Væsentligt nyt om CT Screening for lungecancer

Rigshospitalet
The Heart Center
Department of Cardiothoracic Surgery

Årsmøde for DLCG

Rigshospitalet

22.11.2018

Jesper Holst Pedersen

Overlæge, dr.med

Formand for Screeningsgruppen i DLCG

NELSON 10 års mortalitets data

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Fra verdenskongres i Lunge Cancer (WCLC 2018)
Toronto, Canada

National Lung Screening Trial – NLST Results (N=53454, Cost: 300 mio $)

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(N Engl J Med 2011;365;395-409)

- 20% reduction in lung cancer mortality (p=0.004)
- 6.7% reduction in all cause mortality (p=0.02).
- *Age; 55-74 years with no symptoms of LC*
- *Active or former smoker, 30 pack year history, if quit: within last 15 years*
- Exclusion: life limiting comorbidity, metal implants in chest or back, home oxygen.

CT screening indføres nu gradvist i USA, Canada og Kina.

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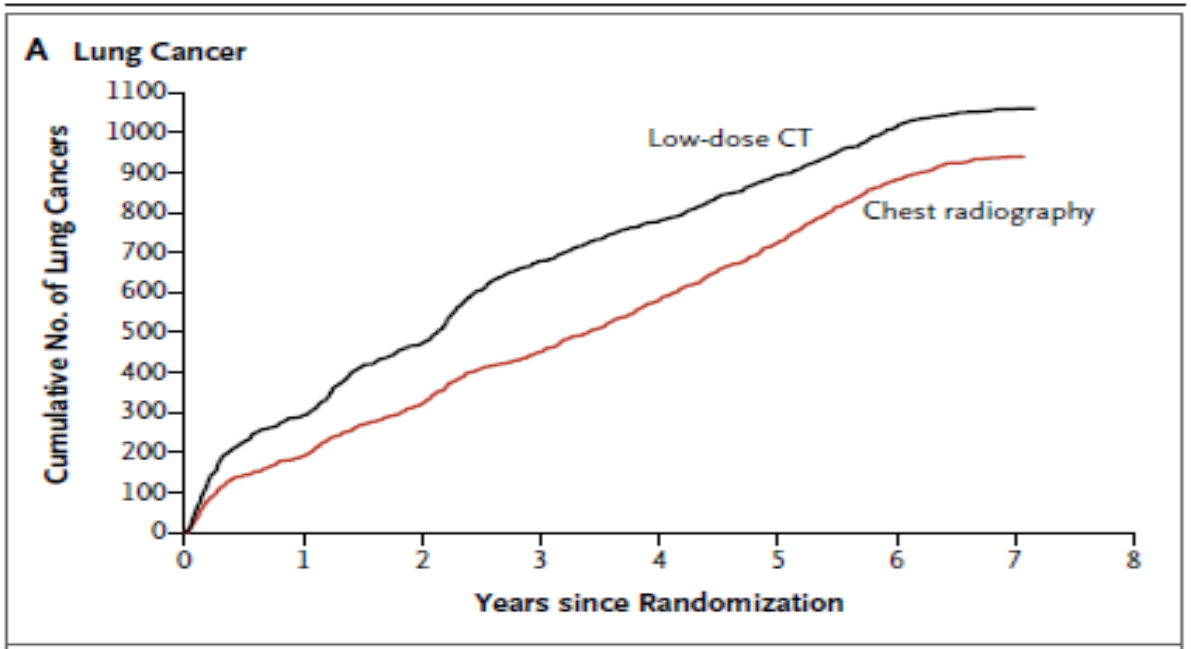

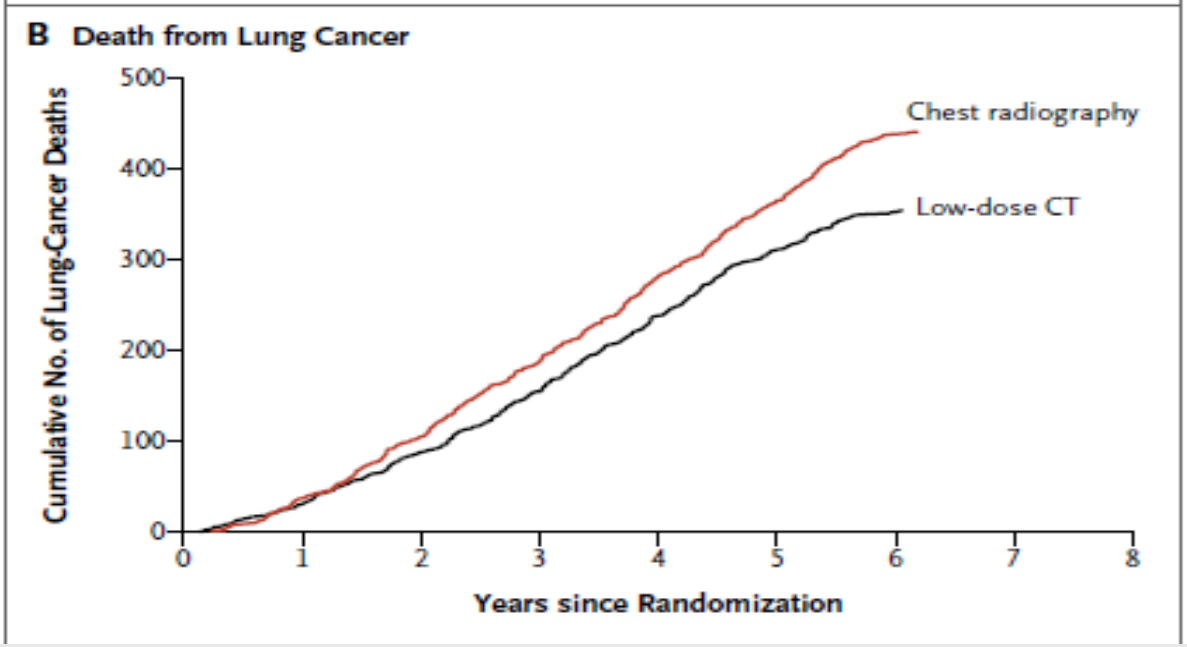

N Engl J Med 2011; 365: 395-409

European Randomized screening trials

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Study	Country	Year start	Subjects enrolled	Age range (years)	Tobac. expos. Pack yrs
UKLS (Field et al, 2011)	UK	2011	4055	50-75	LLP
DANTE (Infante et al, 2008)*	Italy	2001	2 472	60–74	35
NELSON (Klaveren et al, 2008)	NL–B	2003	15 822	50–74	15-20
ITALUNG (Paci et al, 2009)	Italy	2004	3 206	55–69	30
DLCST (Pedersen et al, 2009)*	Denmark	2004	4 104	50–70	20
MILD (Pastorino et al, 2006)*	Italy	2005	4 479	49–75	20
LUSI (Becker et al, 2008)	Germany	2007	4 052	50–69	20
7 European trials	Europe	2001–20011	38 1390	49–75	15-35

* Studies with No mortality benefit all underpowered !!

