Le dépistage du cancer bronchique: Où en est-on?

Toulouse 7-10-2019

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Conlicts of Interest disclosure

I have the following potential conflicts of interest to report

- Grants received from Belgian Cancer League & from Foundation Against Cancer for participation in NELSON trial

GOLF
Groupe d'Oncologie de Langue Française

SPLF
SOCIÉTÉ DE PNEUMOLOGIE DE LANGUE FRANÇAISE

Lung cancer screening: time for implementation?

Toulouse 7-10-2019

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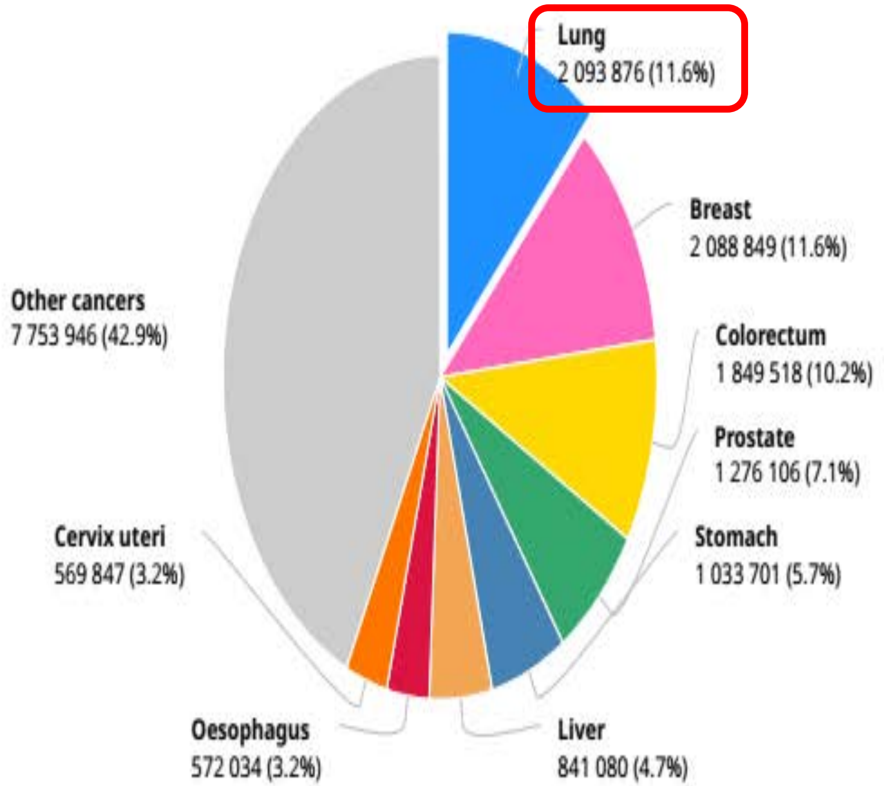
International Agency for Research on Cancer
World Health Organization

