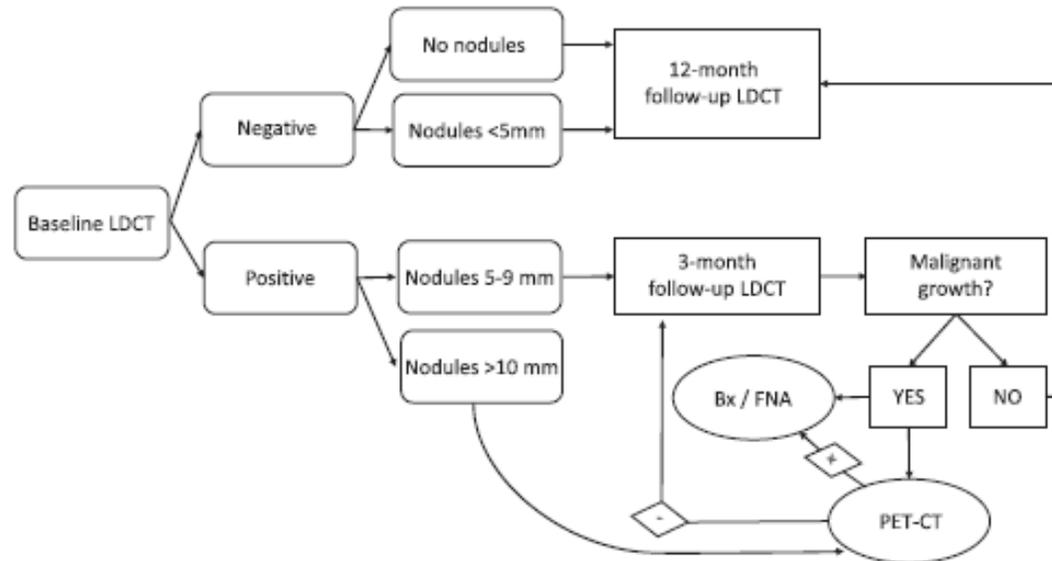
A Global Survey of Self-Reported Cancer Screening Practices by Health Professionals for Kidney Transplant Candidates and Recipients. *Saleem et al. Transpl Int 2025*

Concordance between screening recommendations in CPG among different societies



Prior studies of LDCT screening for LC in liver transplantation

Study	Patients	Criteria	Pack-year Median	Detection rate	Stage I
Herrero, 2013	N=60 2007-12	>10 pack-year	35	1sr round 11.8%	43%
Caballeros, 2023	N=124 2007-22	>10 pack-year	36.5	1st round 1.6% Overall 8.1%	83%
Ranjetoul, 2022	N=206 2005-19	Not reported ALD (retrosp.)	NR	11.2% (NR)	67%





2021 ILTS-SETH CONSENSUS CONFERENCE

Non-hepatic Cancer and Liver Transplantation: Shifting the Paradigm. Dropping the Cancer Stigma.

De Novo Malignancy After Liver Transplantation: Risk Assessment, Prevention, and Management—Guidelines From the ILTS-SETH Consensus Conference