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NELSON - trial ISRCTN 63545820

NELSON

- 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%)

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	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

00:03:40

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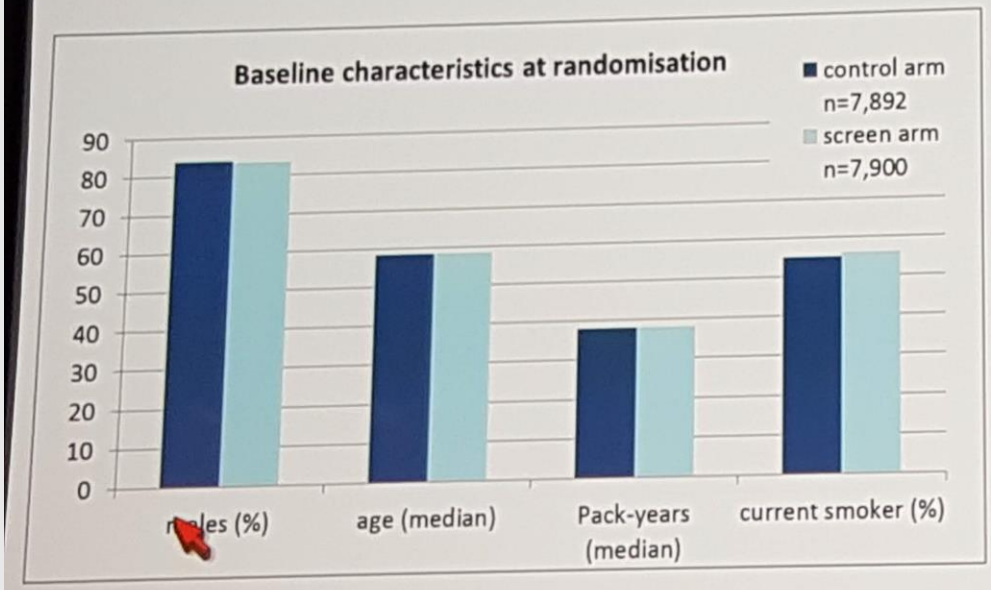

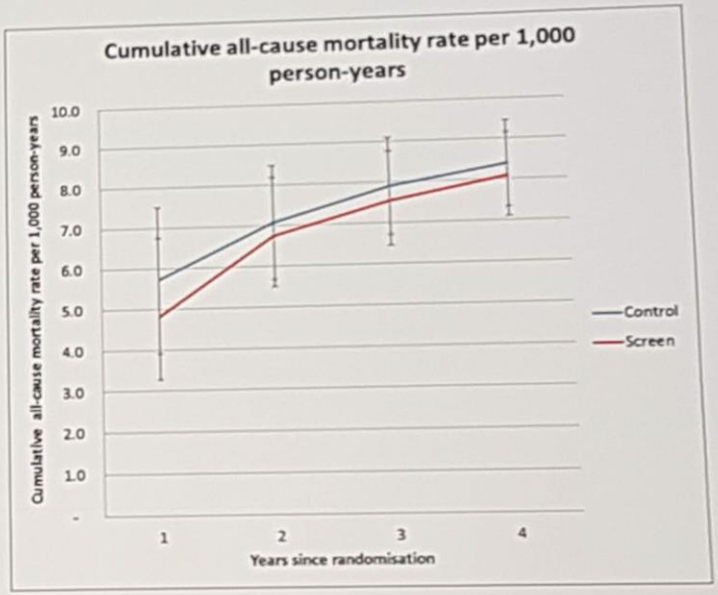

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	screening uptake	indeterminate test result	positive test result (final result)	lung cancer detection (participants)	positive predictive value positive test result
ROUND 1	7,557 (95.6%)	1,451 (19.2%)	197 (2.6%)	70 (0.9%)	36%
ROUND 2	7,295 (92.3%)	480 (6.6%)	131 (1.8%)	55 (0.8%)	42%
ROUND 3	6,922 (87.6%)	471 (6.8%)	165 (2.4%)	75 (1.1%)	45%
ROUND 4	5,279 (66.8%)	101 (1.9%)	105 (2.0%)	43 (0.8%)	41%
TOTAL	**27,053 (85.6%)**	**2,503 (9.3%)**	**598 (2.2%)**	**243 (0.9%)**	**41%**

00:02:50

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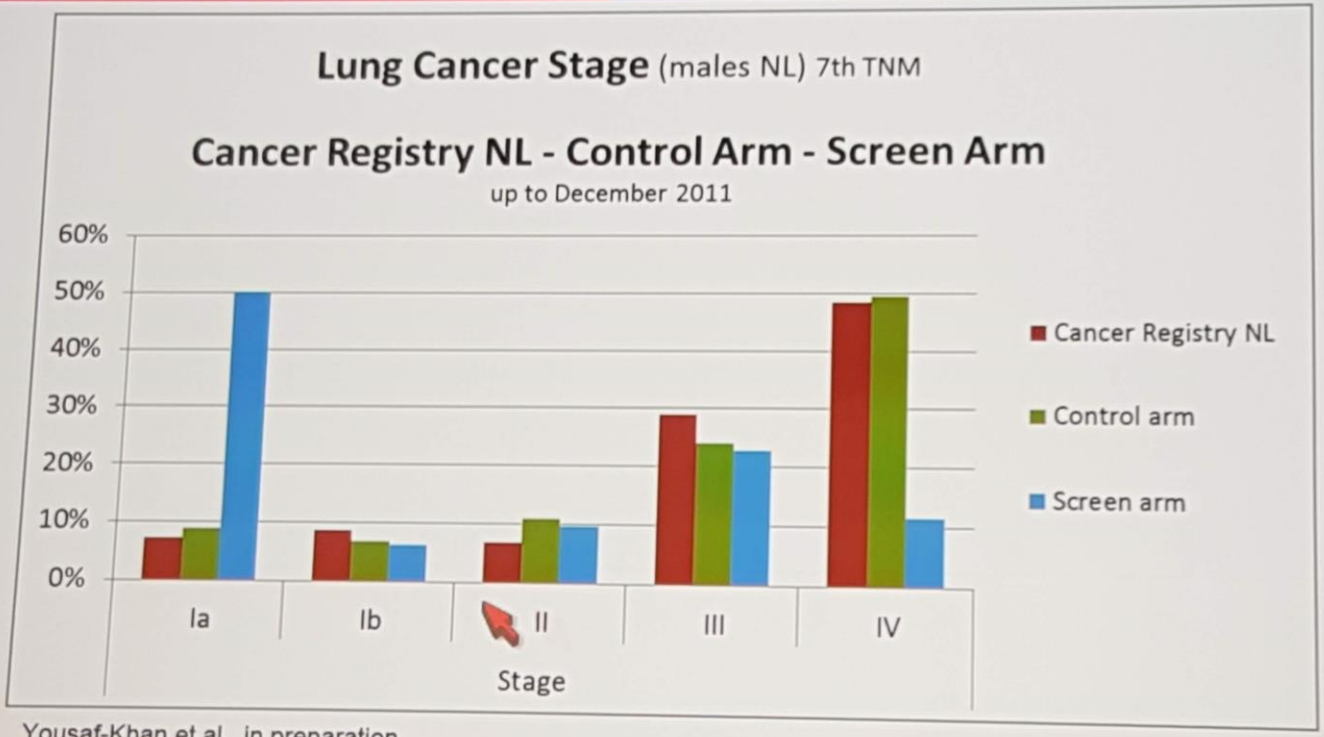