Lung
Source: Globocan 2018

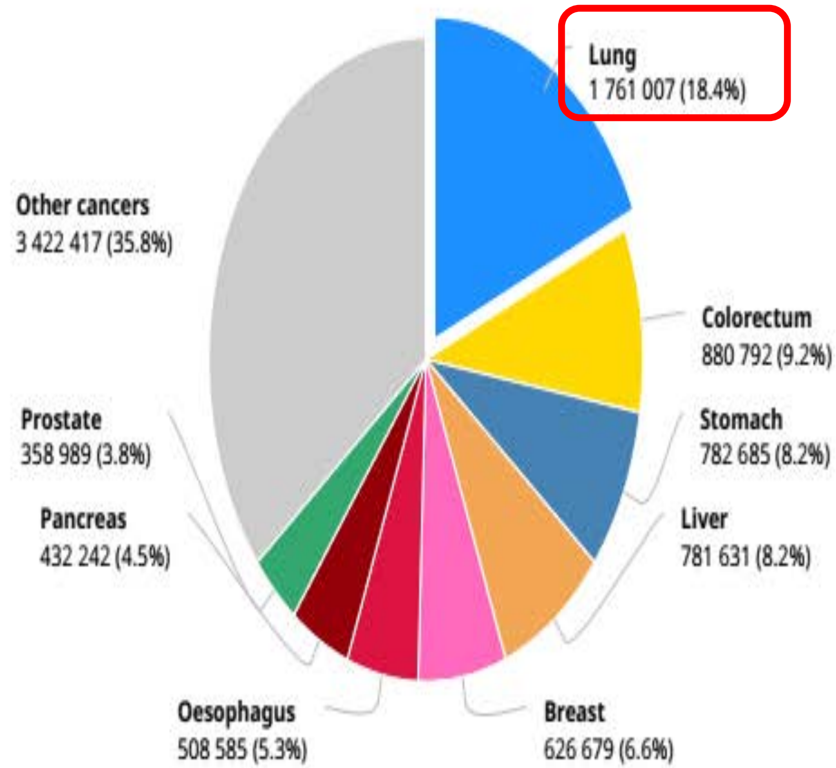
GCO

Number of new cases in 2018, both sexes, all ages



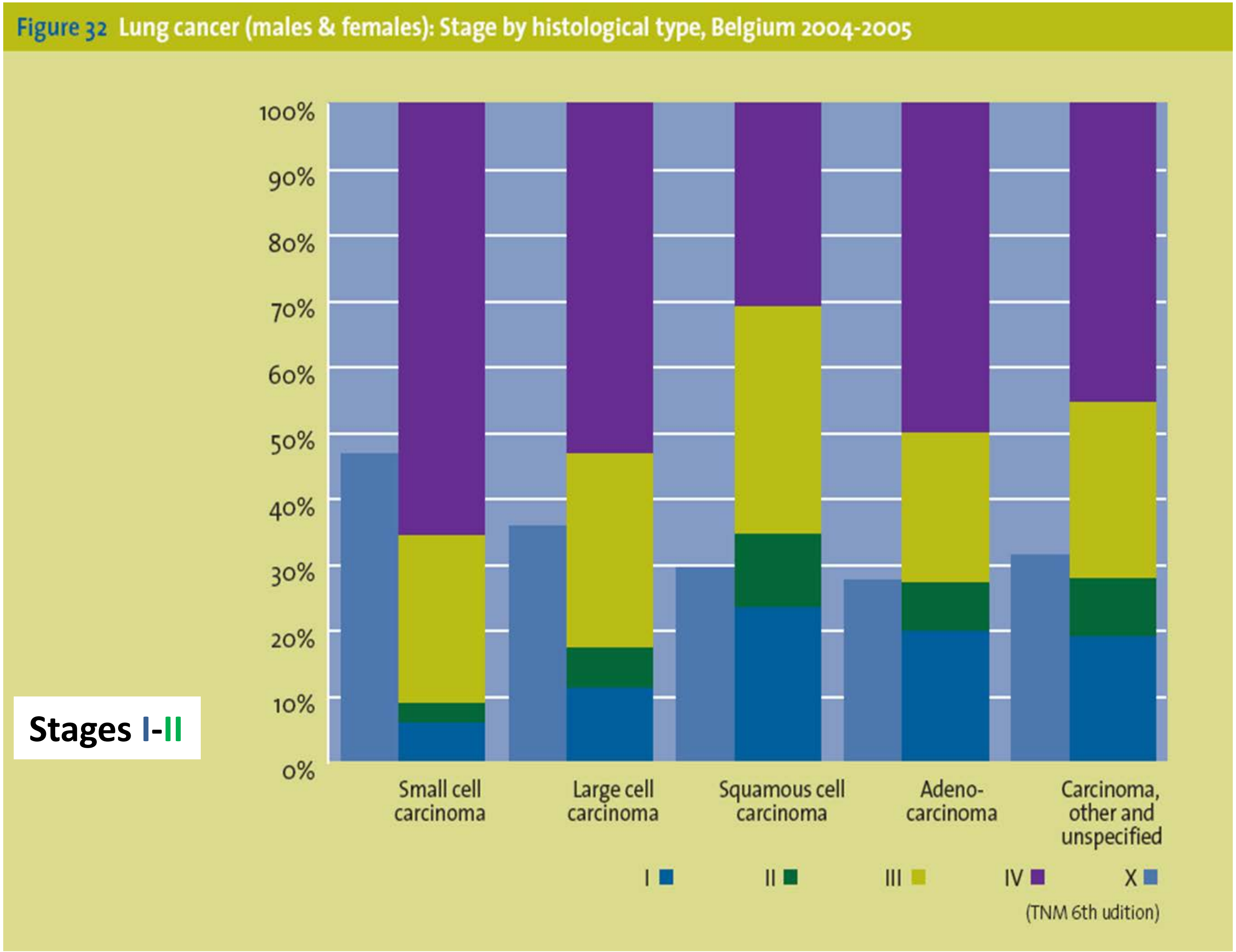
Total: 18 078 957 cases

Number of deaths in 2018, both sexes, all ages



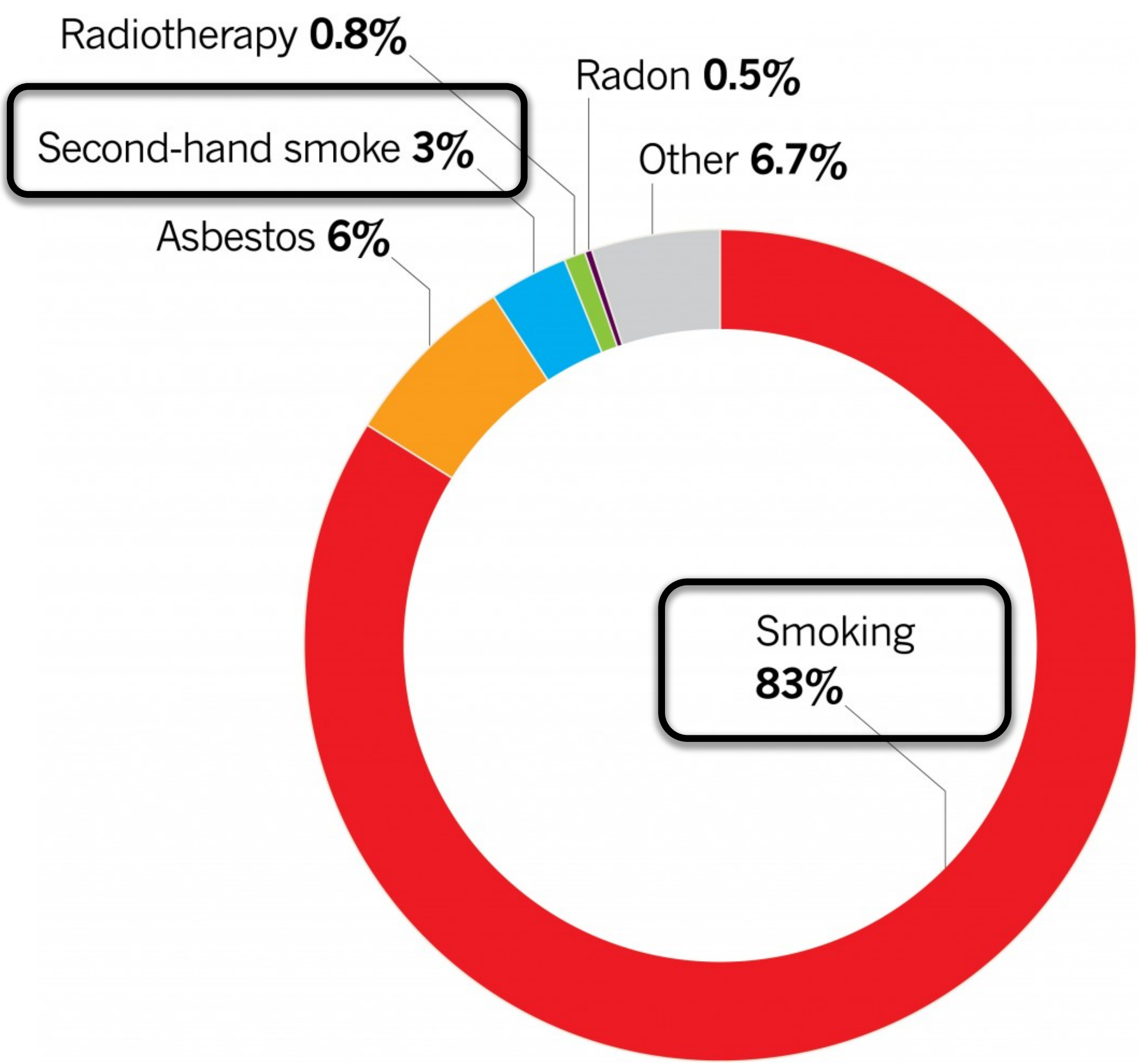
Total: 9 555 027 deaths

Early detection of lung cancer



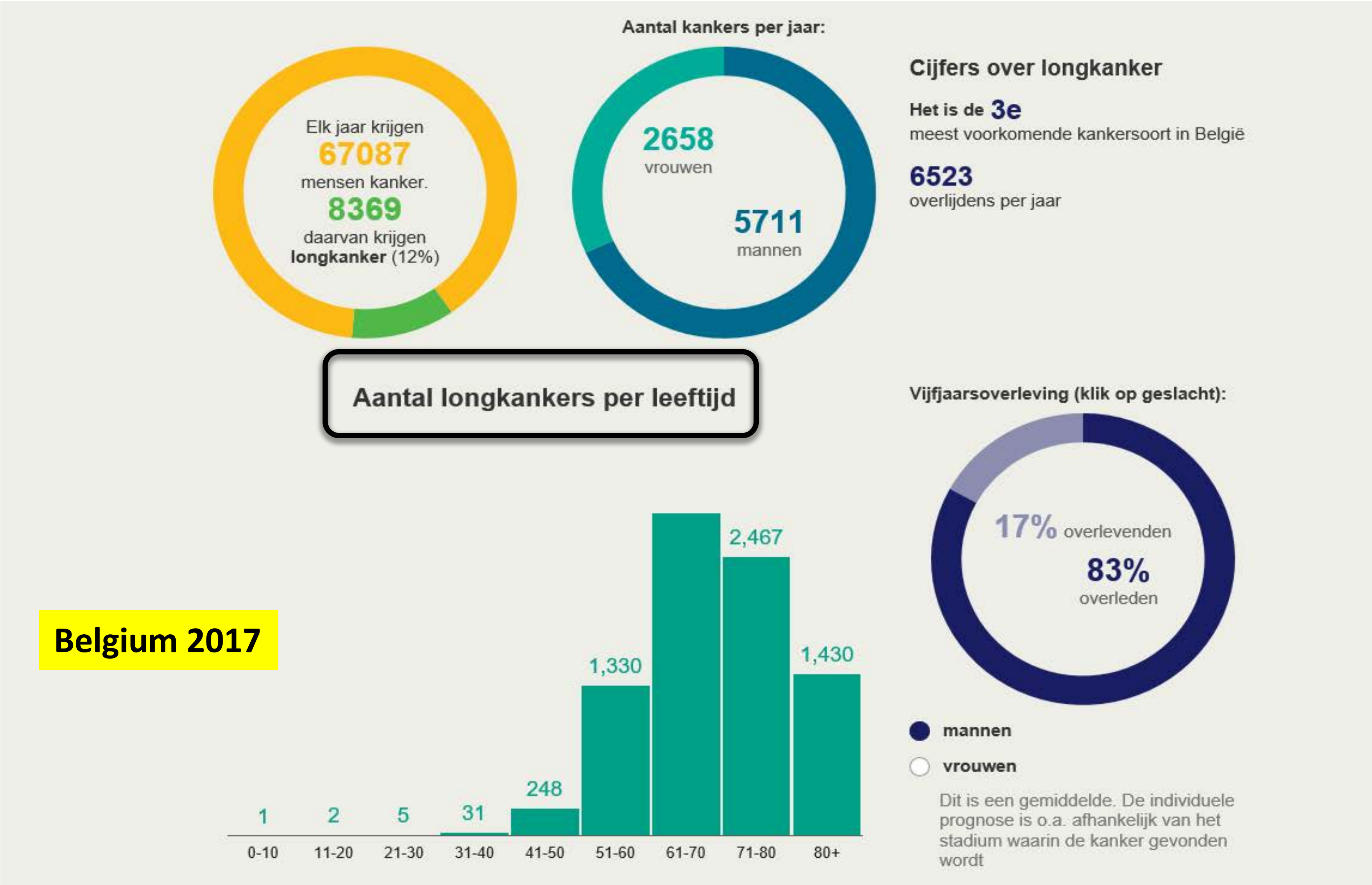
www.kankerregister.org

Persons at high risk for lung cancer



http://blogs.nature.com/ofschemesandmemes/2014/09/11/the-big-issues-affecting-lung-cancer-worldwide

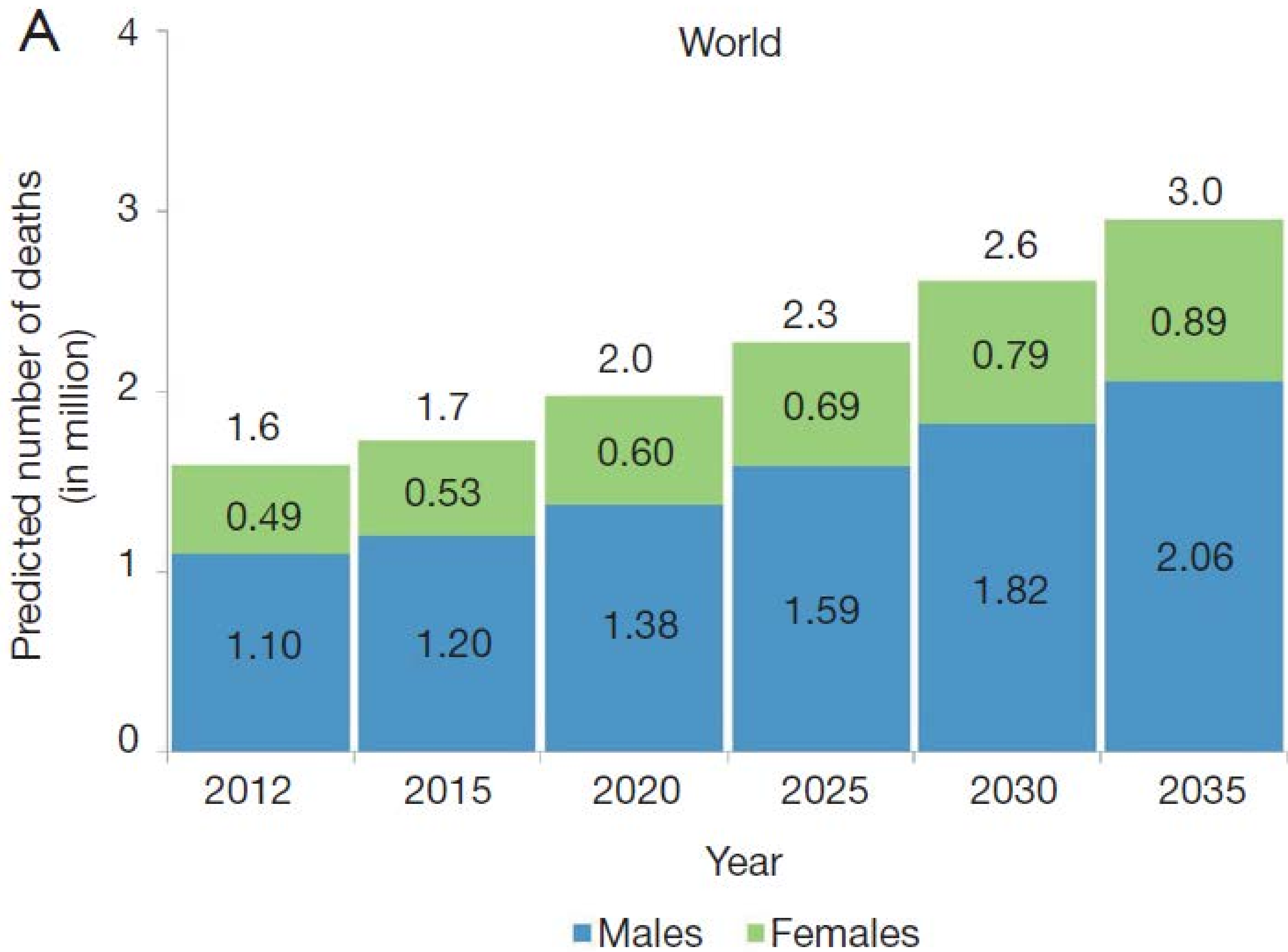
Persons at high risk for lung cancer



Data source: http://www.kankerregister.org

Persons at high risk for lung cancer

Predicted number of deaths



Didkowska J et al Ann Transl Med 2016;4(8):150

Curative lung cancer treatment

Age-adjusted 5 YSR for Lung Cancer

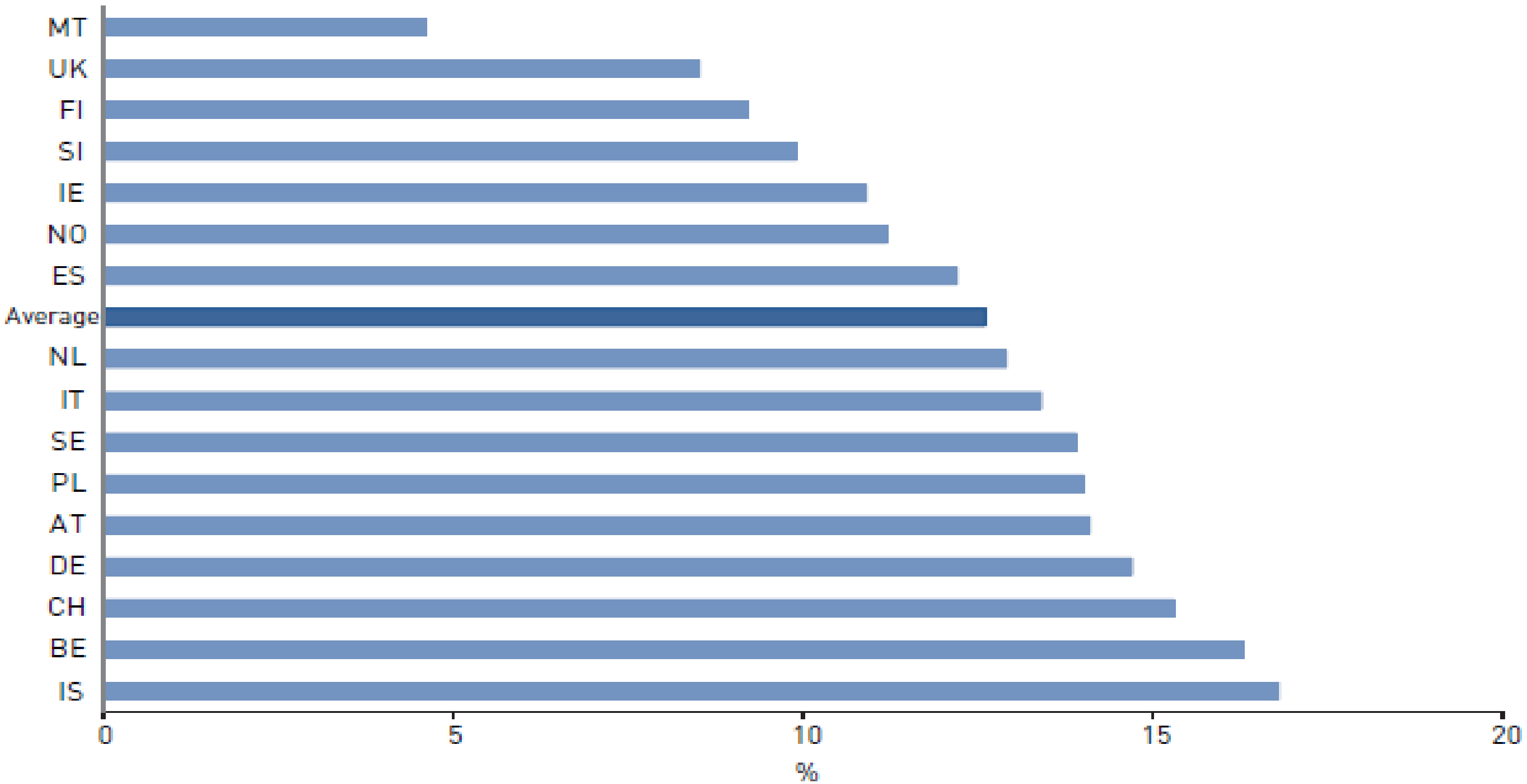
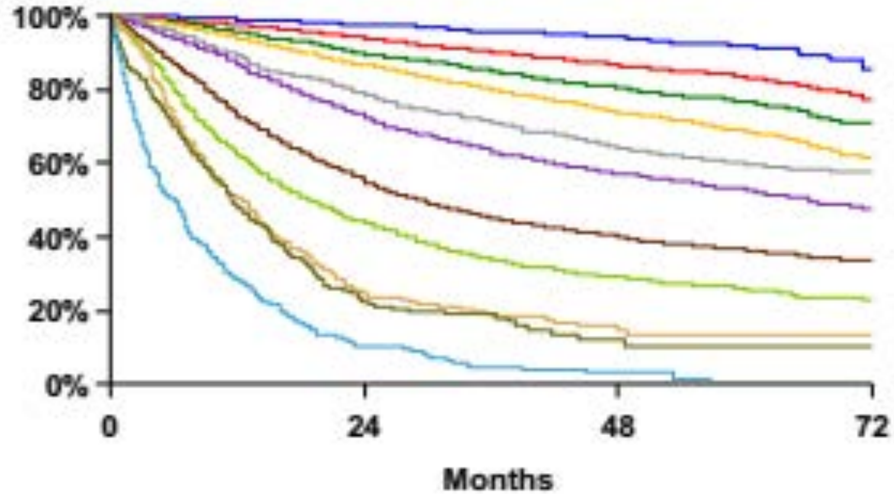


Figure 4 – Age-adjusted 5-year survival from lung cancer in selected European countries among patients diagnosed 2000–2002 relative to that of the general population. Survival for the UK has been derived from estimates for England, Scotland, Wales and Northern Ireland and the average independently calculated. Data from EUROCARE-4 study (www.eurocare.it).