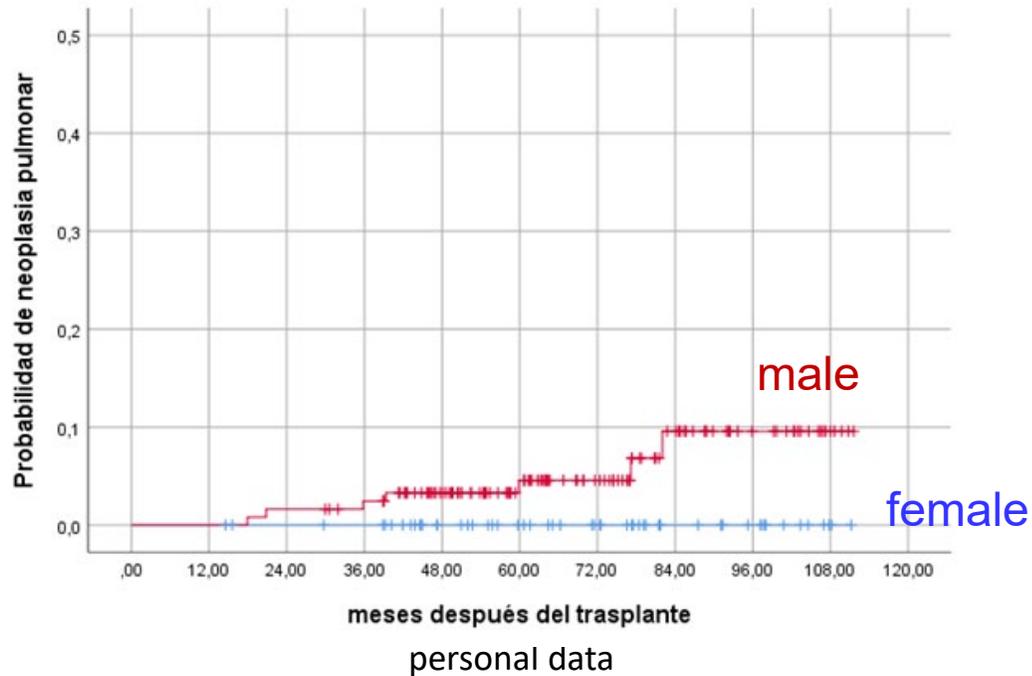
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ALL LT RECIPIENTS WHO ARE ACTIVE SMOKERS (OR HAVE QUIT <15 YEARS BEFORE) WITH A CUMULATIVE SMOKING HISTORY ABOVE 20 PACK-YEAR SHOULD UNDERGO LOW-DENSITY COMPUTED TOMOGRAPHY CHEST IMAGING ANNUALLY

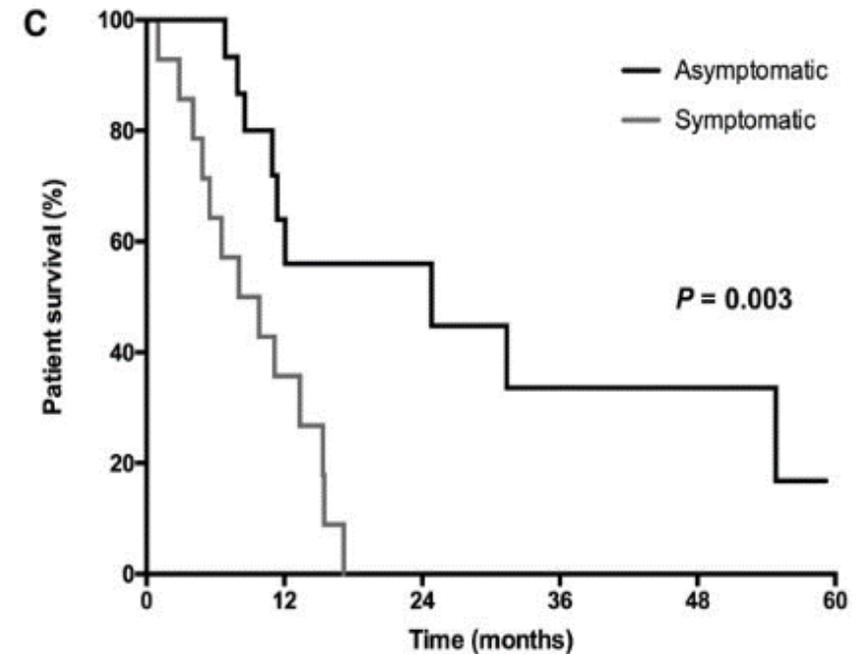
All smokers should receive smoking cessation education and medical intervention after LT (strength of recommendation: strong; level of evidence: high).

Our scenario after liver transplantation

Incidence of Lung Cancer
in Liver Transplant Patients older than 50
(Clinic, Cohort 2009 – 2015)



Small retrospective studies in liver transplantation showed better survival in presymptomatic Lung Cancer