Yousaf-Khan et al., in preparation

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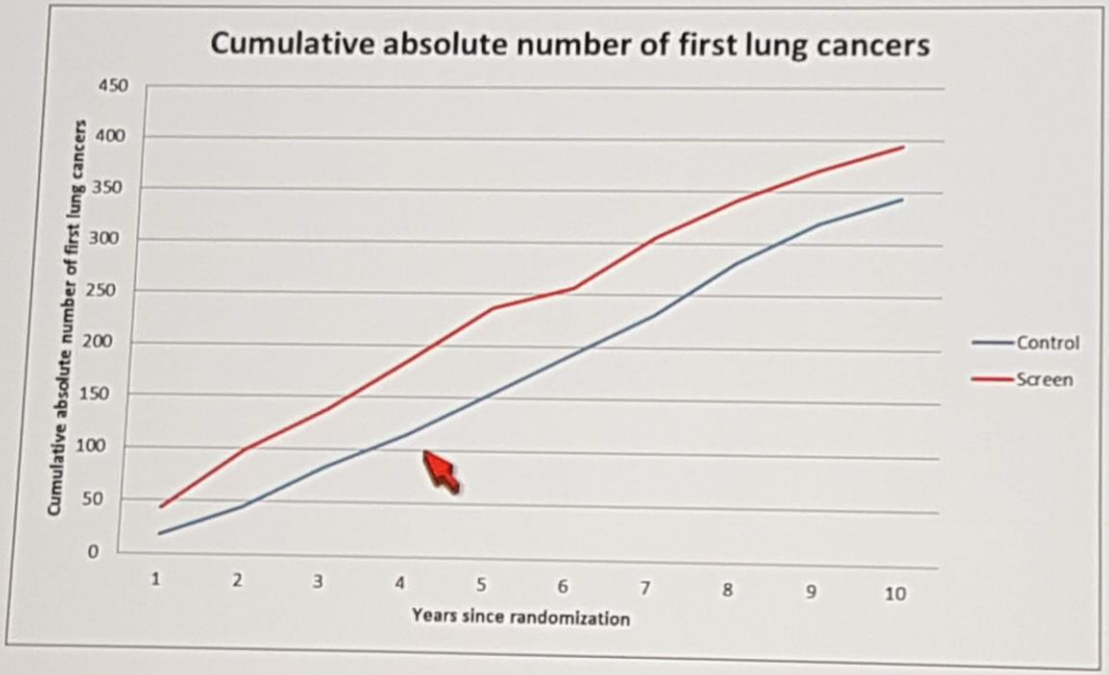

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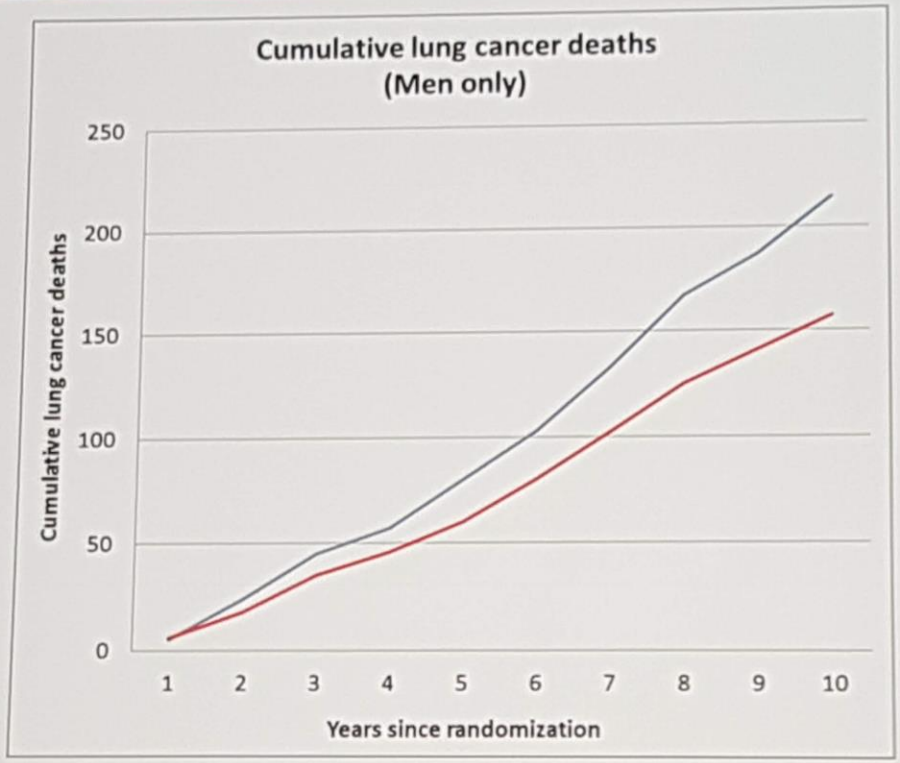

Control arm:
214 lung cancer deaths

Screen arm:
157 lung cancer deaths

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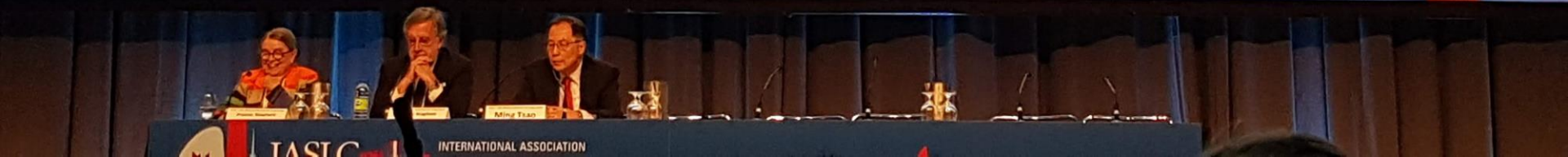

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Lung cancer mortality rate ratio (95% CI)	Year 8	Year 9	Year 10
MALES	0.75 P=0.015 (0.59-0.95)	0.76 P=0.012 (0.60-0.95)	0.74 P=0.003 (0.60-0.91)
FEMALES	0.39 P=0.0037 (0.18-0.78)	0.47 P=0.0069 (0.25-0.84)	0.61 P=0.0543 (0.35-1.04)