European Lung White Book 2013 (ERS publication)

Curative lung cancer treatment



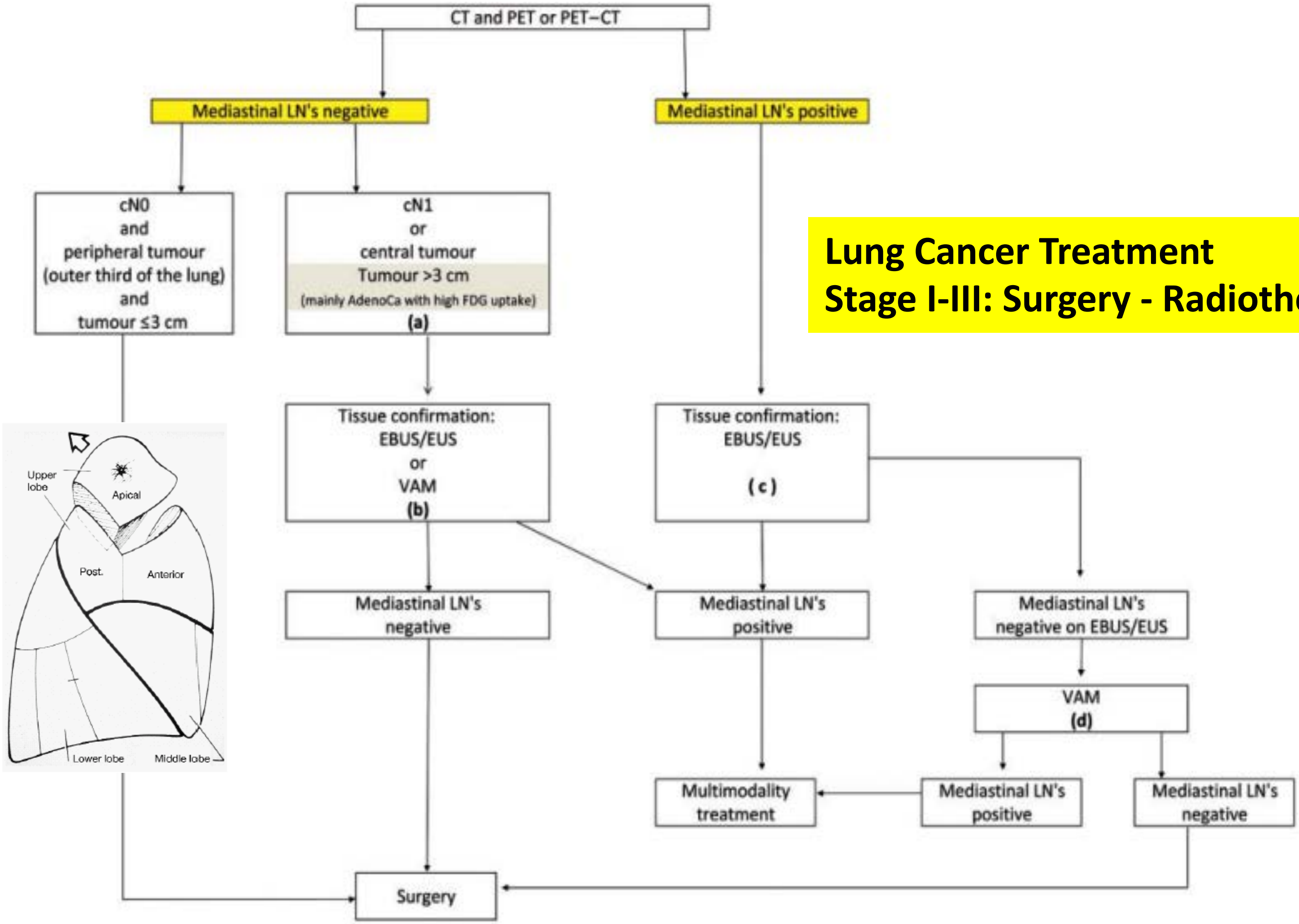
Lung Cancer
Overall Survival by clinical stage

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 P et al The IASLC Lung Cancer Staging Project J Thorac Oncol 2015

Curative lung cancer treatment

Lung Cancer Treatment
Stage I-III: Surgery - Radiotherapy



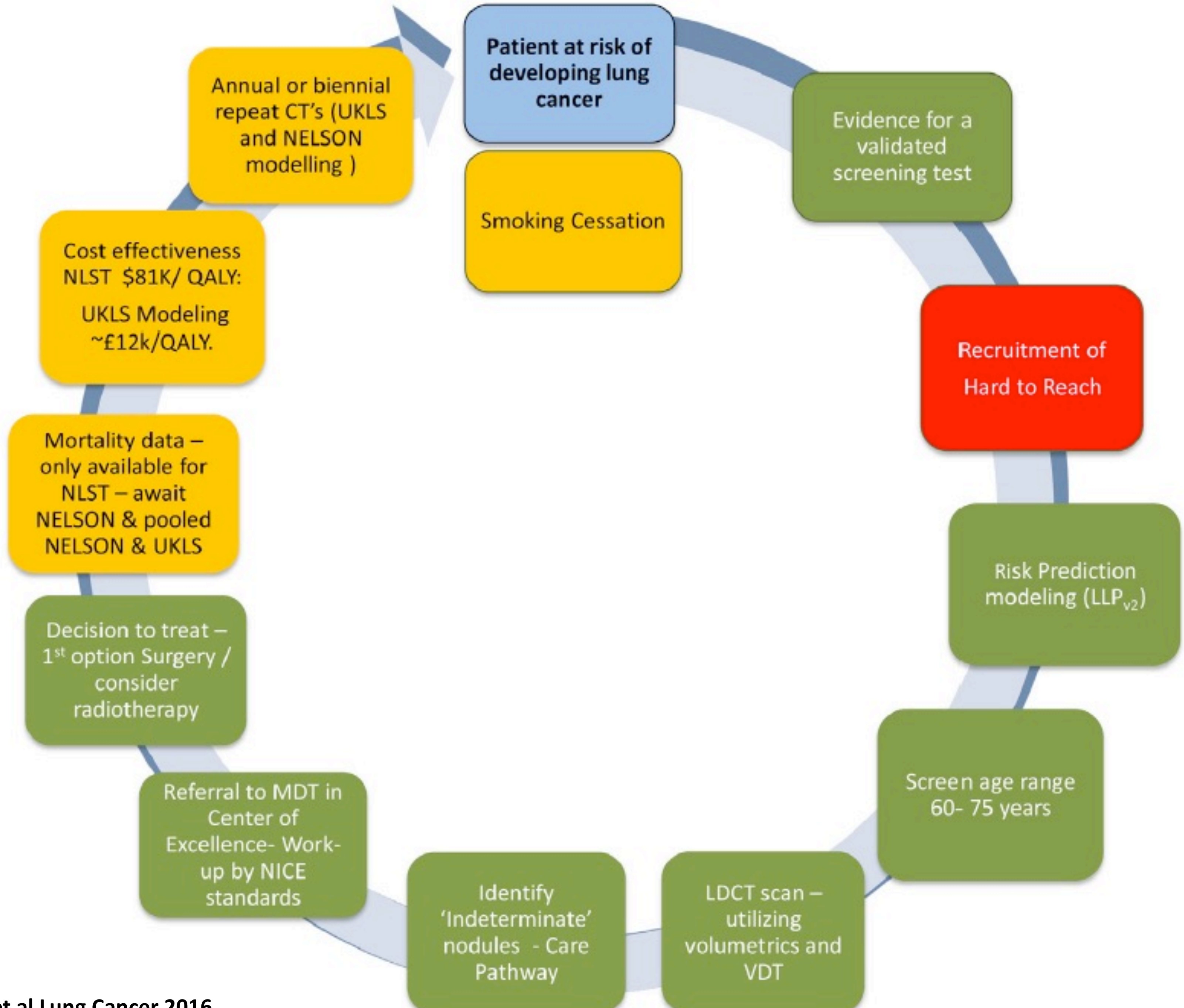
Systemic therapy

- Adjuvant ChT should be offered to patients with resected stage II and III NSCLC [I, A] and can be considered in patients with resected stage IB disease and a primary tumour > 4 cm [II, B]. Pre-existing comorbidity, time from surgery and postoperative recovery need to be taken into account in this decision taken in a multidisciplinary tumour board [V, A].

Postmus PE et al Early and Locally Advanced NSCLC: ESMO Clinical Practice Guidelines Ann Oncol 2017

"Lung cancer screening aims to reduce lung cancer related mortality with relatively limited harm through early detection and treatment"

Van der Aalst CM, ten Haaf K, de Koning H. Lancet Respir Med 2016;4:749-61



Field JK et al Lung Cancer 2016

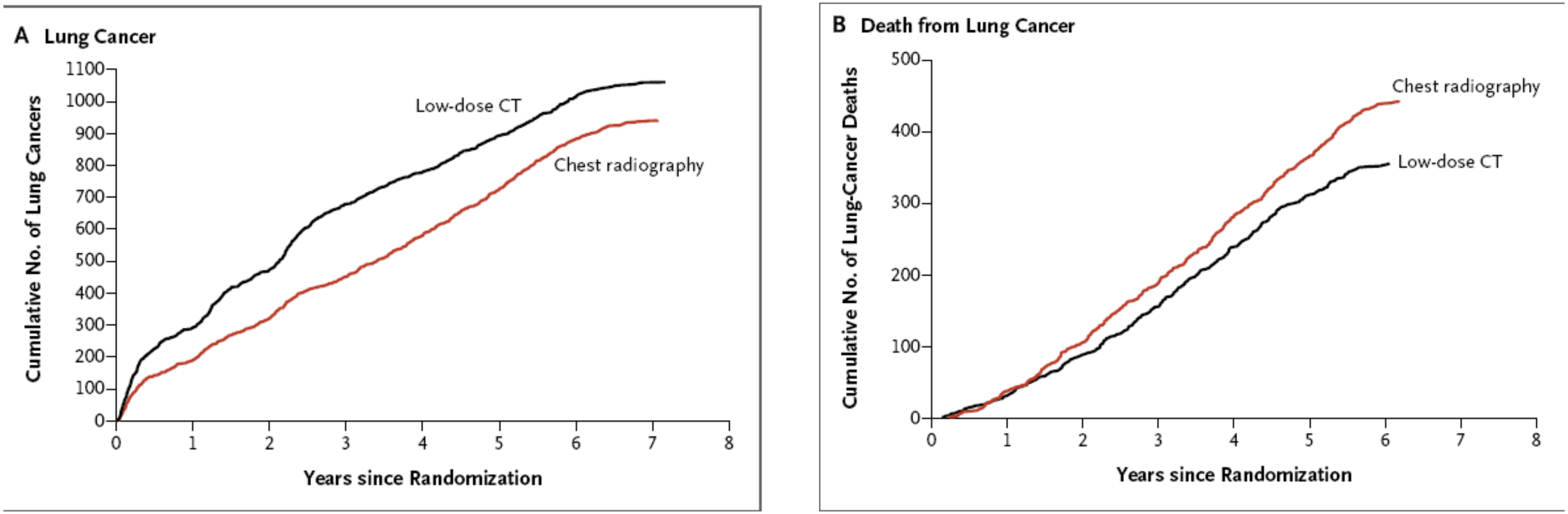
Lung Cancer Screening **PROs**

- Early detection (stage I-II) of lung cancer
- In persons at high(est) risk
- Curative treatment
- Improved lung cancer specific survival
- Smoking cessation

Lung Cancer Screening **CONs**

- Selection of screening (‘highest risk’) participants
- Cost/Benefit of lung cancer screening
- Cumulative Radiation risk (serial CT’s)
- Risks of harm (invasive examinations) in screening-positive participants
- False positive screening results
- Overdiagnosis
- No screening BUT Smoking cessation!

Improved Lung Cancer specific survival



NLST

Total number of deaths due to lung cancer :
247 vs 309 deaths/100.000 pers.yrs (CT vs RX group)

→Relative reduction in LC mortality of 20.0% or HR=0,80 (95%CI 0,73-0,93)
→Reduction in all cause mortality of 6,7% or HR=0,93 (95% CI 0,86-0,99)

Number Needed to Screen with LDCT to prevent 1 death : 320

Aberle DR et al New Engl J Med 2011

	Sample size	Recruitment	Follow-up (years)	Comparison (nodule measurement)	Smoking history	Smoking cessation	Age group (years)	Screening interval	
NLST[8] (USA, 2002)	53 454	Volunteers	6·4*	CT vs chest radiography (D)	≥30 pack-years	<15 years	55–74	Three annual screenings	V
NELSON[9] (Netherlands/ Belgium, 2004)	15 822	Population-registry	7·4*	CT vs usual care (V)	≥15 cigarettes per day for ≥25 years or ≥10 cigarettes per day for ≥30 years	≤10 years	50–75	Four screenings with different screening intervals: 1 year, 2 years, and 2·5 years	(V)
DLCST[10] (Denmark, 2004)	4104	Volunteers	9·8*	CT vs usual care (V)	≥20 pack-years	≤10 years	50–70	Five annual screenings	X
MILD[11] (Italy, 2000 and 2005)	1035 (pilot) and 4099 (main study)	Volunteers	4·4*	CT vs usual care (V)	≥20 pack-years	≤10 years	≥49	Five annual vs three biennial screenings	V longterm
UKLS[12] (UK, 2011–12)	4055	Population-registry	..	CT vs usual care (V)	Predicted risk of ≥5% of lung cancer diagnosis within 5 years, and 5-year risk for lung cancer	≤10 years	50–75	One screening	?
LUSI[13] (Germany, 2007)	4052	Population	3–6·5	CT vs usual care (D)	≥15 cigarettes per day for ≥25 years or ≥10 cigarettes per day for ≥30 years	≤10 years	50–69	Four annual screenings	V
ITALUNG[14] (Italy, 2003)	3206	General practitioners	6	CT vs usual care (D)	≥20 pack-years	≤10 years	55–69	Four annual screenings	V longterm
DANTE[15] (Italy, 2005)	2450	Volunteers	8·4	CT vs clinical review (D)	≥20 pack-years	≤10 years	60–74	Four annual screenings	X

Dates provided are trial start dates. D=diameter. V=volume. *Median.

