Erasmus MC
Universitair Medisch Centrum Rotterdam

Cancer Institute

European Reference Network
for rare or low prevalence complex diseases
Network Respiratory Diseases (ERN-LUNG)

Screening for Mesothelioma

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Pulmonologist
Erasmus MC, Rotterdam, The Netherlands

Pulmonary rare diseases and orphan drugs, Milan, March 1st

Disclosures

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- Consultancy Roche, Boehringer Ingelheim, BMS, MSD
- Speakers fee Roche, Pfizer, Boehringer Ingelheim, Novartis, BMS
- None relevant for this presentation

Screening for malignancies

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- Individuals at significant risk for the disease
- Apply adequate test for early detection
  - High number of false positives leads to increased number of complications
- Improved treatment option for early-detected disease

NELSON trial –
CT screening for lung cancer

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Population

- Aged 50-74 years
- Smoking history
  - >10 cig/day for >30 years
  - >15 cig/day for >25 years
- Smoking cessation ≤10 years

NELSON

Coordinated by

NELSON trial

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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%**

NELSON trial

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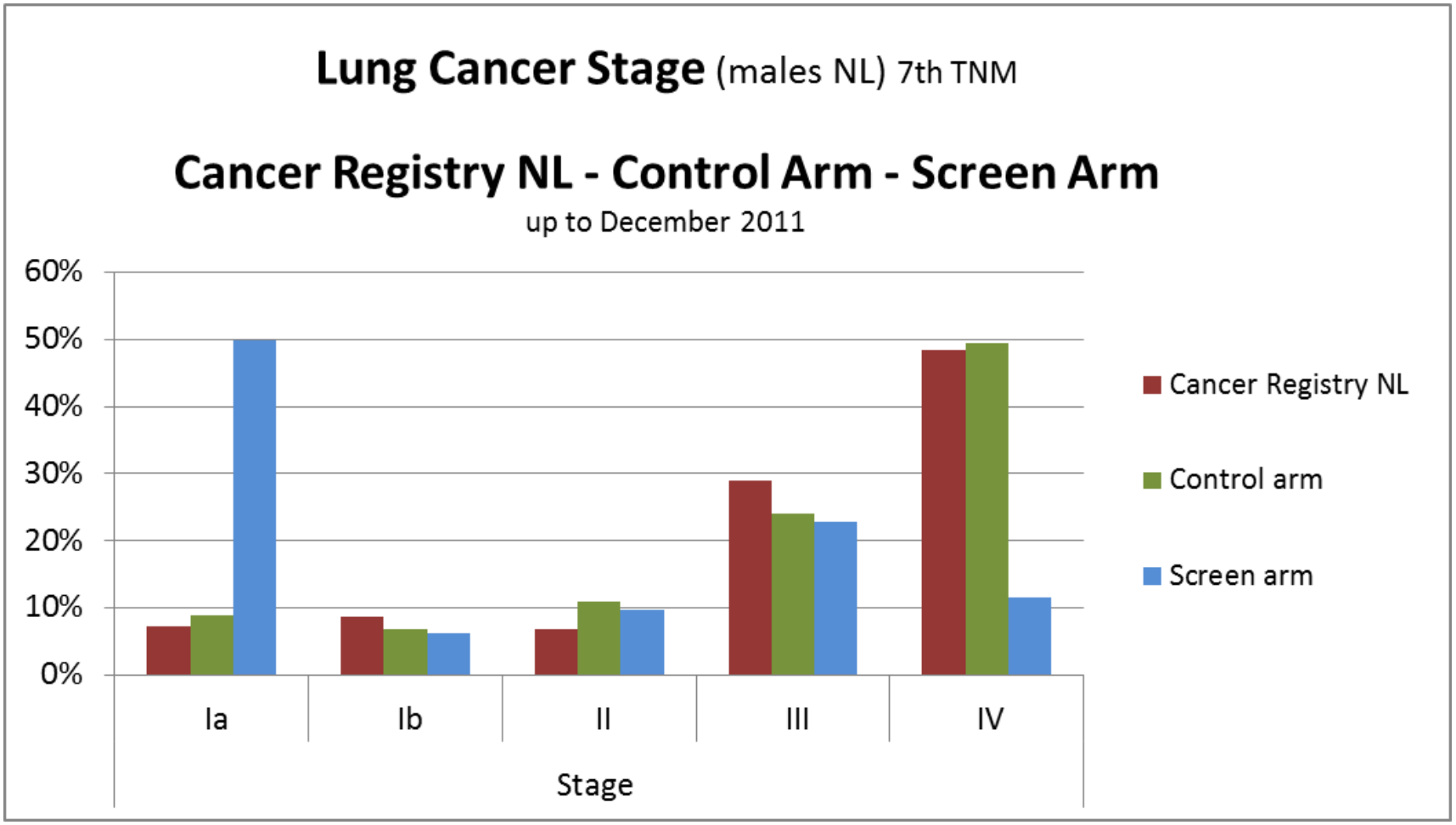