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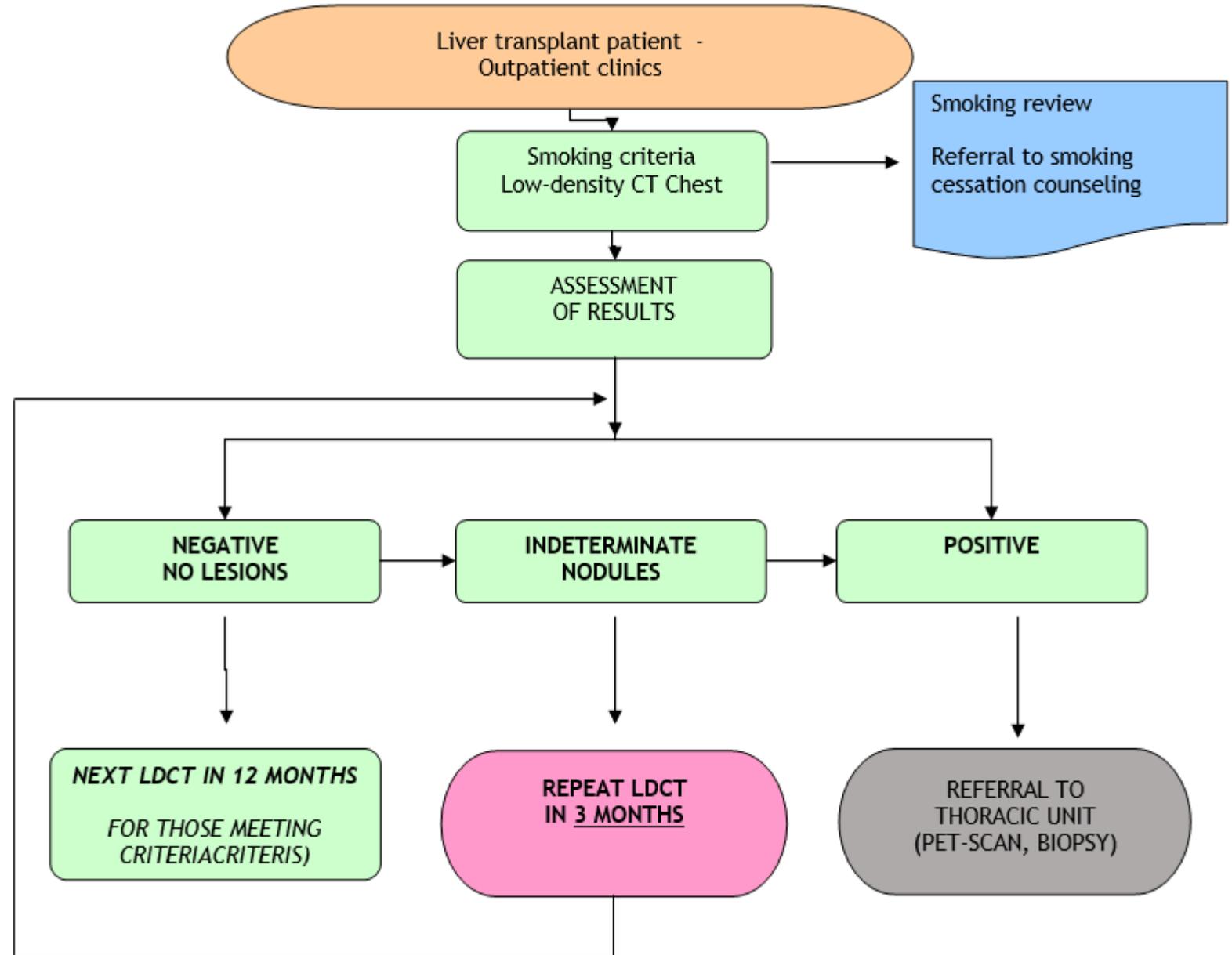
CLINIC-BARCELONA 2023