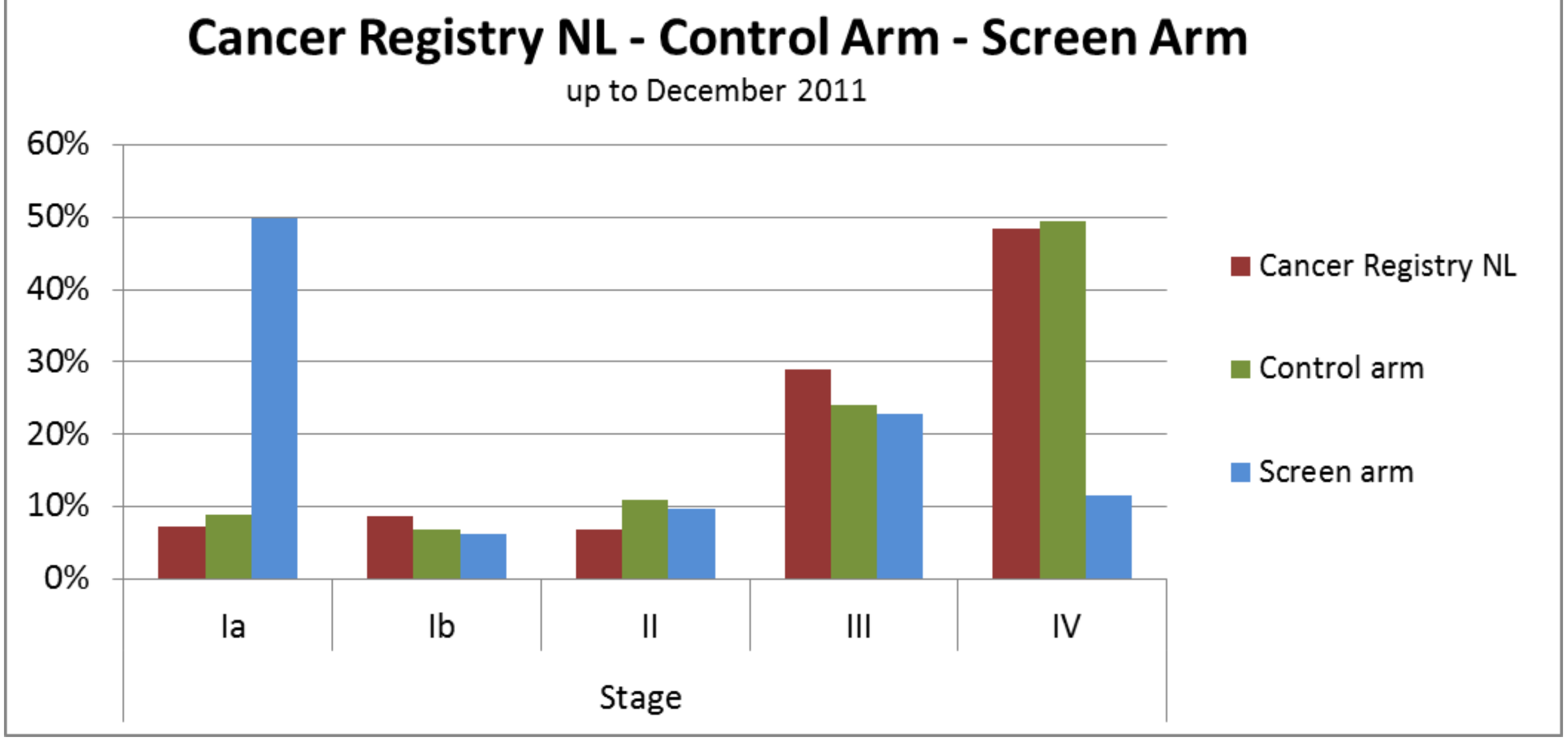
Table 1: Large-scale randomised controlled lung cancer screening trials

Van der Aalst CM, ten Haaf K, de Koning H. Lancet Respir Med 2016;4:749-61

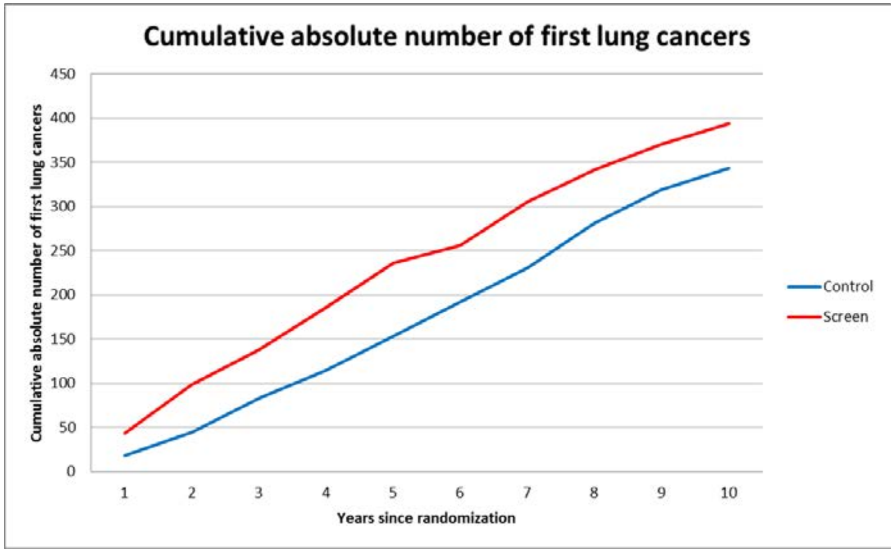
LDCT lung cancer screening RCTs

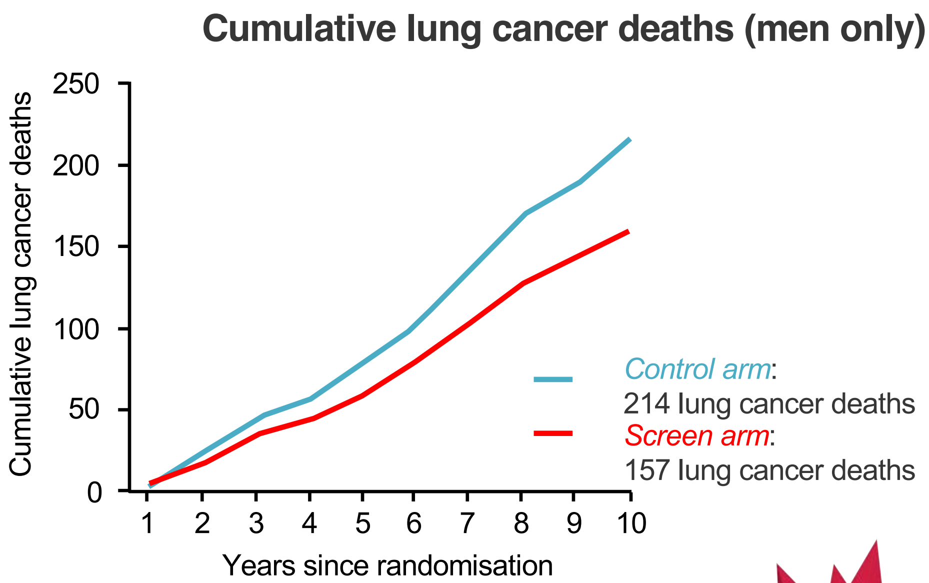
	Year 1	Year 2	Year 4	Year 6.5	Year 10
	CT screening	CT screening	CT screening	CT screening	
Screen arm n=7,900	 n=7,557 95.6% uptake	 n=7,295 92.3% uptake	 n=6,922 87.6% uptake	 n=5,279 66.8% uptake	
Control arm n=7,892	**Usual care (no screening)**				NATIONAL LINKAGES - Statistics Netherlands/ Belgium - Dutch/ Belgium Cancer Registry - Centre for Genealogy CAUSE OF DEATH REVIEW

Lung Cancer Stage (males NL) 7th TNM



Yousaf-Khan et al., in preparation





de Koning H. et al J Thorac Oncol 2018;13(10):S185 PL02.05

Lung cancer mortality rate ratio (95% CI)	Year 8	Year 9	Year 10
MALES	**0.75** P=0.015 (0.59-0.95)	**0.76** P=0.012 (0.60-0.95)	**0.74** P=0.003 (0.60-0.91)
FEMALES	**0.39** P=0.0037 (0.18-0.78)	**0.47** P=0.0069 (0.25-0.84)	**0.61** P=0.0543 (0.35-1.04)

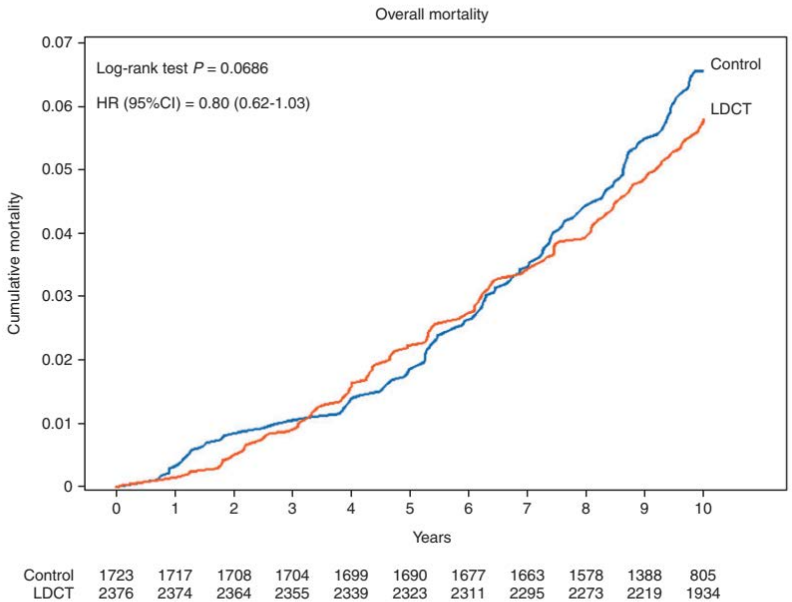
Rand: 23-12-2003 – 06-07-2006

FU: 23-12-2003 – 31-12-2015

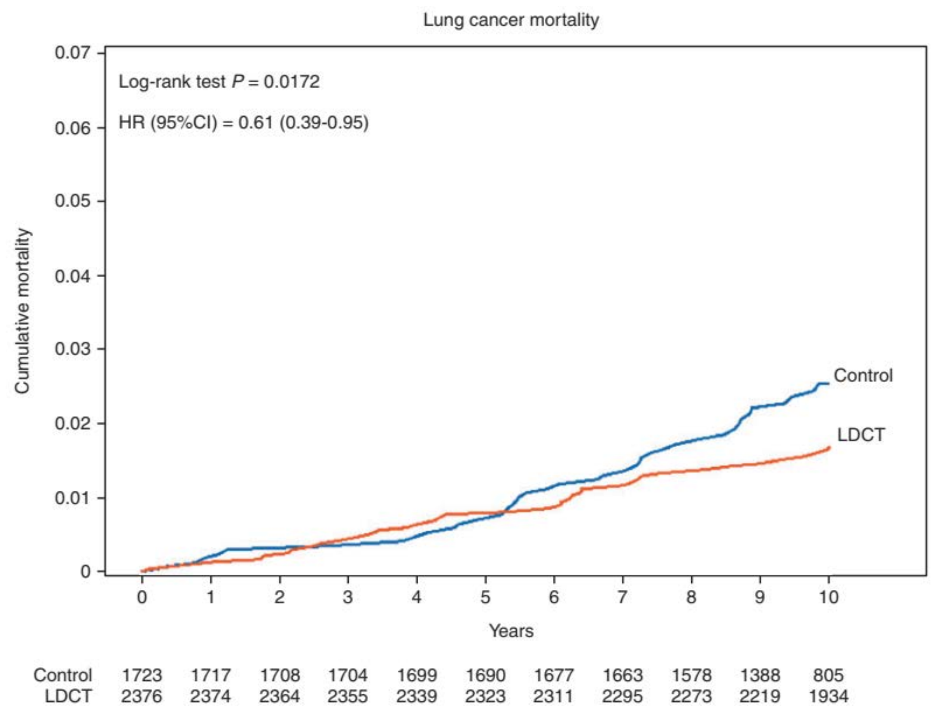
FU 94% complete
year 10

Improved Lung Cancer specific survival

Prolonged lung cancer screening reduced 10-year mortality in the MILD trial: new confirmation of lung cancer screening efficacy



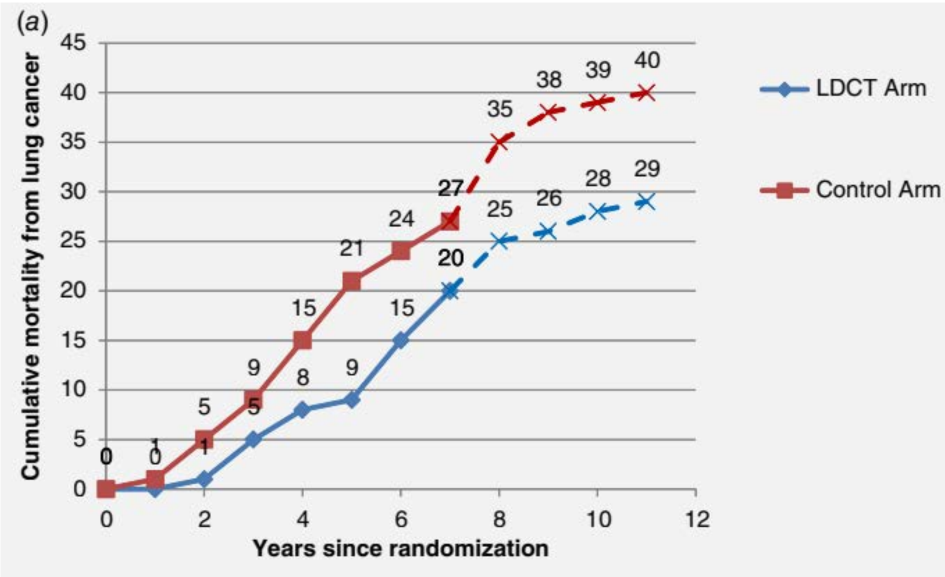
Cumulative Overall mortality by arm, over 10 yrs of FU
Reduction of 20%



Cumulative Lung Cancer Mortality by arm, over 10 yrs of FU
Reduction of 39%

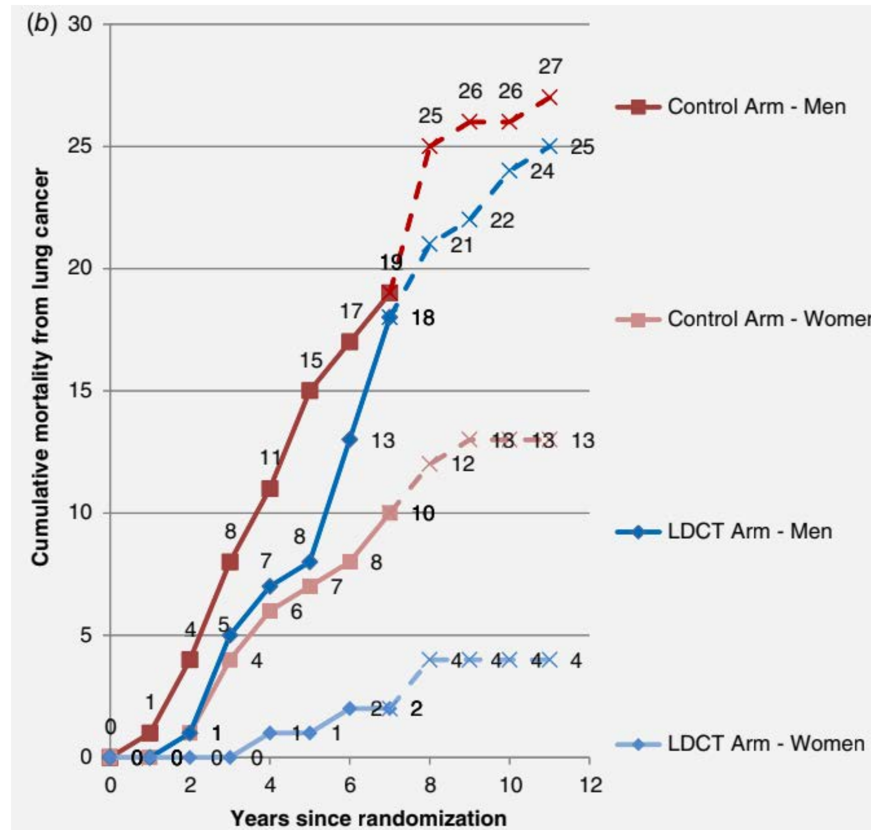
Pastorino U et al Ann Oncol 2019

Improved Lung Cancer specific survival



Lung cancer mortality reduction by LDCT screening—Results from the randomized German LUSI trial