Rand: 23-12-2003 – 06-07-2006

FU: 23-12-2003 – 31-12-2015

FU 94% complete year 10

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NELSON Volume CT screening

- MALES at high risk for lung cancer have a reduced risk of dying from lung cancer of **26%** in the screen arm compared to the male control arm (95% CI 9-40%)
- In WOMEN, reductions are consistently more favourable: **39-61%**
- These results are more favourable than the NLST-results & suggest gender differences
- Volume CT lung cancer screening of high risk former and current smokers results in low referral rates (2.3%), and a very substantial reduction in lung cancer mortality (in both genders)

00:00:30

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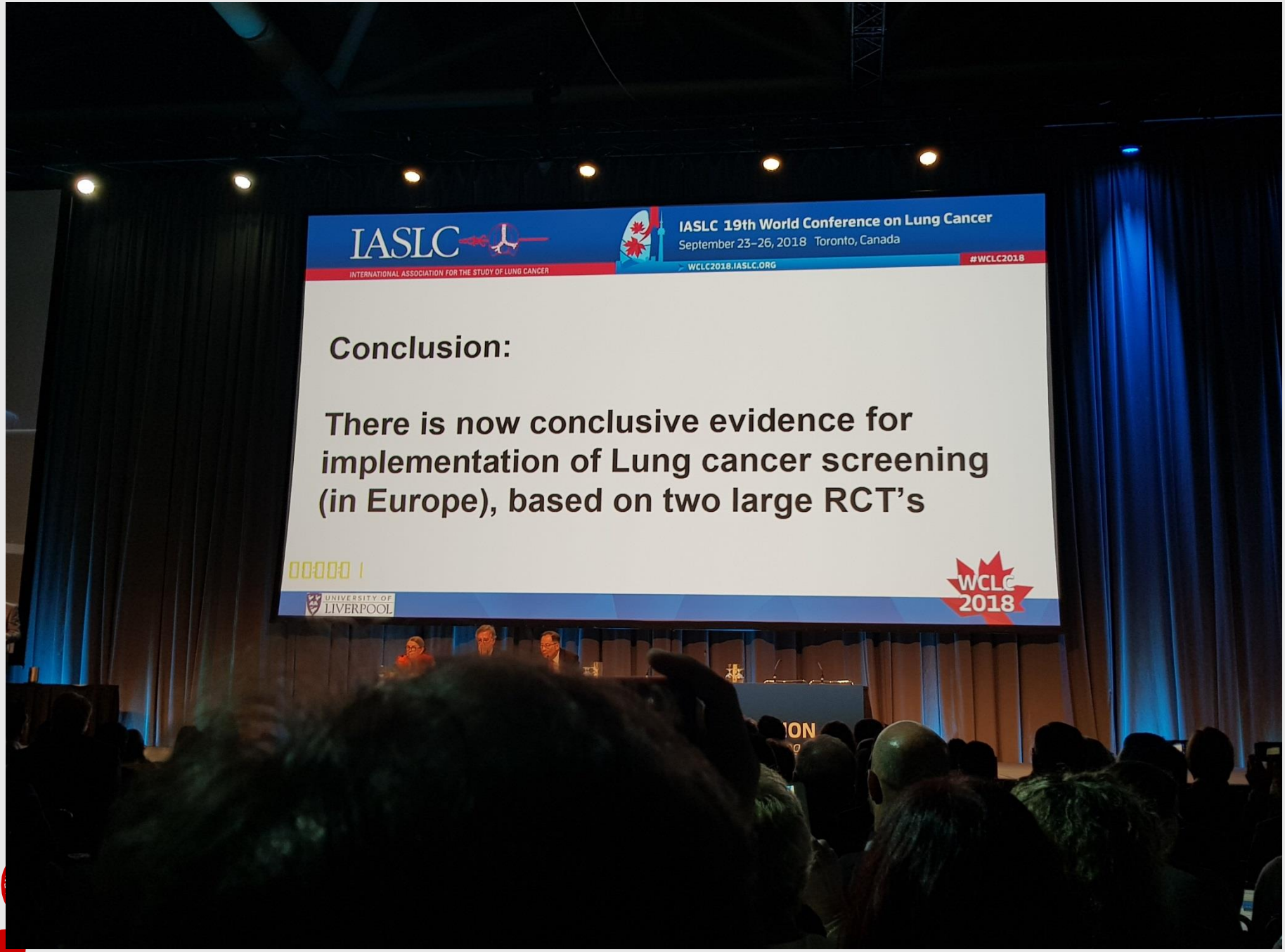
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Conclusion:
There is now conclusive evidence for implementation of Lung cancer screening (in Europe), based on two large RCT's
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KONKLUSION

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The Heart Center
Department of Cardiothoracic Surgery

Tiden er kommet til at implementere CT screening for lungecancer i Danmark.

Screeningsgruppen under DLCG skal derfor forberede dette og tilvejebringe beslutningsgrundlaget herfor.

Kommisorium besluttes og godkendes af bestyrelsen i DLCG.

Kommisorium
DLCG SCreeningsgruppe

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Gruppen skal på vegne af DLCG, udarbejde en Rapport (hvidbog) der kan danne grundlag for en anbefaling og beslutning om indførelse af CT screening for lungekræft i Danmark. Rapporten skal beskrive de hidtidige erfaringer med CT screening i Danmark og udlandet, og beskrive evidensen for de forventede fordele og ulemper ved CT screening for lungekræft. Rapporten skal derudover beskrive: Hvem der skal tilbydes CT screening, den konkrete screeningsteknologi samt hvorledes udredning af positive og tilfældige fund skal ske, samt deltager undervisning og ryge stop hjælp og undervisning. Derudover vurdering af costeffektivtet af screeningsprogrammet og hvilke krav der skal stilles til de enkelte screeningcentre og til den nationale monitorering og kontrol af screeningsprogrammet. Rapporten skal desuden beskrive en plan for hvorledes den konkrete implementering tænkes at foregå og hvilke resurser og forudsætninger der skal være tilstede.