Yousaf-Khan et al., in preparation

NELSON trial

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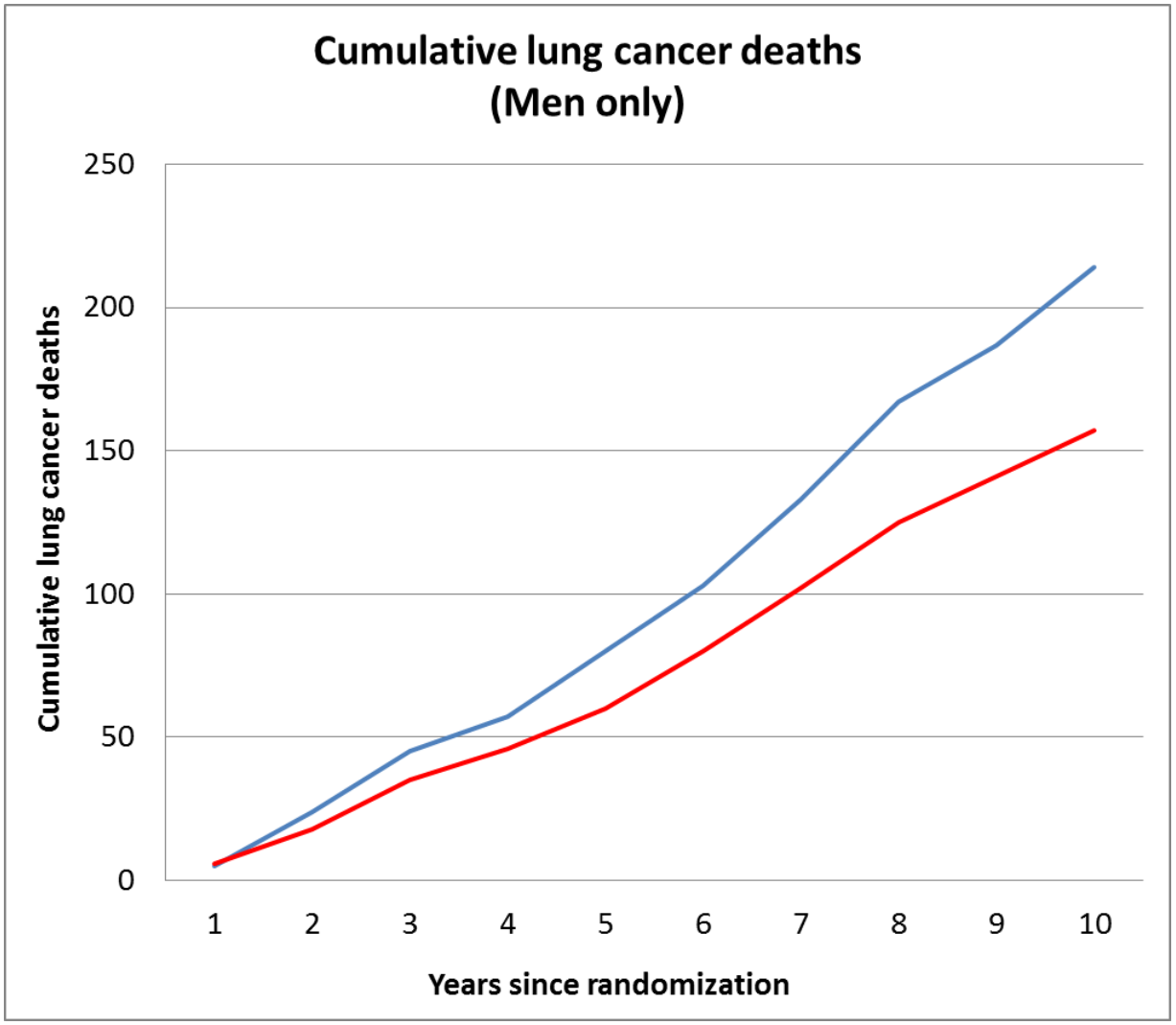
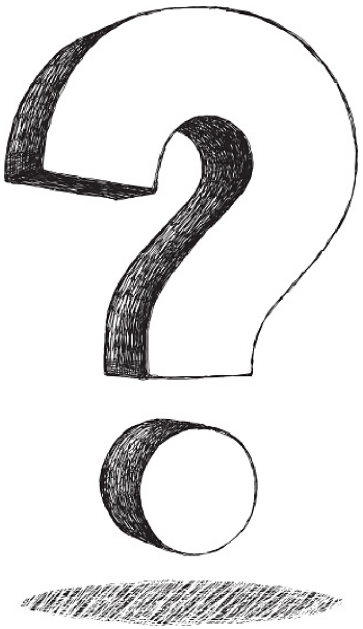