Cumulative LC mortality over 5 yrs of FU
Reduction of 26% (p=0,21 NS)



Cumulative LC Mortality by sex over 5 yrs of FU
HR 0,31 p=0,04 in women
HR 0,94 p=0,81 in men

Becker N et al Int J Cancer 2019

Smoking Cessation in Lung Cancer Screening

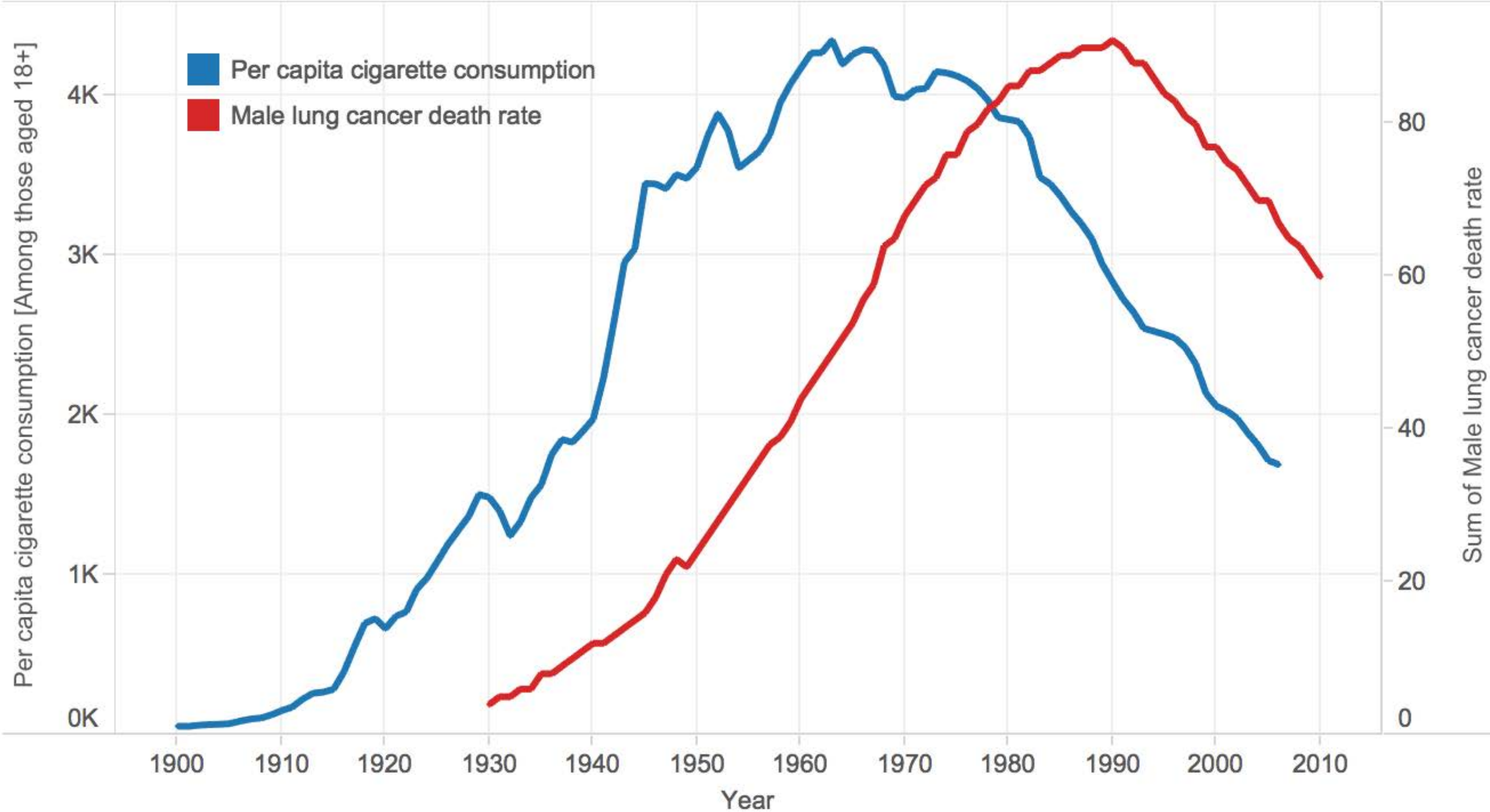
Interventions for Smoking Cessation

- **Non-pharmacologic**
  - Self help (also Internet) **NNT 50**
  - Advice/information **NNT 50**
  - Individual counselling **NNT 25**
  - Group counselling **NNT 20**
  - Telephone counselling **NNT 40**
- **Pharmacologic**
  - NRT **NNT 20**
  - Bupropion **NNT 15**
  - Varenicline **NNT 8**
- **Alternative interventions**
  - hypnosis, acupuncture, laser therapy ??

NNT = number needed to treat

Report from Federaal Kenniscentrum voor de Gezondheidszorg (KCE), Belgium 2004

Trends in Tobacco Use and Lung Cancer Death Rates in the U.S.



Death rates source: US Mortality Data, 1960-2010, US Mortality Volumes, 1930-1959, National Center for Health Statistics, Centers for Disease Control and Prevention.
Cigarette consumption source: US Department of Agriculture, 1900-2007.

Does smoking cesstion lead to a decrease in lung cancer deaths? YES

No screening BUT JUST Smoking Cessation!

VLAANDEREN STOPT MET ROKEN.BE

ACTIEZONE | NIEUWS | VORMING & TOOLS | LOKAAL AANBOD | VOLWASSENEN | JONGEREN | OUDERS | PROFESSIONALS

Vlaanderen stopt met roken > Professionals > Basisfeiten over roken > Wie rookt?

WIE ROOKT?

ALGEMENE CIJFERS

GEZONDHEIDSENQUÊTE

Uit de in 2015 gepubliceerde cijfers van de laatste Gezondheidsenquête blijkt dat nog altijd bijna één op de vier Belgen rookt: 23% rookt, 19% doet het dagelijks, 4% occasioneel. In Vlaanderen gaat het in totaal over 22% rokers.

Sinds 2008 is het aantal rokers met amper 2% verminderd. De prevalentie van roken is op haar hoogst in de bevolking op actieve leeftijd (25 tot 64 jaar), daar vindt men tussen 26% en 29% rokers. Er is een verontrustende stijging van het roken en dagelijks roken bij jonge vrouwen.

Het aantal sigaretten dat dagelijks wordt gerookt – gemiddeld 16 – is sinds tien jaar onveranderd gebleven. Eén dagelijkse roker op zes vertoont tekenen van zware tabaksafhankelijkheid. In de leeftijdsgroep van 35-44 jaar is het aantal rokers en dagelijkse rokers het hoogst (respectievelijk 29% en 24%).

ROOKENQUÊTE

Een andere infobron is de jaarlijkse rookenquête van de Stichting tegen Kanker. Uit de meest recente (2017) blijkt dat in België nog 1 op 5 Belgen rookt en dat er geen significant verschil is in het aantal rokers tegenover 2015.

17% rookt dagelijks.

PROFESSIONALS

- Basisfeiten over roken
- Boodschap over stoppen
- Werk
- Gemeente
- Eerstelijnszorg
- school

Since 2008 smoking prevalence barely declined

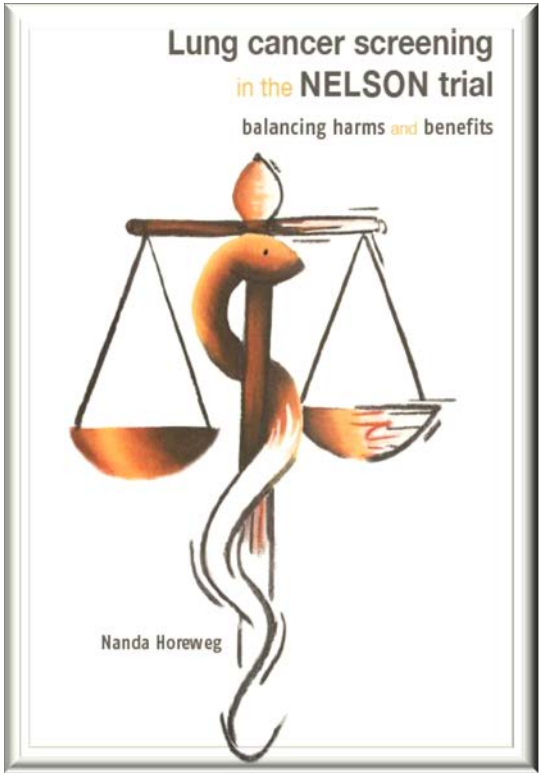
Vlaanderen.be Website accessed 01/2019

LDCT Lung Cancer Screening

Benefits

LC mortality reduction

Reduction in stages III-IV



Harms

False positives

Overdiagnosis

Overtreatment

Radiation exposure

Costs

QOL

Smoking behaviour

In: European Guide on Quality Improvement in Comprehensive Cancer Control (2017)
by Tit Albreht, R. Kiasuwa & M. van den Bulcke

- The step-wise decision-making concerning **potential new cancer screening programmes** include the establishment of evidence of effectiveness, benefits that outweigh the harms, and cost-effectiveness.

Slide by courtesy of H de Koning

Selection of screening ('highest risk') participants

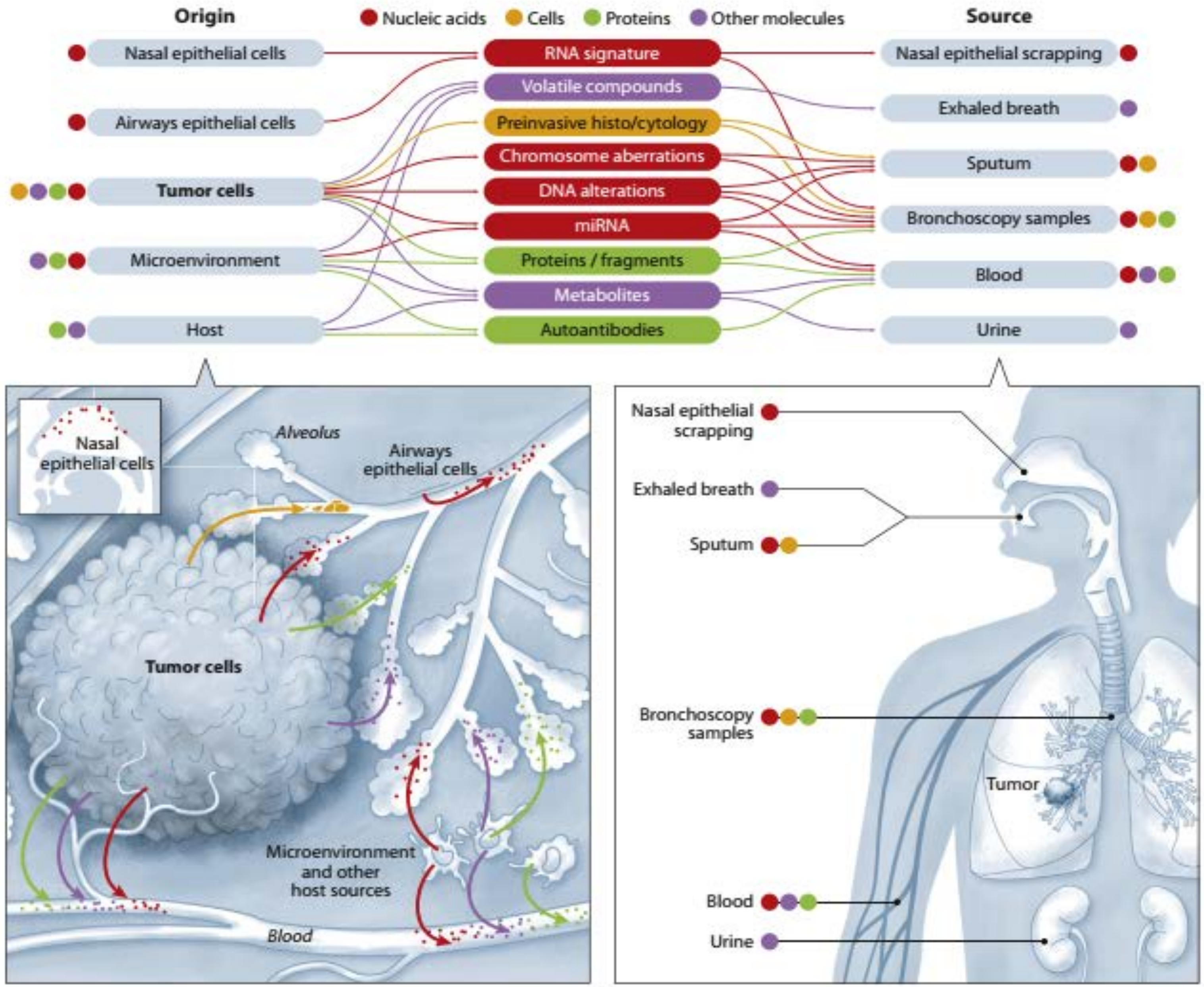
Best selection of screening participants

- USPSTF Age (55-80 yrs) & smoking behaviour (30PY)
- PLCOm2012 model
- LLPv2 Liverpool Lung Project risk prediction model, used inRCT, Subjects selected with a ≥ 5% risk of developing LC in next 5 yrs
- Using other inclusion criteria (biological data, …)

Table 2. Modified Logistic-Regression Prediction Model ($PLCO_{M2012}$) of Cancer Risk for 36,286 Control Participants Who Had Ever Smoked.*