DLCG Screeningsgruppe Medlemmer - 2018

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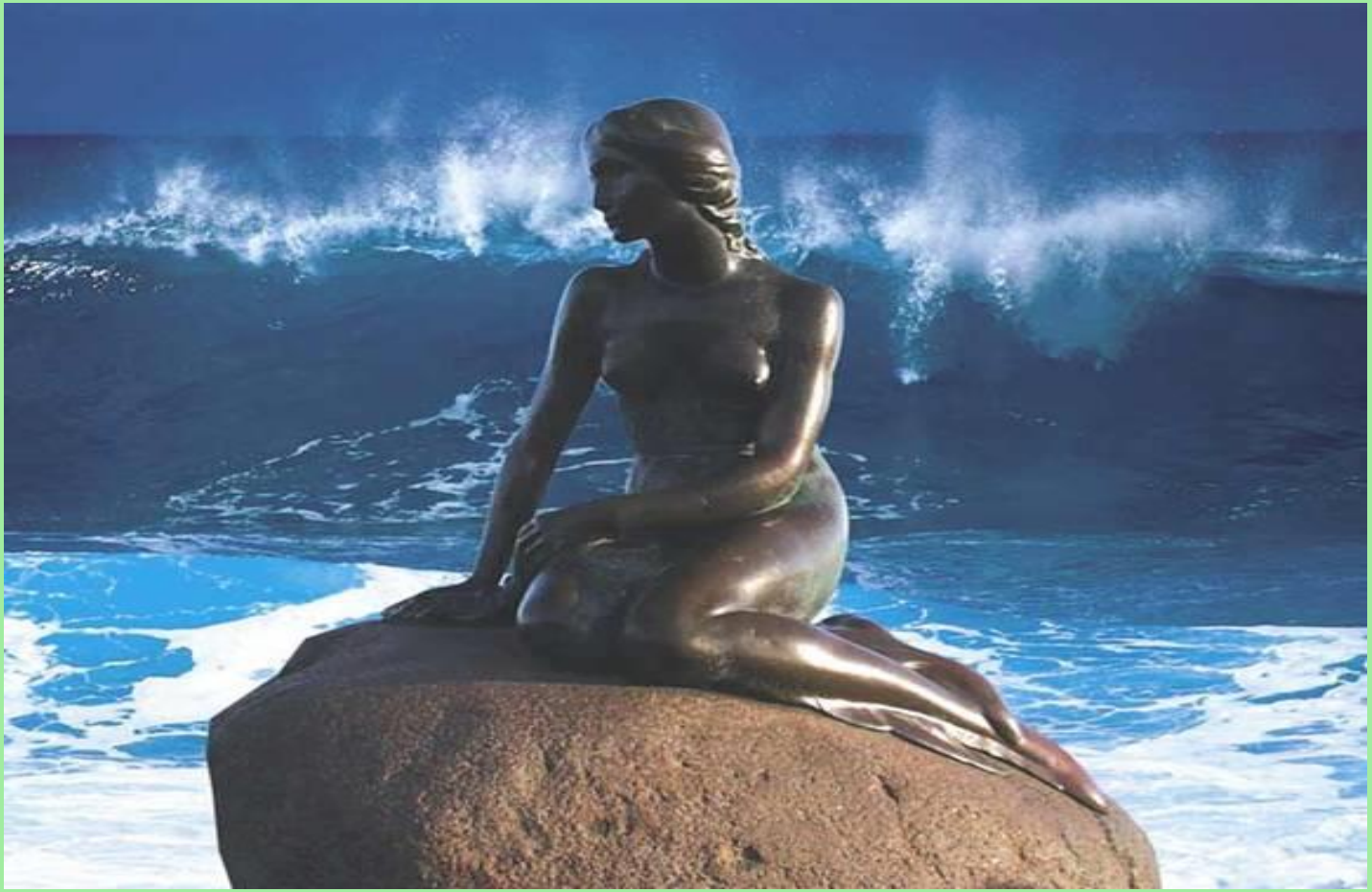
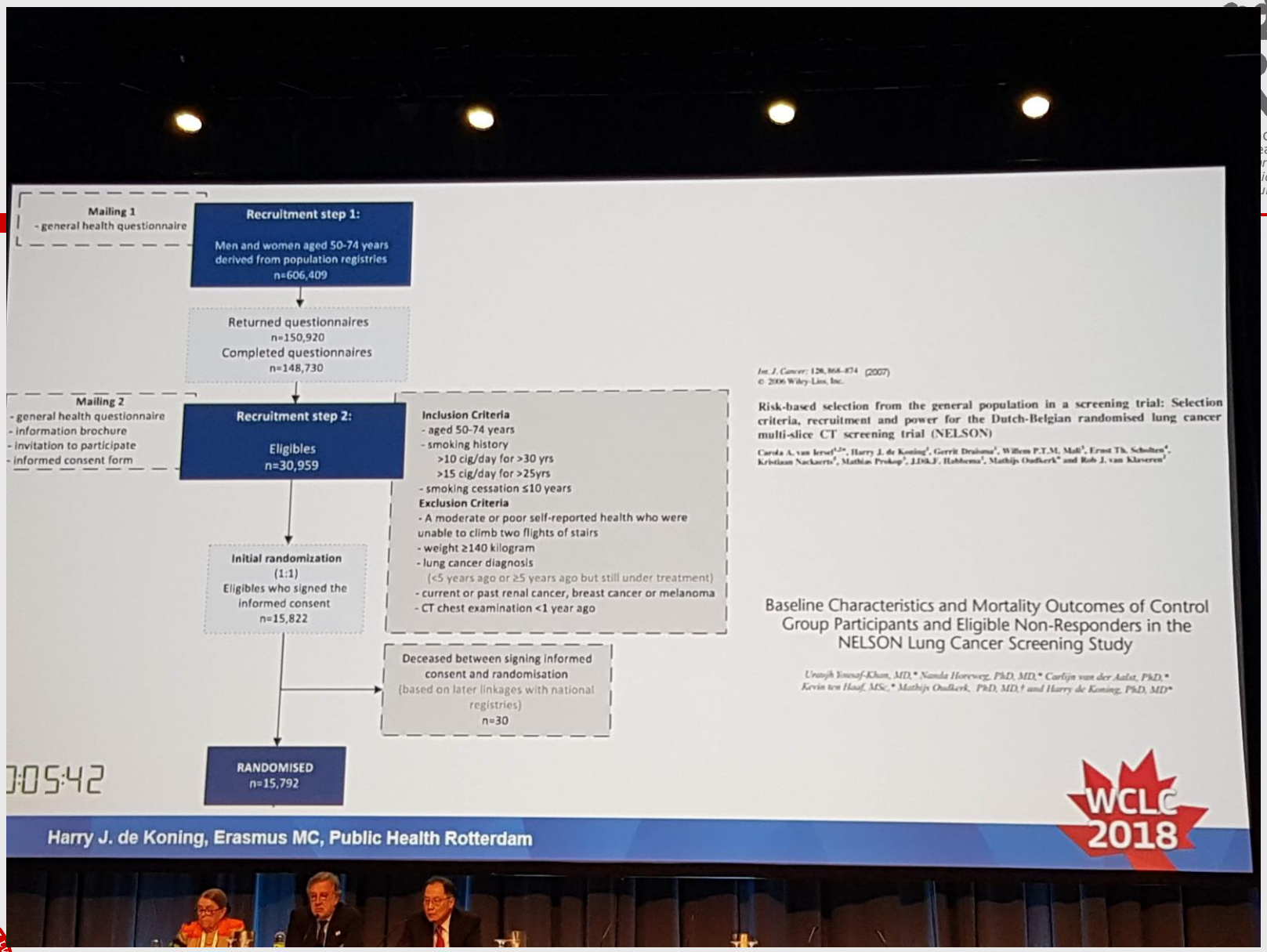
- Jesper Holst Pedersen (Formand, Thoraxkirurgi)
- Zaigham Saghir (Næstformand, Lungemedicin)
- Torben Riis Rasmussen (Lungemedicin)
- Niels Seersholm (Lungemedicin)
- Klaus Richter Larsen (Lungemedicin)
- Rene Horsleben Petersen (Thoraxkirurgi).
- Finn Rasmussen (Radiologi)
- Hans Henrik Torp Madsen (Radiologi)
- Michael Brun Andersen (Radiologi)
- Haseem Ashraf (Radiologi)
- Birgit Guldhammer Skov (Patologi)
- Jann Mortensen (Klin.Fysiologi)
- John Brodersen (Almen Praksis)
- Asger Dirksen (lungemedicin)

Spørgsmål ?