Control arm:
214 lung cancer deaths

Screen arm:
157 lung cancer deaths

Harry J. de Koning, WCLC 2018



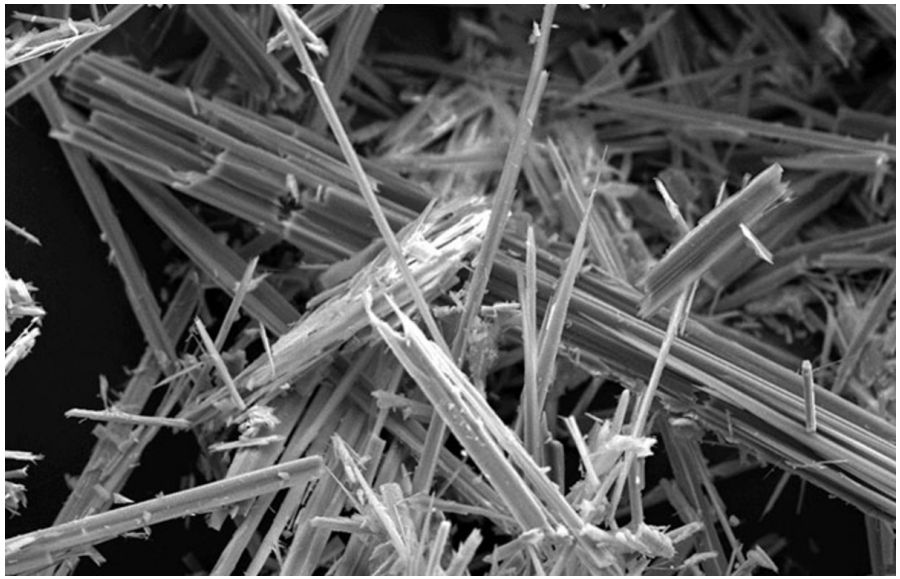
CAN WE DO THE SAME IN MESOTHELIOMA?

Male mesothelioma mortality 2010

Mesothelioma risk

- Dependent of asbestos exposure

- Varies from immeasurably low from occasional exposure to 10% in the highest-exposed asbestos workers



Serum biomarker

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Studies Reporting Sensitivity and Specificity of Mesothelin in Undiagnosed Effusions