Variable	Odds Ratio (95% CI)	P Value	Beta Coefficient
Age, per 1-yr increase†	1.081 (1.057–1.105)	<0.001	0.0778868
Race or ethnic group‡			
White	1.000		Reference group
Black	1.484 (1.083–2.033)	0.01	0.3944778
Hispanic	0.475 (0.195–1.160)	0.10	−0.7434744
Asian	0.627 (0.332–1.185)	0.15	−0.466585
American Indian or Alaskan Native	1		0
Native Hawaiian or Pacific Islander	2.793 (0.992–7.862)	0.05	1.027152
Education, per increase of 1 level†§	0.922 (0.874–0.972)	0.003	−0.0812744
Body-mass index, per 1-unit increase†	0.973 (0.955–0.991)	0.003	−0.0274194
Chronic obstructive pulmonary disease (yes vs. no)	1.427 (1.162–1.751)	0.001	0.3553063
Personal history of cancer (yes vs. no)	1.582 (1.172–2.128)	0.003	0.4589971
Family history of lung cancer (yes vs. no)	1.799 (1.471–2.200)	<0.001	0.587185
Smoking status (current vs. former)	1.297 (1.047–1.605)	0.02	0.2597431
Smoking intensity¶			−1.822606
Duration of smoking, per 1-yr increase†	1.032 (1.014–1.051)	0.001	0.0317321
Smoking quit time, per 1-yr increase†	0.970 (0.950–0.990)	0.003	−0.0308572
Model constant			−4.532506

Humphrey LL et al Ann Intern Med 2013; Tammemägi MC et al NEJM 2013 & JAMA Network Open 2019; Cassidy A et al Br J Cancer 2008



Seijo LM et al J Thorac Oncol 2018

Overdiagnosis

The excess of lung cancers detected by LDCT divided by all lung cancers detected by screening in a LDCT arm

- In NLST about 18,5% overdiagnosis in screen-detected LCs
- Expected to be less in NELSON (results awaited)

Estimates of P_A and P_s

	Overdiagnosis, % (95% CI)	
Lung Cancer Type	P_A	P_S
All lung cancers	11.0 (3.2 to 18.2)	18.5 (5.4 to 30.6)
All NSCLC, including BAC and NOS	14.4 (6.1 to 21.8)	22.5 (9.7 to 34.3)
All NSCLC, excluding BAC and including NOS	7.1 (−2.3 to 15.6)	11.7 (−3.7 to 25.6)
BAC only	67.6 (53.5 to 78.5)	78.9 (62.2 to 93.5)

Abbreviations: BAC, bronchioloalveolar cell carcinoma; NOS, not otherwise specified; NSCLC, non-small cell lung cancer.

P_A : the total amount of excess LC cases between LDCT and CXR arm over the total number of LCs diagnosed in the screen arm
P_S : the total amount of excess LC cases between LDCT and CXR arm over all screen-detected LCs in LDCT screening arm

Patz EF Jr et al JAMA Intern Med 2014;

False positive screening results

Low rate of false positive screening scans

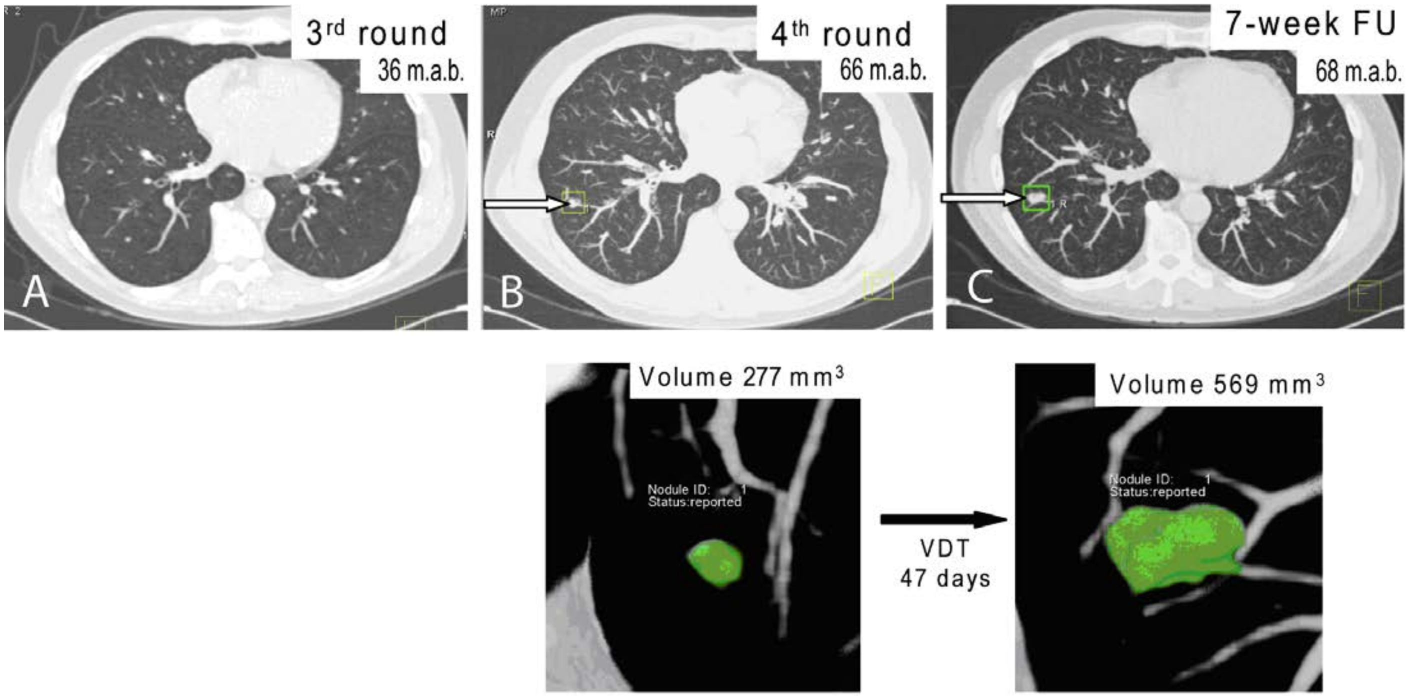
	High referral protocol	Low referral protocol with published mortality analyses			Low referral protocol with no published mortality analyses			
	NLST[16] (n=53 454)	DLCST[17,18] (n=4104)	DANTE[19] (n=2450)	MILD[11,20] annual and biennial (n=4099)	NELSON[21,22] (n=15 822)	LUSI[23] (n=4052)	ITALUNG[24] (n=3206)	UKLS[25] (n=4055)
(Continued from previous page)								
Interval lung cancers	44	32	38	Annual: 5; biennial: 5	52	4	2	..
Positive screening tests (%)								
Overall	24·2%	3·8%	37·3%	..	2·0%	8·8%	19·6%	5·7%
At least one positive test	39·1%	..	..	..	6·0%‖	..	52·7%	..
T_0	27·3%	8·7%	..	Annual: 14·0%; biennial: 15·0%	2·6%	22·2%	30·3%	5·7%
T_1	27·9%	2·3%	..	..	1·8%	4·7%	17·3%	..
T_2	16·8%	2·7%	..	..	2·4%	4·0%	16·1%	..
T_3	..	2·2%	..	..	2·0%	5·7%	13·7%	..
T_4	..	2·8%	..	..	..	5·7%	..	..
False-positives (%)								
Of all scans	17 497/75 126 (23·3%)	302/9800 (3·1%)	..	..	355/29735 (1·2%)	747/9121 (8·2%)	1003/5333 (18·8%)	72/1994 (3·6%)
Of all positive scans	17 497/18 146 (96·4%)	302/371 (81·4%)	..	..	355/598 (59·4%)	747/805 (92·8%)	1003/1044 (96·1%)	72/114 (63·2%)
Per participant basis	..	..	22·9 %	..	273/7582 (3·6%)‖	..	..	..

- **False positives of all scans: 1,2%(NELSON) - 23,3%(NLST)**
- **False positives of all positive scans: 59,4%(NELSON) – 96,4%(NLST)**

Van der Aalst CM et al Lancet Respir Med 2016

Nodule management

- NELSON nodule management plan



Heuvelmans M.A. et al, J Thorac Imaging 30, 101-107, 2015

Results: nodule volume algorithm based on LC probability

Screening result	Nodule volume
negative	< 100 mm³
indeterminate*	≥ 100 to 300 mm³
positive	≥ 300 mm³

*Follow-up CT for VDT assessment:

- final screening result negative for VDT ≥ 600 days
- final screening result positive for VDT < 600 days

End-to-end lung cancer screening with three-dimensional deep learning on low-dose chest computed tomography

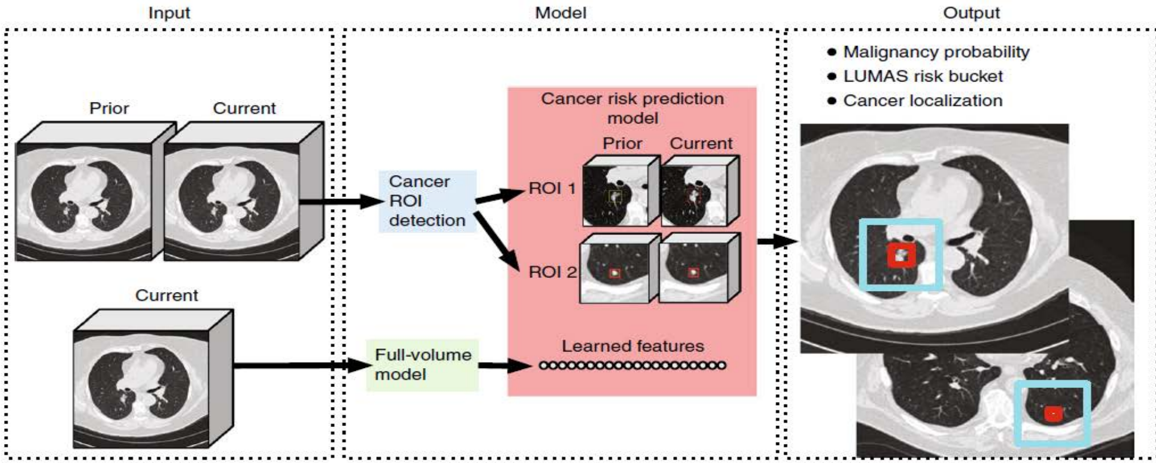
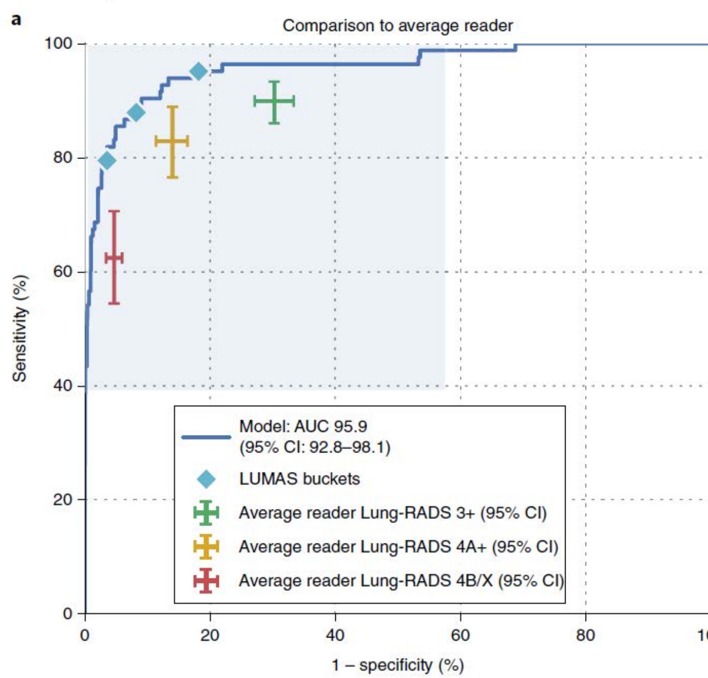


Fig. 1 | Overall modeling framework. For each patient, the model uses a primary LDCT volume and, if available, a prior LDCT volume as input. The model then analyzes suspicious and volumetric ROIs as well as the whole-LDCT volume and outputs an overall malignancy prediction for the case, a risk bucket score (LUMAS) and localization for predicted cancerous nodules.



Ardila D et al Nature Med 2019

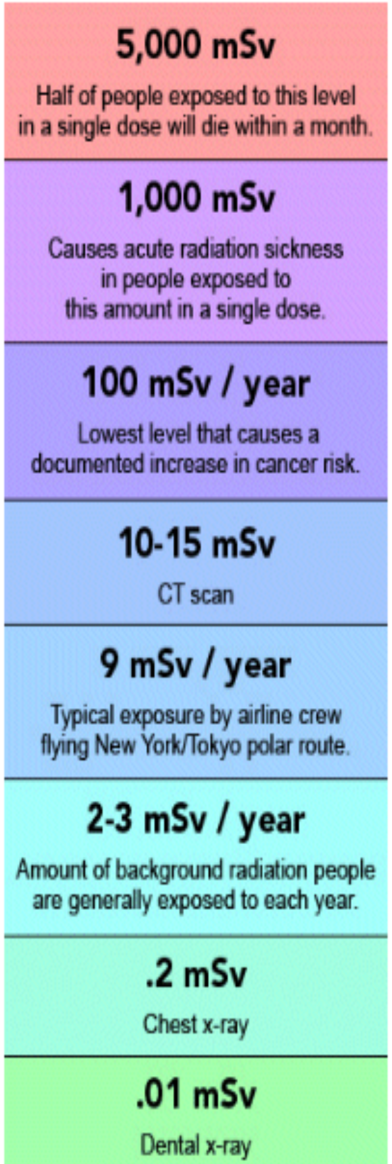
Risks of harm (invasive examinations)

Maximal protection of screening participants

- Unintended harms of screening (radiation exposure)
- Psychosocial consequences of false positives and overdiagnosis
- Invasive examinations for screen-detected lung nodules

Van der Aalst CM et al Lancet Respir Med 2016

Cumulative Radiation risk (serial CT's)



Radiation exposition to screening participants

Table 5 Recently reported effective dose values from lung cancer screening LDCT studies

Report (year of publication)	Effective dose	Method of estimation
Rampineli et al. (2017) [23]	1.2	DLP
Lee et al. (2017) [33]	2.01-2.80	Organ doses **NLST**
Messerli et al. (2017) [34]	0.13*	DLP
	0.3*	DLP+SSDE**
Jacobs et al, (2017) [35]	1.3	DLP
	3.8	DLP+SSDE**
Miao et al. (2017) [36]	0.67*	DLP
	1.20	DLP
Current study	0.71	Organ doses
	0.52	DLP+SSDE

*Described as ultra-low dose chest CT protocol

**DLP-derived effective dose corrected for body size to provide size specific dose estimates (SSDE)

Screening (bi-)annually?