Mailing 1
- general health questionnaire
Recruitment step 1:
Men and women aged 50-74 years derived from population registries
n=606,409
Returned questionnaires
n=150,920
Completed questionnaires
n=148,730
Mailing 2
- general health questionnaire
- information brochure
- invitation to participate
- informed consent form
Recruitment step 2:
Eligibles
n=30,959
Inclusion Criteria
- aged 50-74 years
- smoking history
>10 cig/day for >30 yrs
>15 cig/day for >25yrs
- smoking cessation ≤10 years
Exclusion Criteria
- A moderate or poor self-reported health who were unable to climb two flights of stairs
- weight ≥140 kilogram
- lung cancer diagnosis
(<5 years ago or ≥5 years ago but still under treatment)
- current or past renal cancer, breast cancer or melanoma
- CT chest examination <1 year ago
Initial randomization
(1:1)
Eligibles who signed the informed consent
n=15,822
Deceased between signing informed consent and randomisation
(based on later linkages with national registries)
n=30
RANDOMISED
n=15,792
Int. J. Cancer: 120, 868–874 (2007)
© 2006 Wiley-Liss, Inc.
Risk-based selection from the general population in a screening trial: Selection criteria, recruitment and power for the Dutch-Belgian randomised lung cancer multi-slice CT screening trial (NELSON)
Carola A. van Iersel, Harry J. de Koning, Gerrit Draisma, Willem P.T.M. Mali, Ernst Th. Scholten, Kristiaan Nackaerts, Mathias Prokop, J.Dik.F. Habbema, Mathijs Oudkerk and Rob J. van Klaveren
Baseline Characteristics and Mortality Outcomes of Control Group Participants and Eligible Non-Responders in the NELSON Lung Cancer Screening Study
Uranjh Yousaf-Khan, MD, Nanda Horeweg, PhD, MD, Carlijn van der Aalst, PhD, Kevin ten Haaf, MSc, Mathijs Oudkerk, PhD, MD, and Harry de Koning, PhD, MD
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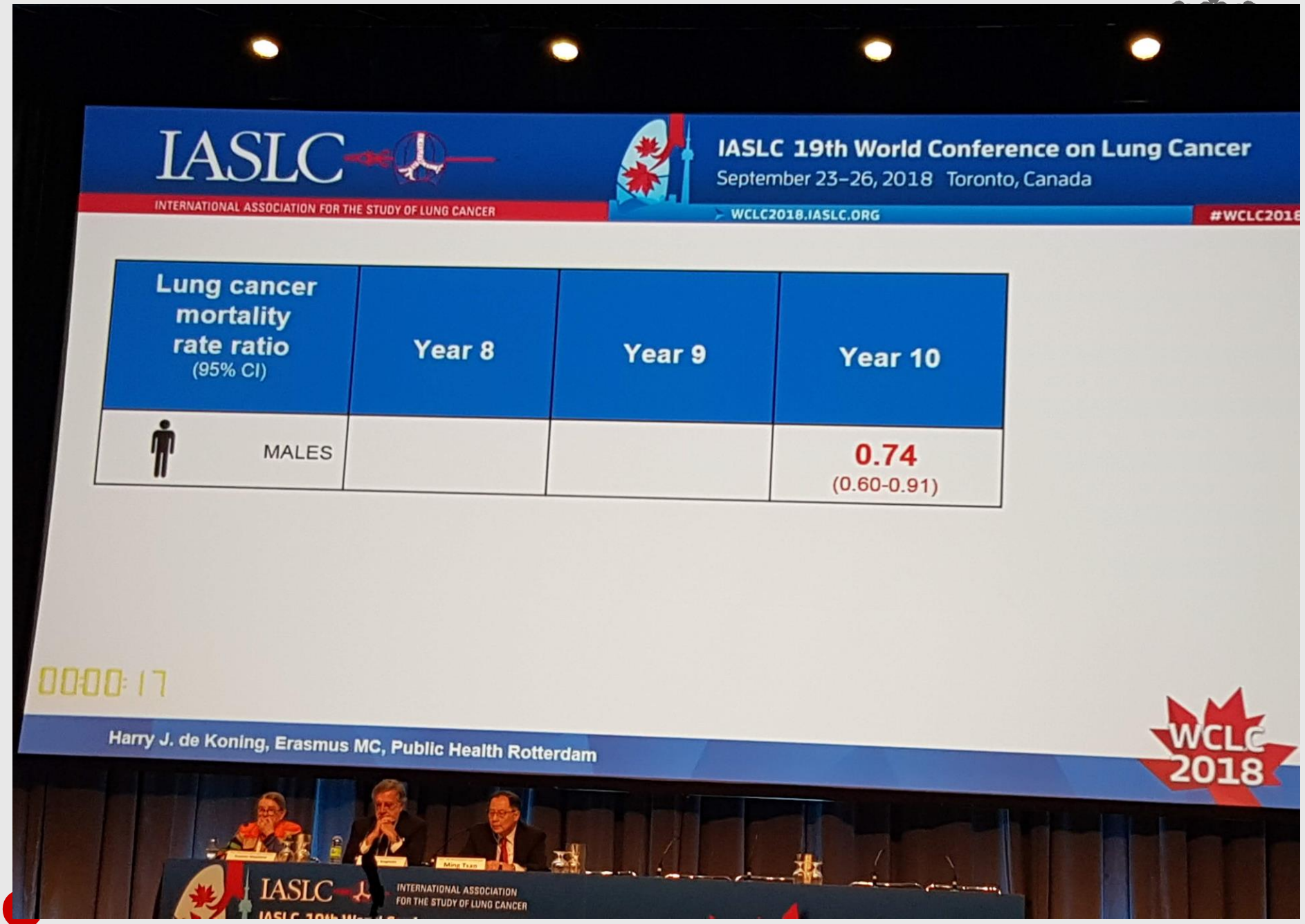
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Lung cancer mortality rate ratio (95% CI)
Year 8
Year 9
Year 10
MALES
0.74
(0.60-0.91)
00:00:17
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Message indeterminate screening test result

"We have observed a very small abnormality in your lung (5–10 mm long). Such a small abnormality is often detected in many persons and it usually represents a small scar or a minor inflammation. Therefore, at this moment there is no need for any further investigations. However, in order to see whether there has been any change in this abnormality, a new CT scan of the lungs will be made after 3 to 4 months."