Study	Study Setting	Study Cohort	Cytologic Analysis	Total No.	No. MM	Sens,[a] %	Spec,[a] %	NPV,[a] %	PPV,[a] %
Davies et al[15]	Oxford Centre for Respiratory Medicine, Oxford, UK	166 consecutive patients with possible malignant PE	Atypical Nondiagnostic/ nonmalignant	11 94	8 7	63 57	100 97	50 97	100 57
Hooper et al[16]	North Bristol Lung Centre, Bristol, UK	206 consecutive patients with a new undiagnosed PE	Atypical Nondiagnostic	26 148	13 15	73 64	70 96	70 96	73 69
Canessa et al[17]	Division of Pneumology, La Spezia, Italy	275 consecutive patients with undiagnosed PE	Undiagnosed	NR	NR	76	94	NR	NR
Creaney et al[18]	PathWest Diagnostic Laboratory, Perth, WA, Australia	1,331 consecutive patients with possible malignant PE	Atypical/suspicious Nondiagnostic/ nonmalignant	81 855	34 43	62 44	98 99	78 97	95 65

Creaney et al. CHEST 2017; 152(1):143-149

Serum biomarker

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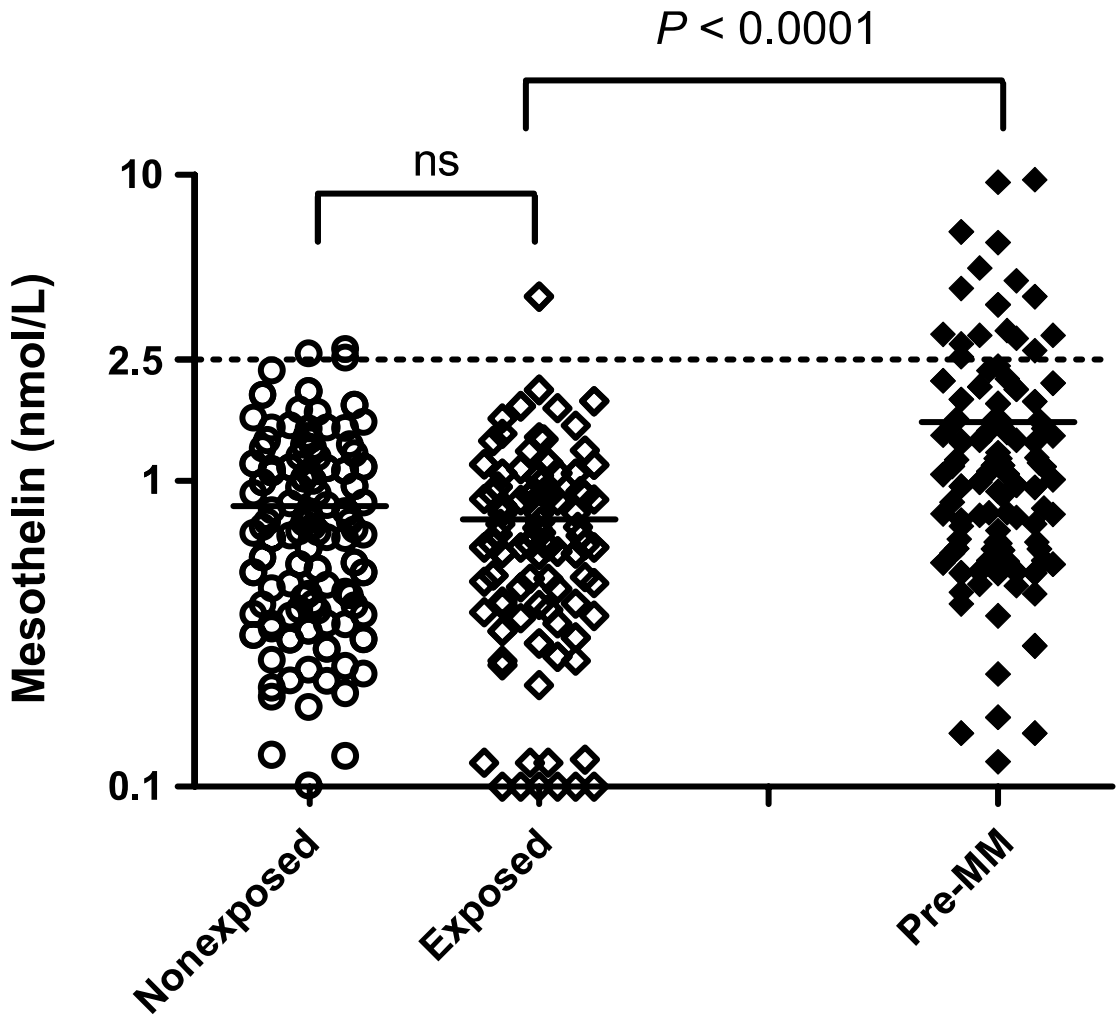