Key Points

- *Effective dose from lung cancer screening low-dose CT may be <1 mSv.*
- *Screening with modern low-dose CT minimally aggravates lifetime cancer induction intrinsic risk.*
- *Dosimetry of lung cancer screening low-dose CT should encounter the radiation burden from the localizing scan projection radiography.*
- *DLP method may underestimate effective dose from low-dose chest CT by 27 %.*

Persinakis K et al Eur Radiol 2018; Figure from: http://www.aboutcancer.com/radiation_imaging_risks_0311.htm (accessed 2019)

Cost/Benefit of lung cancer screening

Cost per country

- Influence of smoking eligibility criteria for screening trial on Cost effectiveness
- But also the amount of CT's and CT detected nodule management plan (volumetry)
- Tobacco cessation measures

- NLST: 81,000 US dollars/QALY
- UKLS modeling study: 12,000 Pound/QALY
- Canada: 52,000 CAD dollars/QALY
- Switzerland (MISCAN Modeling study): less than 50,000 € per LYG (Life Year gained) or less than 70,000 € per QALY

Field JK et al Lung Cancer 2016; Black WC et al NEJM 2015; Goffin WL et al JAMA Oncol 2015; Whynes DK et al Cost Eff Resour Alloc 2008; Tomonaga Y et al Lung Cancer 2018

…or screening AND Smoking Cessation!

Impact of low-dose CT screening on smoking cessation among high-risk participants in the UK Lung Cancer Screening Trial

Kate Brain,[1] Ben Carter,[1,2] Kate J Lifford,[1] Olivia Burke,[1] Anand Devaraj,[3] David R Baldwin,[4] Stephen Duffy,[5] John K Field[6]

Key messages

What is the key question?
What is the effect on smoking cessation of taking part in the UK randomised pilot trial of low dose CT lung screening?

What is the bottom line?
CT lung cancer screening does not appear to falsely reassure smokers or reduce their motivation to stop smoking.

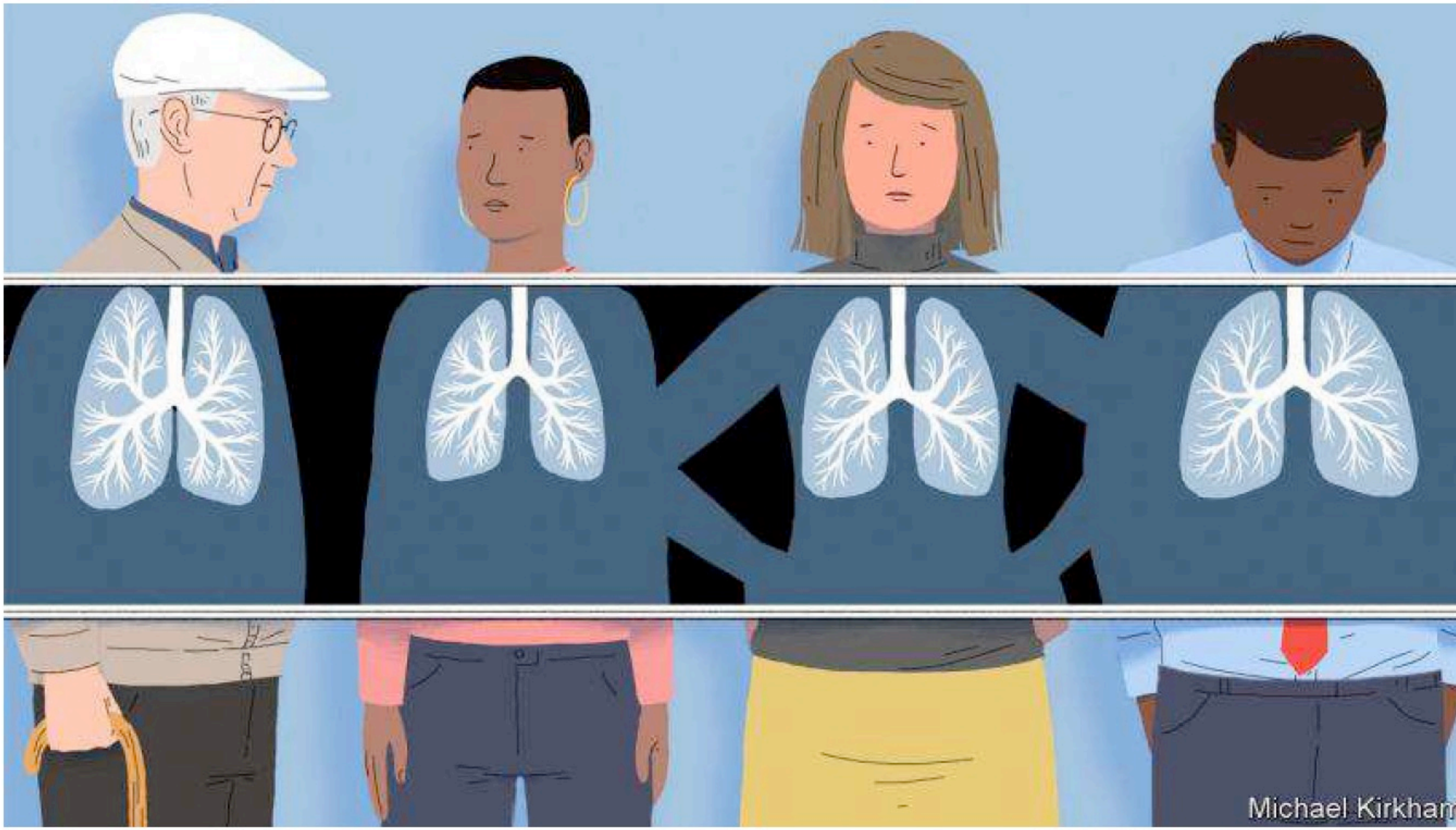
Why read on?
For clinicians and policy makers who are considering implementation of risk-stratified lung cancer screening, this study adds to evidence suggesting that integrating CT screening with evidence-based smoking cessation interventions could prompt quitting in motivated high-risk smokers.

Brain K et al Thorax 2017

Cancer

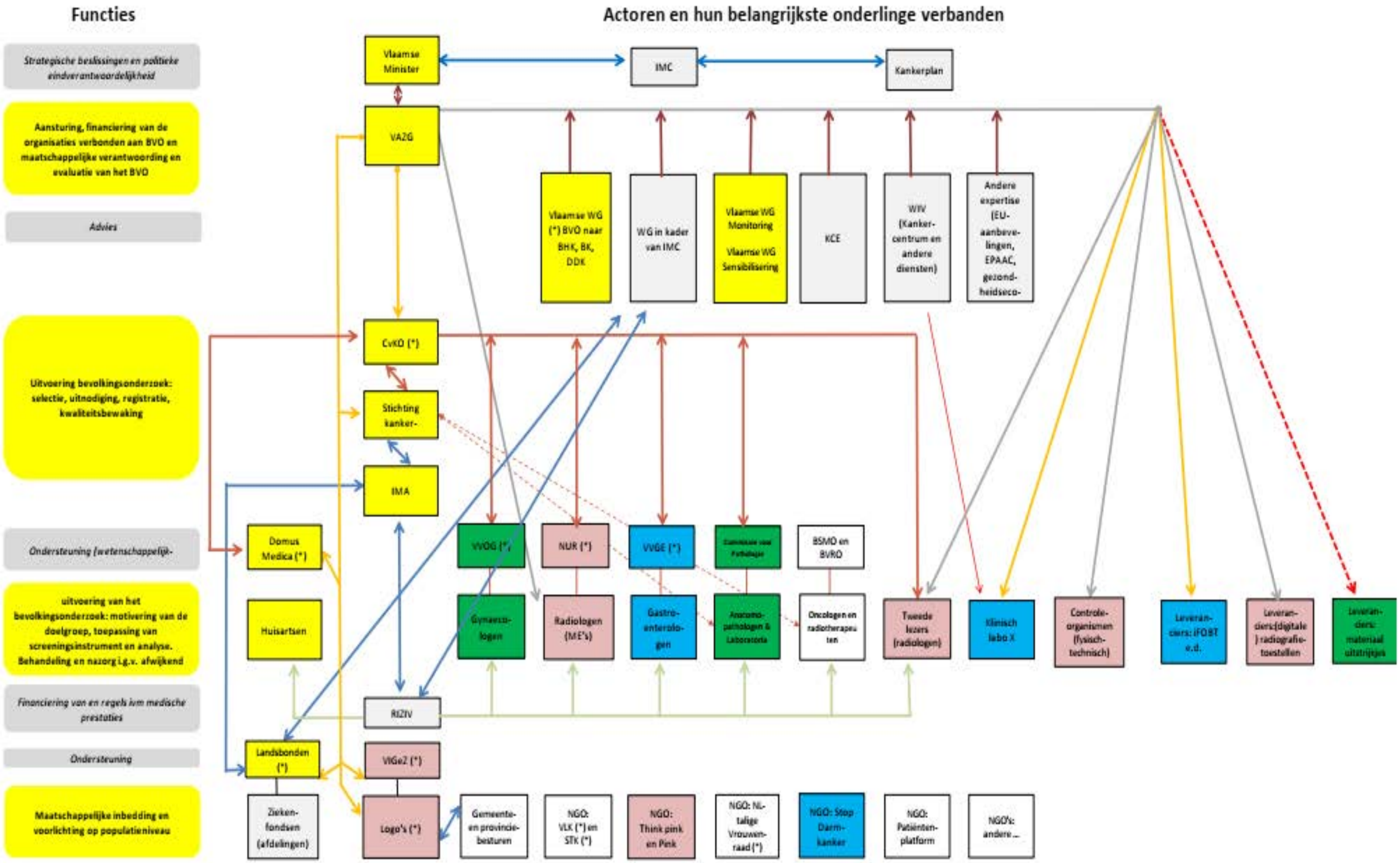
Screening for lung cancer is a controversial idea

But the evidence now suggests it can work



https://www.economist.com/science-and-technology/2019/04/27/screening-for-lung-cancer-is-a-controversial-idea

Figuur 7: Organisatiestructuur van het Vlaams bevolkingsonderzoek naar kanker



LUCSO-1—French pilot study of LUng Cancer Screening with low-dose computed tomography in a smokers population exposed to Occupational lung carcinogens: study protocol

Delva F, *et al. BMJ Open* 2019;**9**:e025026.

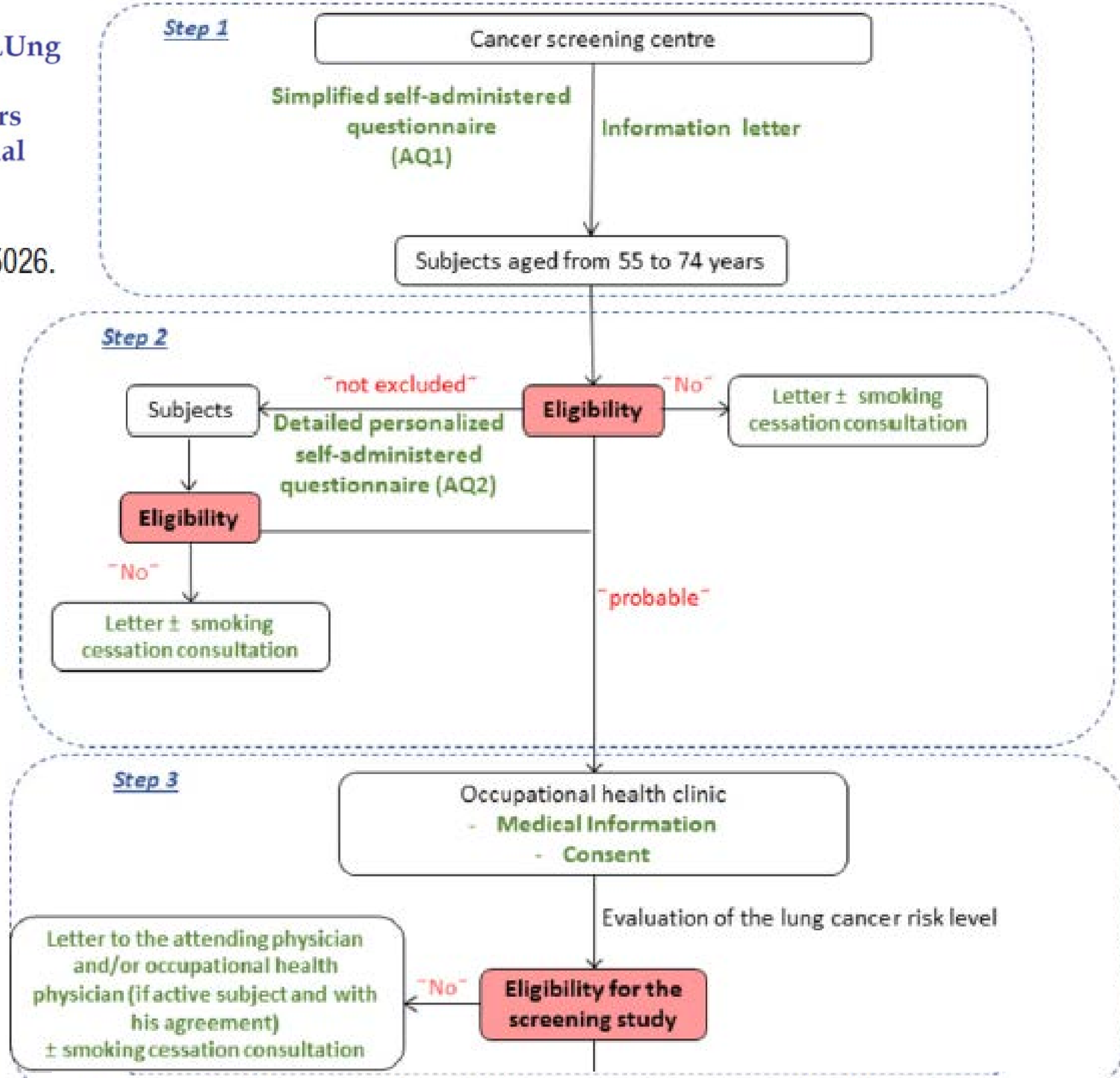


Figure 3 Organisation of lung cancer screening in subjects at high risk of lung cancer in France.