Lancet Oncol 2014; 15: 1332–41

Lung cancer probability in patients with CT-detected pulmonary nodules: a prespecified analysis of data from the NELSON trial of low-dose CT screening

Lancet Oncol 2016; 17: 907–16

Occurrence and lung cancer probability of new solid nodules at incidence screening with low-dose CT: analysis of data from the randomised, controlled NELSON trial

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Lung cancer mortality rate ratio (95% CI)	Year 8	Year 9	Year 10
MALES	0.75 (0.59-0.95)	0.76 (0.60-0.95)	0.74 (0.60-0.91)

00:00:06

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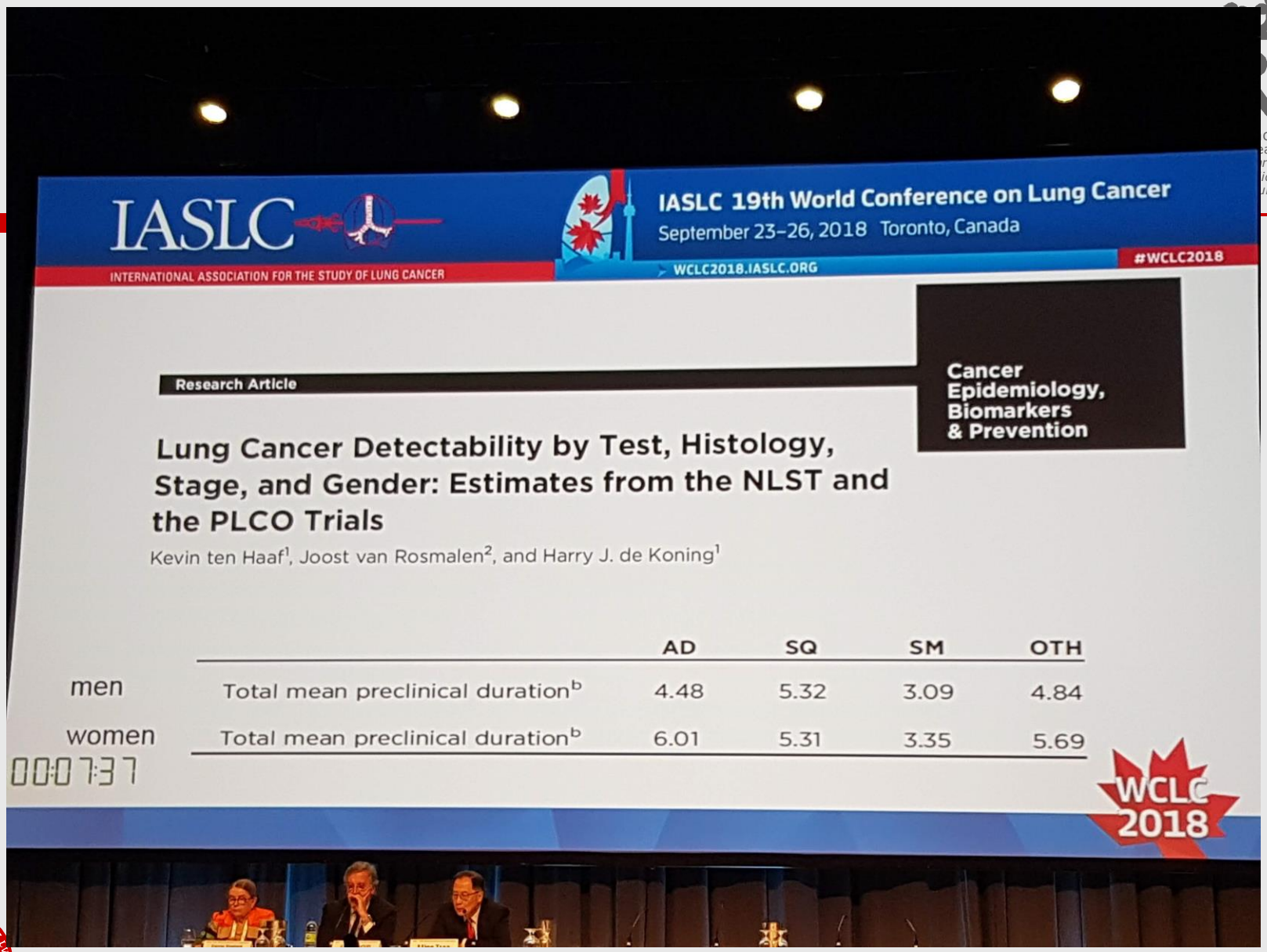
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Research Article
Cancer Epidemiology, Biomarkers & Prevention
Lung Cancer Detectability by Test, Histology, Stage, and Gender: Estimates from the NLST and the PLCO Trials
Kevin ten Haaf[1], Joost van Rosmalen[2], and Harry J. de Koning[1]
AD SQ SM OTH
men Total mean preclinical duration[b] 4.48 5.32 3.09 4.84
women Total mean preclinical duration[b] 6.01 5.31 3.35 5.69
00:07:37
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Table 3. Eligibility for lung cancer CT screening in the Nordic countries according to NLST criteria.

	Total population age 55–75 years	NLST criteria age 55–75 years	Age 60–75 years
Denmark	1.325511	106.041	81.331
Norway	1.070000	96.300–128.400	NA
Sweden	2.315320	265.049	173.512
Finland	1.408876	125.130	98.963
Iceland	333,000	9.711	NA

NLST criteria: age 55–75, >30 pack years smoking history and not quit more than 15 years ago.
NA: not available.

A minimal invasive VATS surgery program is required to allow a full spectrum of surgical options (wedge resection, anatomical segmental resections, lobectomy, lymph node dissection, etc.) [5,7,10,36,61].

Acta Oncologica 2017 oct;56(10);1249-1257

The German Lung Cancer Screening Intervention Trial (LUSI)