Creaney et al. Cancer Epidemiol Biomarkers Prev 2010;19:2238-2246

Biomarkers

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- Old
  - Mesothelin
  - Osteopontin
  - Fibulin-3

- New
  - ENOX2
  - Circulating microRNA
  - High-mobility group box 1
  - Proteomics
  - Deep learning

NOTYETKNOWN

Ultra-Low-Dose Chest Computer Tomography Screening of an Asbestos-exposed Population in Western Australia

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Characteristic	LDCT	No LDCT
Total subjects	906	402
Mean (SD) age, yr		
Male		
Smoking status		
Current		
Ex		
Never		
Mean (SD), pack-years		
Asbestos exposure		
Wittenoom worker		
Wittenoom resident		
Other occupational		
Mean (SD) time since first exposure, yr		
Mean (SD) exposure duration,		
Spirometry		
Percentage predicted FEV_1		
Percentage predicted FVC		
FEV_1/FVC ratio		
D_{LCO}	21.60 (6.45)	21.02 (5.62)

Brims, AJRCCM 2015

Results

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	Year 1	Year 2
Total subjects	906	973
1st scan	906 (100%)	115 (11.8%)
Indeterminate nodule	79 (8.85%)	42 (4.3%)
Recall	77 (8.4%)	37 (3.8%)
Lung cancer	7 (0.77%)	3 (0.3%)
Mesothelioma	4 (0.44%)	1 (0.1%)

NELSON trial

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CT screening

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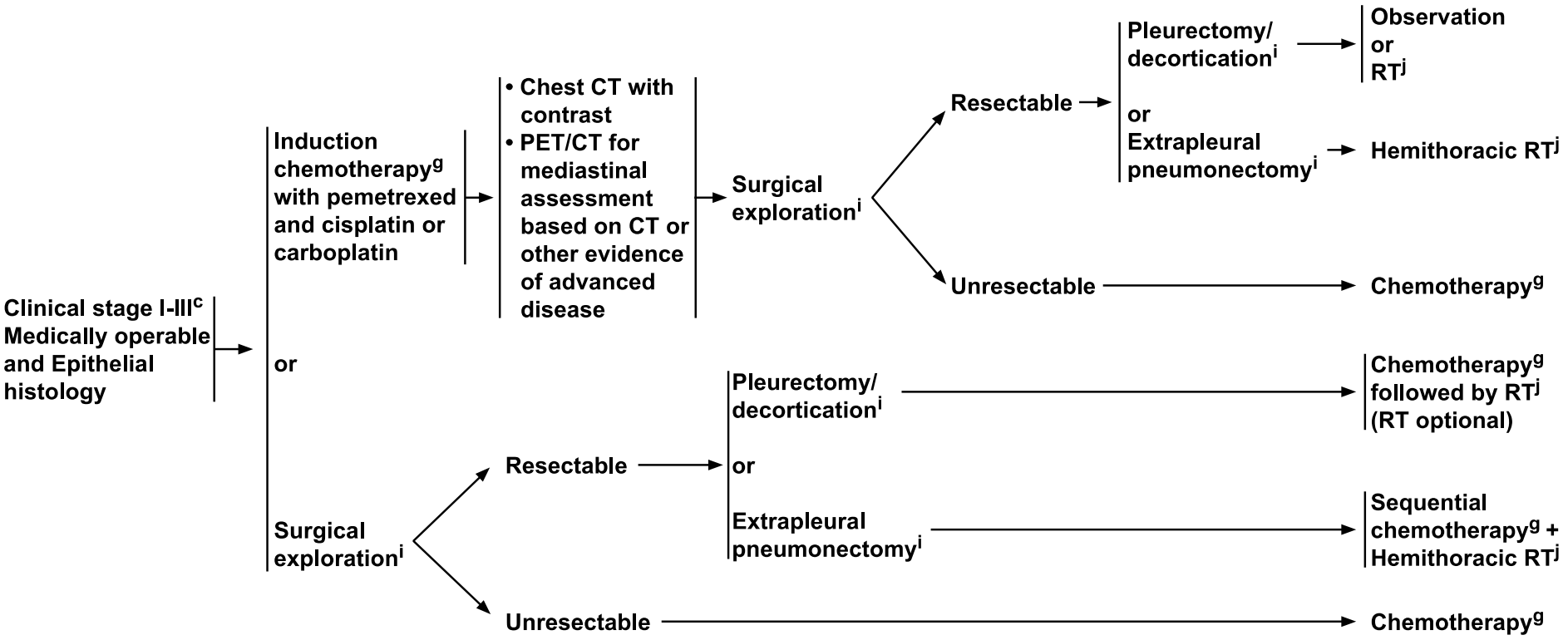
- Even in the highest asbestos exposed workers, the incidence of mesothelioma is lower than lung cancer in lung cancers screening studies.