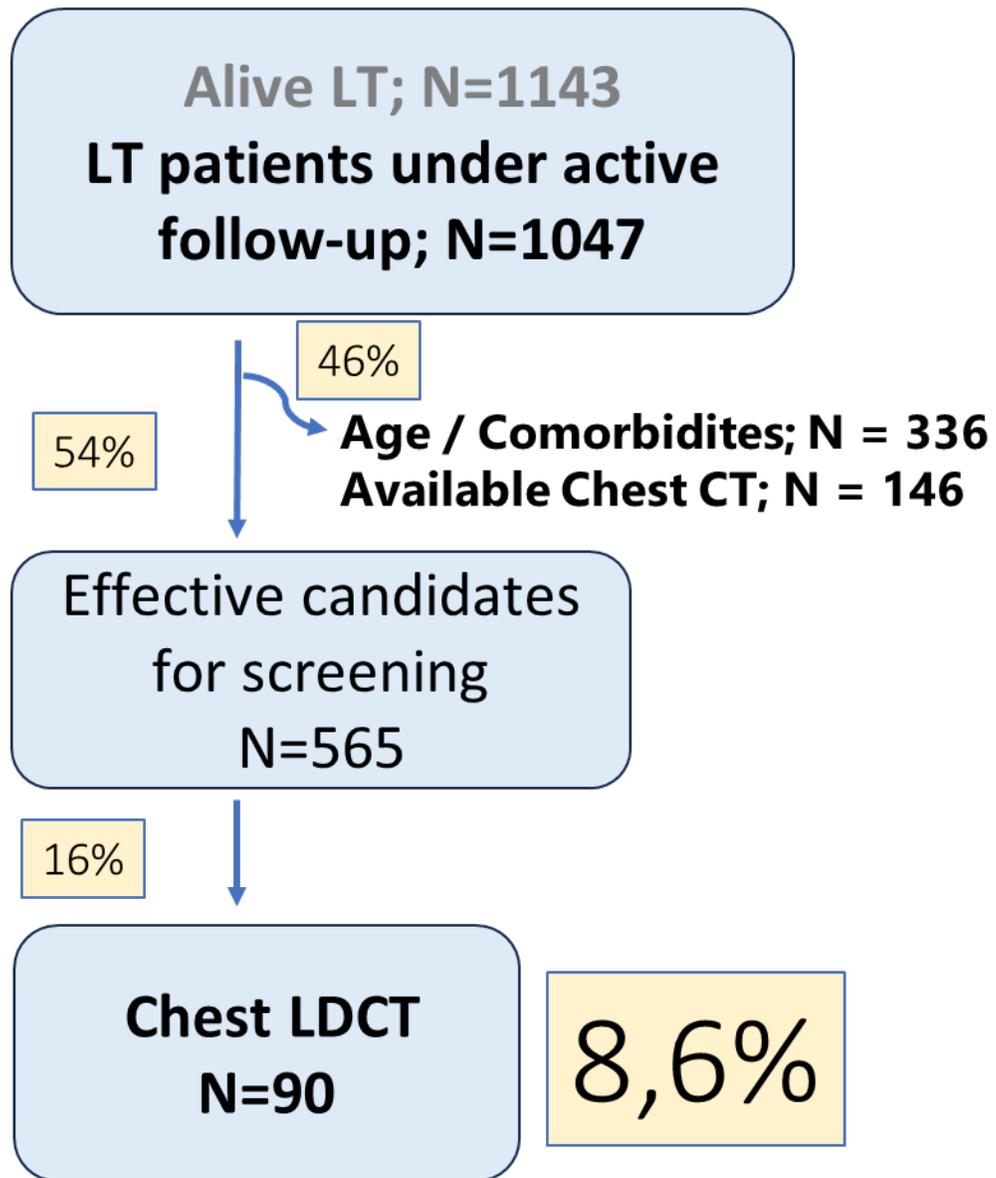
Inclusion Criteria for Screening :

- ≥ 20 pack-year
(active or quit < 15 y)
- age ≥ 50 and <80

Exclusion criteria: Chest CT within 12 months and/or contraindication to surgery or severe comorbidities.

End-of-screening: > 15 years after smoking cessation and /or onco-specific follow-up for solid cancer: hepatocellular carcinoma within 5-years after transplantation or other neoplasia.





Baseline characteristics (n=90)

Age (year old)	63 (58-69)
Gender (male)	70 (78%)
Liver disease before LT	
Alcohol (+/- viral)	59 (66%)
Viral	32 (35%)
Other	15 (17%)
Prior HCC	32 (36%)
Prior non-HCC cancer	5 (6%)
Years after LT	8 (3-14)
Cumulative dose (pack/year)	30 (20-41)
Active smoking	49 (54%)
Years after quitting (ex-smokers)	6 (3-9)

HCC: hepatocellular carcinoma. LT: liver transplantation.
 Median (interquartile range) or number (percentage).

Main Results of First Round of Chest LDCT (n=89, n=1 excluded by new-onset symptoms)

NEGATIVE

INDETERMINATE

POSITIVE

excluded

n=61 (68,5%)

n=18 (20,3%)

n=10 (11,2%)

n=1; HIV+

E IV

Squamous cell carc.