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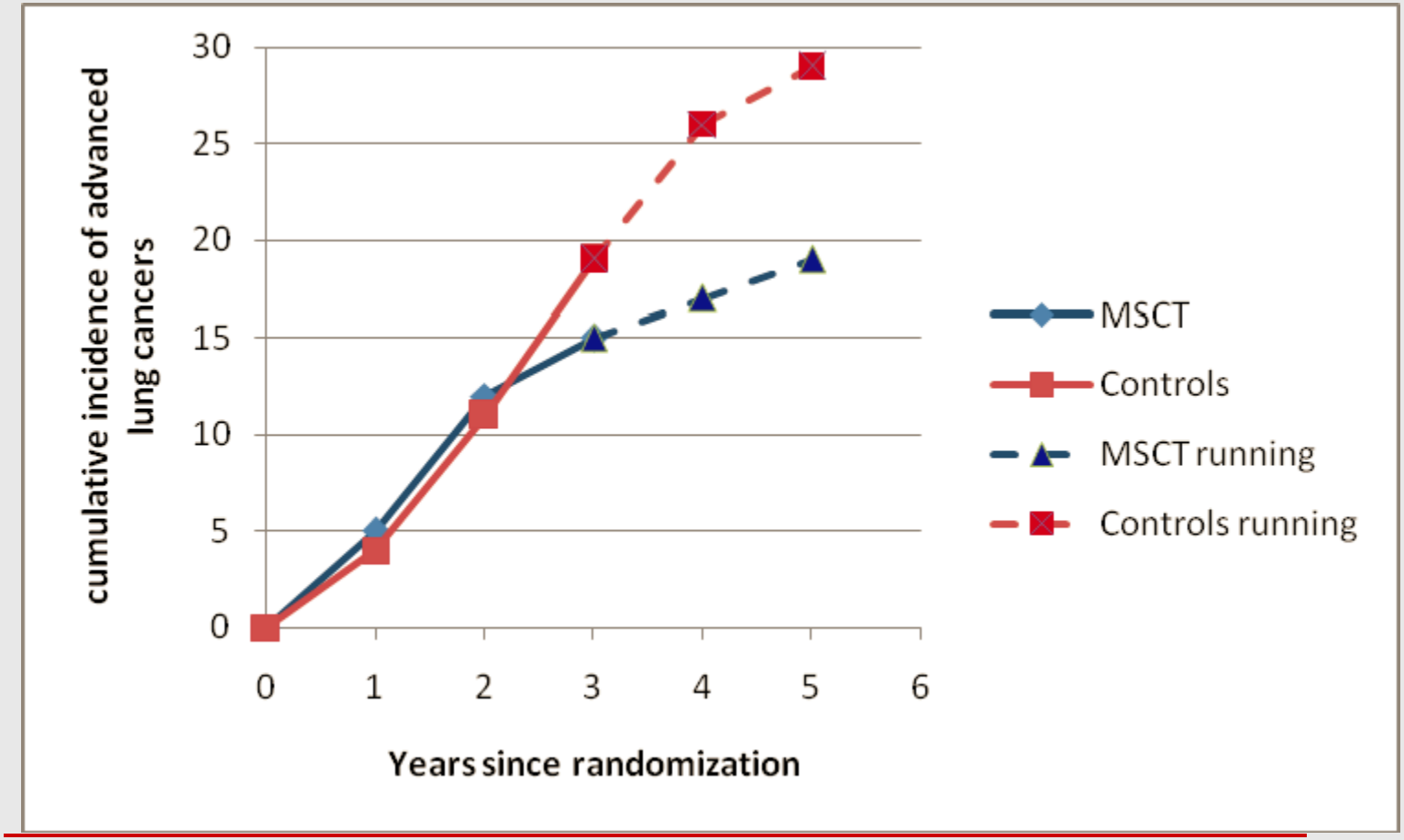
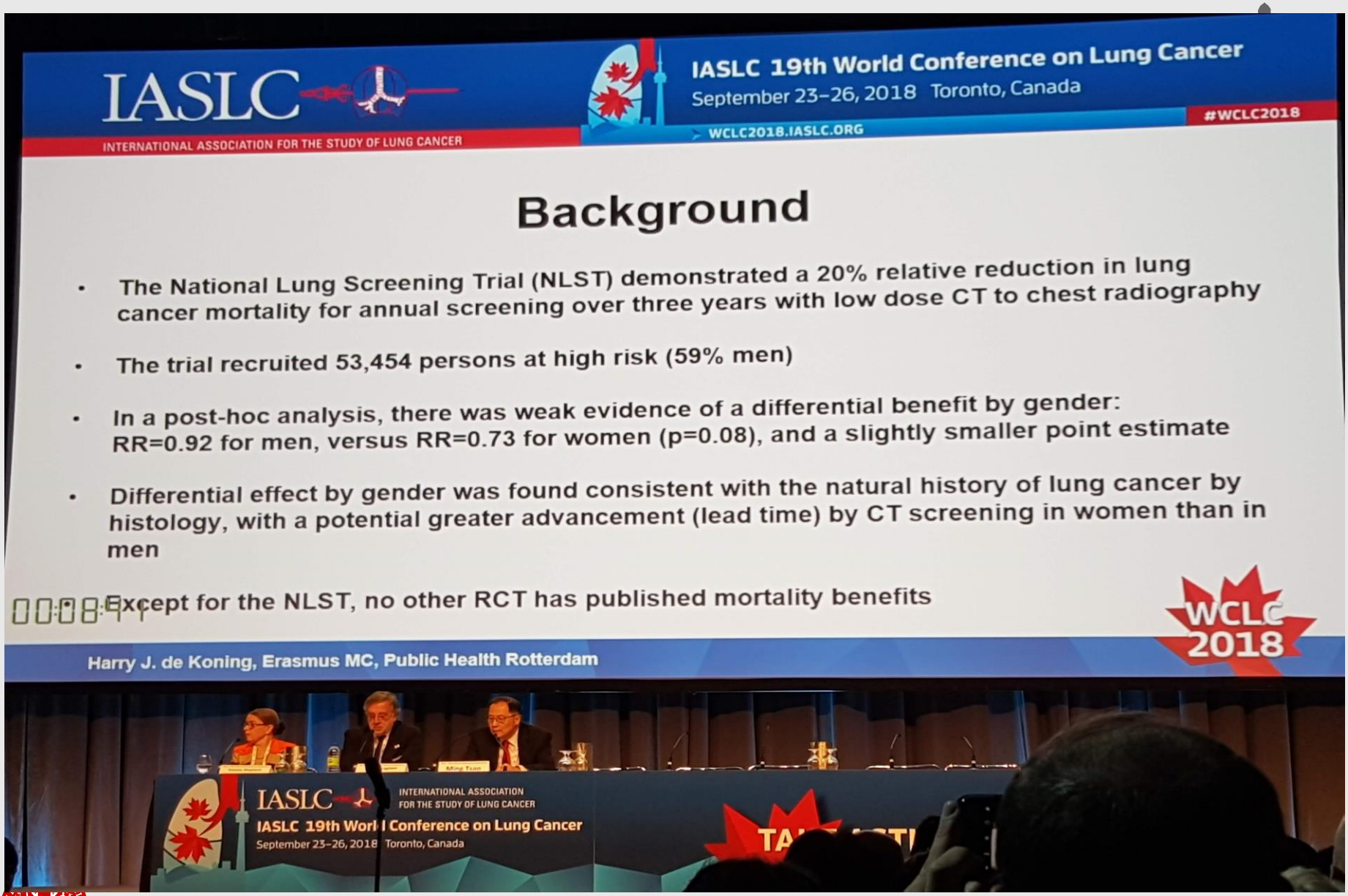


Becker N et al JTO 2015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Background
The National Lung Screening Trial (NLST) demonstrated a 20% relative reduction in lung cancer mortality for annual screening over three years with low dose CT to chest radiography
The trial recruited 53,454 persons at high risk (59% men)
In a post-hoc analysis, there was weak evidence of a differential benefit by gender: RR=0.92 for men, versus RR=0.73 for women (p=0.08), and a slightly smaller point estimate
Differential effect by gender was found consistent with the natural history of lung cancer by histology, with a potential greater advancement (lead time) by CT screening in women than in men
Except for the NLST, no other RCT has published mortality benefits
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