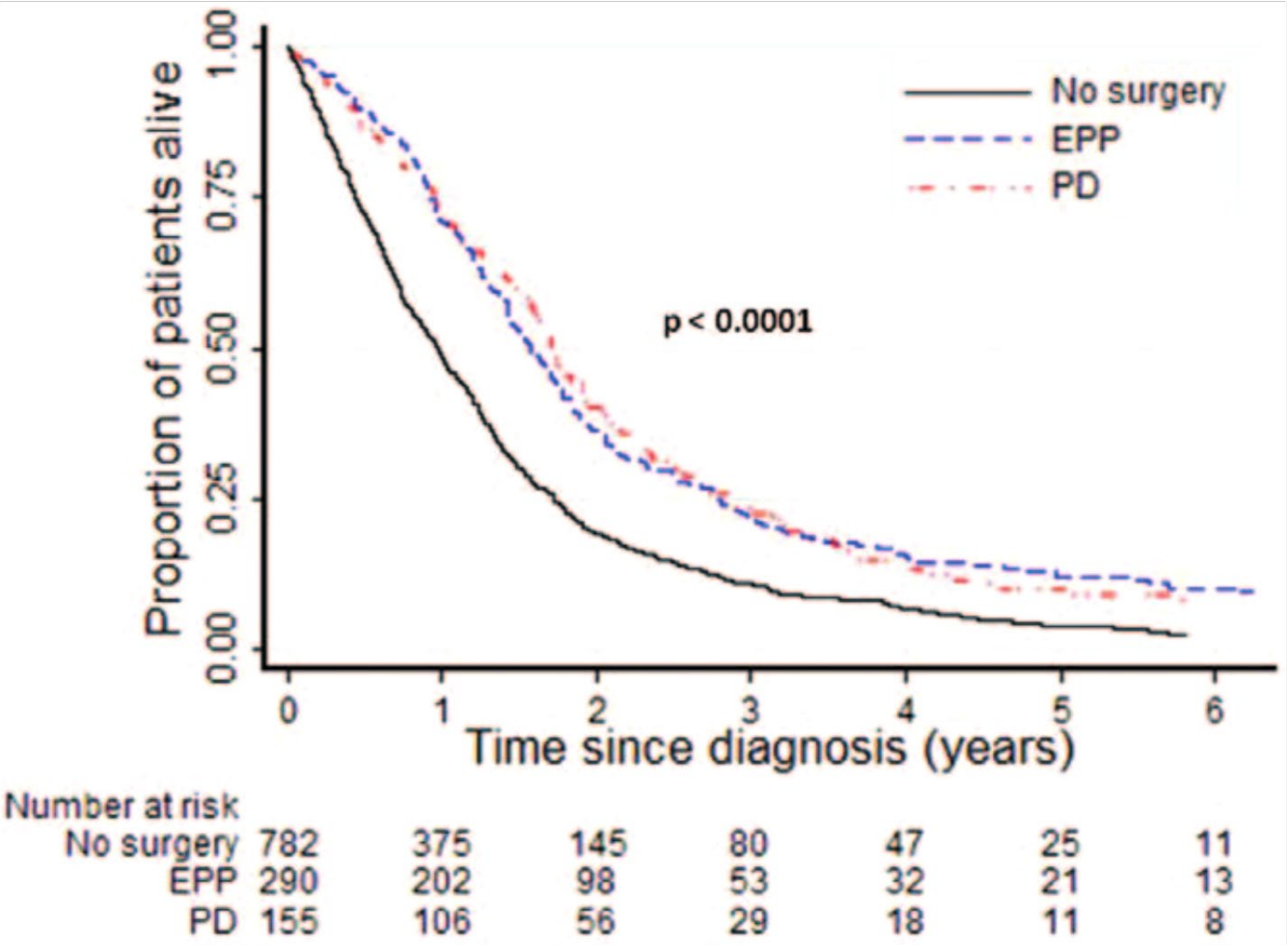
- A positive outcome of such trials is unimaginible:
  - Number needed to screen vs number of asbestos exposed persons
  - Harm done by unneccessary interventions