LDCT at 3 months

16 negative

2 positive

n=12 (13,4%)

PET-TC

NO CANCER

n=78 (86,6%)

N=1

Lesion 40mm

Negative PET-TC

FNB neg, resolution (3 mo)

CONFIRMED LUNG CANCER

n=11 (12,4%)

ALL POSITIVE PET-TC

1 negative

Age (years)	Gender	Years After LT	Liver disease prior to LT	Cumulative doce (pack/y)	Nodule size (mm)	Estadio tumoral	Histology (all NSLC)	Treatment	Inmunosupression at diagnosis
66	M	8	ArLD	30,0	9,00	EIA ₁ (T1N0M0)	Adenoc.	Segmentectomy	monotherapy TAC <5
58	M	8	ArLD +HCC	20,0	18,00	EIA ₃ (T1cN0M0)	Adenoc.	Chemotherapy	monotherapy TAC <5
74	M	20	HCV + HCC	50,0	32,00	EIB (T2aN0M0)	Adenoc.	Bilobectomy + chemo	EVE-MMF
59	M	2	HCV + HCC	30,0	8,00	EIB <i>pre</i> (T2aNx)	Squamous	Lobectomy (prehab)	TAC 3-5 + MMF/EVE
69	M	12	HCV	50,0	37,00	EIB (T2aN0M0)	Squamous	Lobectomy (prehab)	TAC 3-5 + MMF/EVE
63	F	19	ArLD	95,0	34,00	EIIA (T2bN0M0)	Squamous	Lobectomy	monotherapy TAC <5
70	M	4	HCV + HCC	50,0	63,00	EIIB (T3N0M0)	Squamous	Lobectomy,chemo/RT	TAC 3-5 + MMF/EVE
67	M	5	ArLD	50,0	24,00	EIIB (T3N0M0)	Squamous	Lobectomy (prehab)	monotherapy TAC <5
70	M	19	ArLD	40,0	38,00	EIIIA (T2N2M0)	Squamous	Bilobectomy, chemo	monotherapy TAC <5
56	M	7	ArLD	30,0	48,00	EIVA (T3N2M1)	Squamous	Chemotherapy	TAC 3-5 + MMF/EVE
70	M	12	ArLD +HBV	45,0	30,00	EIVA(T4N3M1)	Adenoc.	Chemo, pleurodesis	monotherapy TAC <5

M: male, F: female. ArLD: alcohol-related liver disease. HCV: hepatitis C virus. HBV: hepatitis B virus. HCC: hepatocellular carcinoma; NSLC: non-small cell lung cancer; TAC: tacrolimus; EVE: everolimus; MMF: mycophenolate.

- ✓ All NSLC: 64% squamous, 36% adenoc.
- ✓ Median size in LDCT: **31(22-35) mm**
- ✓ 45 % stage I
- ✓ 63 % surgical treatment
- ✓ Only CD>30pack/y was associated with lung cancer →

	No lung cancer	Lung Cancer	p
Age (years)	61 (57-66)	64 (57-69)	0,148
Male	76 %	91 %	0,264
Alcohol-related	64 %	72 %	0,593
Prior HCC	37,5 %	36,4 %	0,982
Time from LT to LDCT (years)	7 (3-14)	13 (7-19)	0,059
Asctive smoking	53,2 %	63,6 %	0,344
Smoking cessation (years)	6 (4-8)	4 (0-8)	0,109
Cumulative dose (pack/y)	29 (20-40)	45 (30-50)	0,163
C.D. > 30 pack/year	2,3 %	21.2 %	0,007
Prior cancer (any)	39,2%	54,5%	0,112
Enphysema by LDCT	40,5%	63,6%	0,147

Conclusions after implementation in LT in our center

- Applicability: < 10% of transplant patients met the criteria for Lung Cancer Screening.
- The first round of screening yielded a high rate of lung cancer detection ($\approx 12\%$)
- Second round yielded no cases (some indetermined nodules ungoing).
- **Lower false-positive rate** (1/89) compared to general population.
- 2/3 patients were diagnosed at **early stages** and underwent surgical resection.
- Heart transplantation now enrolling patients

Take home messages

- ✓ Smoking cessation strategies, starting at listing, should be a priority and standard of care for all SOT.
- ✓ SOT at risk of Lung Cancer are more likely to benefit from screening due to higher SIR and SMR.
- ✓ LDCT screening in SOT is feasible and represent an opportunity to improve the outcomes.