PREVENTING OVERDIAGNOSIS

5-7 December 2019 SYDNEY

ACCREDITED CATEGORY 2 ACTIVITY WITH RACGP

https://www.preventingoverdiagnosis.net/

Thank you for your attention … on lung cancer screening!

H.J. de Koning, C. van der Aalst, P.A. de Jong, E.T. Scholten, K. Nackaerts, M. Heuvelmans, J-W. Lammers, W.P. Mali, C. Weenink, A.U. Yousaf-Khan, N. Horeweg, S. v. 't Westeinde, M. Prokop, J.G.J.V. Aerts, M.A. den Bakker, E.F. Blom, F.B. Thunnissen, J. Verschakelen, R. Vliegenthart, J.E. Walter, K. ten Haaf, H.J.M. Groen, M. Oudkerk

&

NELSON-investigators

NEderlands-Leuvens Longkanker Screenings ONderzoek

NELSON

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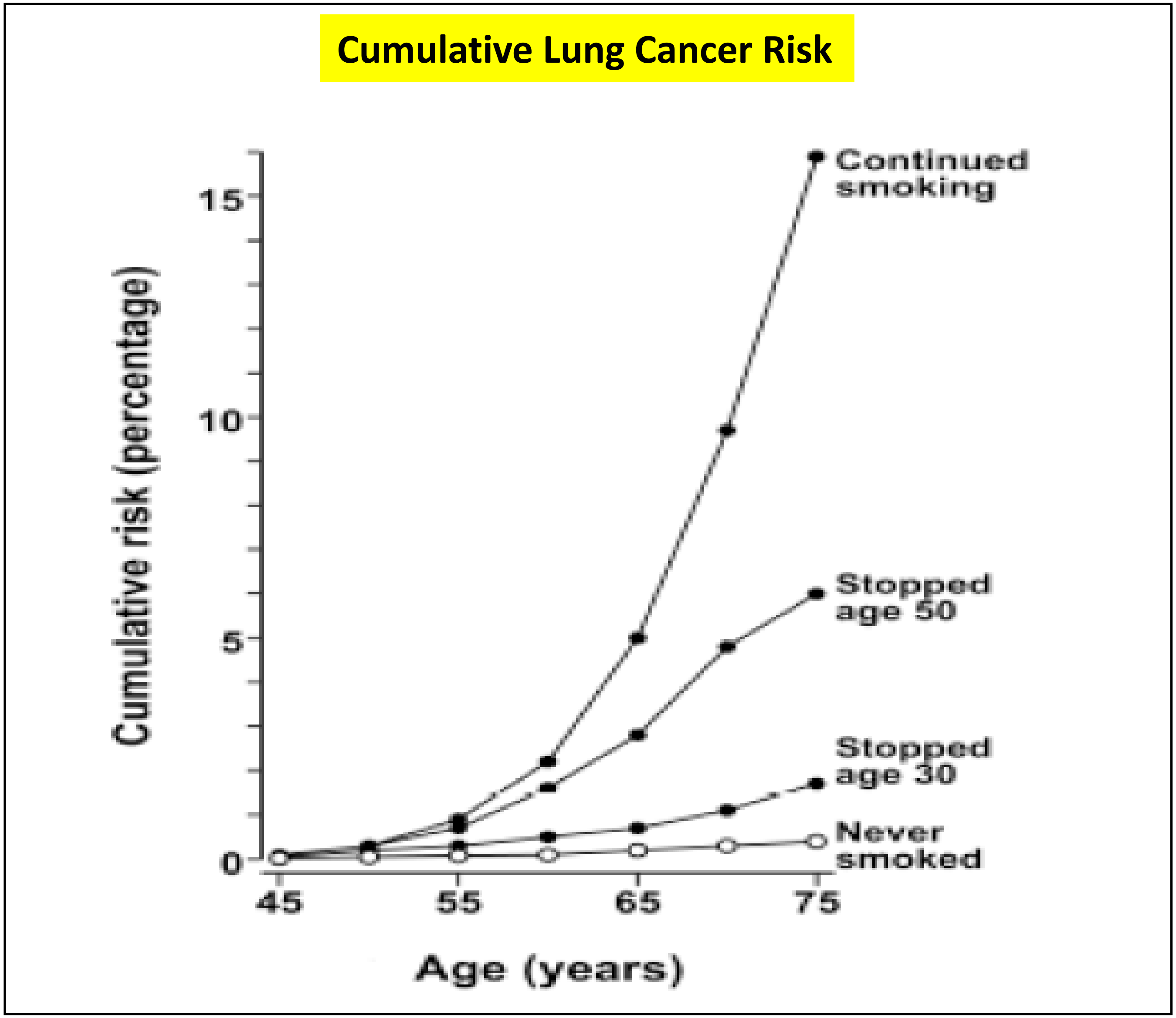
Table 6 Lung nodule and cancer prevalence in series of incidentally detected nodules and screening trials

	Studies (n)	Patients (n)	Nodule prevalence (%), mean (range)	Lung cancer prevalence (%), mean (range)
Incidental	11 [3 5 7 13–18 31 32]	11 683	13 (2–24)	1.5 (0–4.0)
Screening	21 [4 6 8–12 19–30 34 35]	116 300	33 (17–53)	1.4 (0.5–2.7)

▶ The reported prevalence of malignant nodules is similar in screening studies and in studies reporting nodules as incidental findings. **Evidence level 3**

Callister MEJ et al, Thorax 2015;70:ii1-ii54

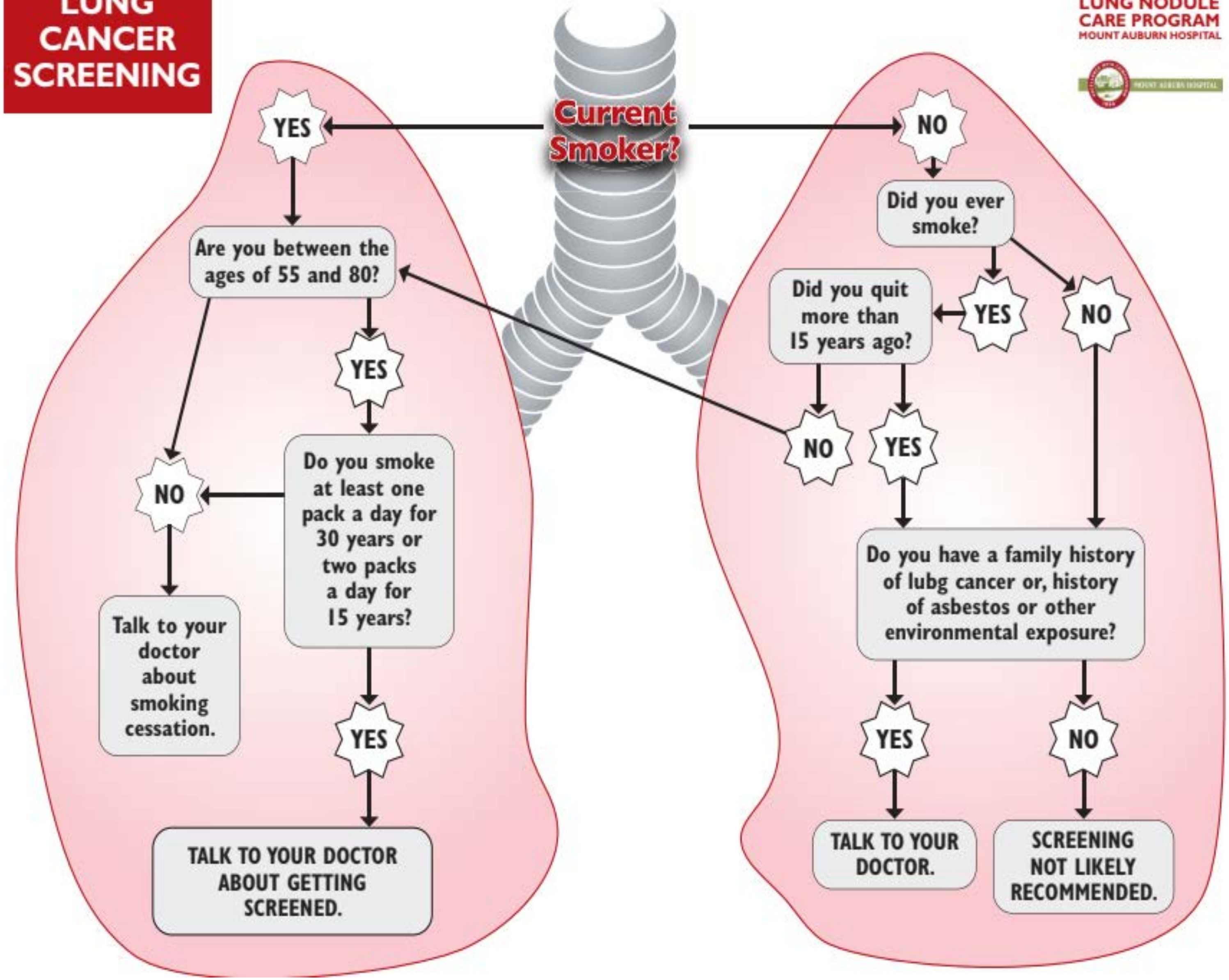
Persons at high risk for lung cancer



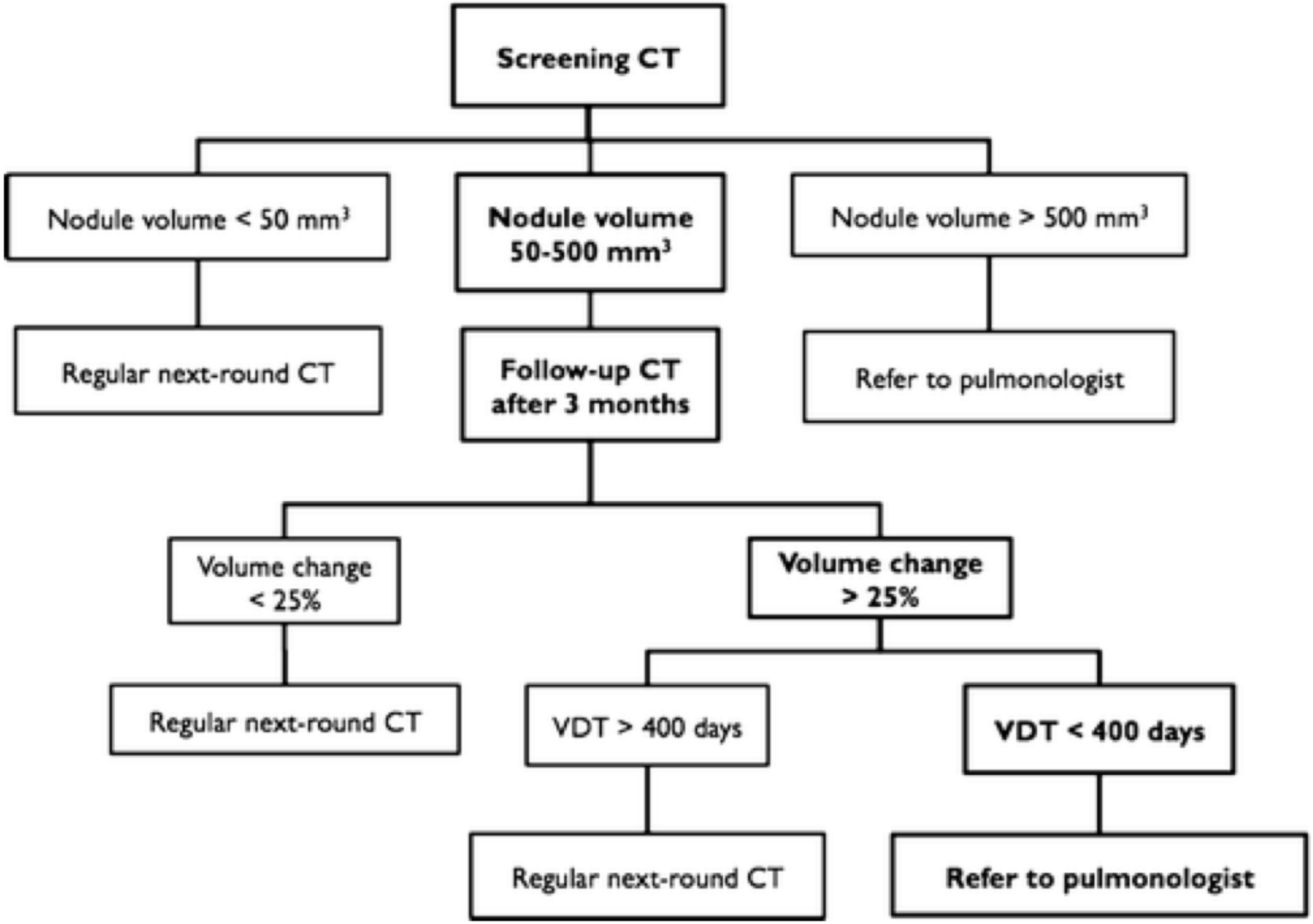
Slide from P Brennan IARC

LUNG CANCER SCREENING

MULTIDISCIPLINARY
LUNG NODULE
CARE PROGRAM
MOUNT AUBURN HOSPITAL



OVERVIEW OF NELSON SCREENING PROTOCOL



Heuvelmans M.A. et al, J Thorac Imaging 30, 101-107, 2015

NELSON : 5,5 YEARS CALCULATIONS

1st screening result	Risk screen-detected lung cancer
Negative	1,0%
Indeterminate	5,7%
Positive	48,3%

Horeweg N et al Eur Respir J 2013;42:1659-67