  - In addition….

NCCN guidelines 2018.2

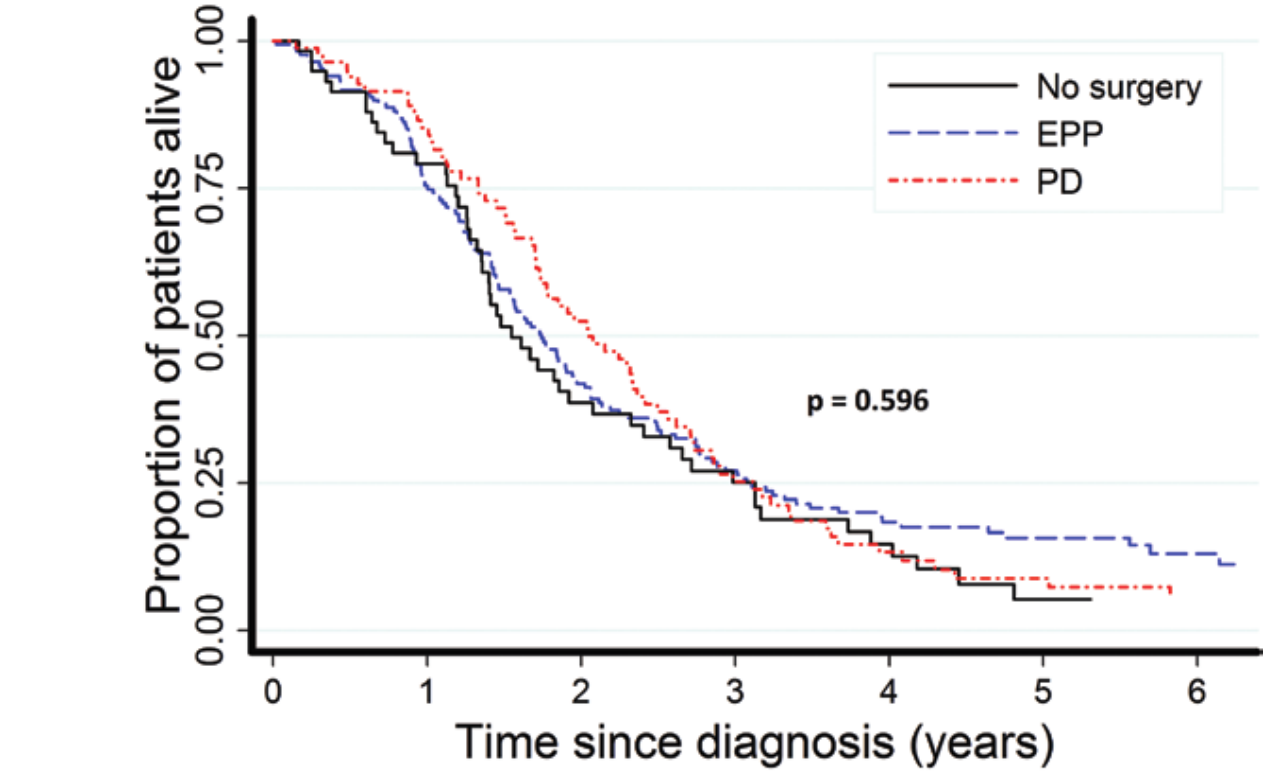


Surgery in mesothelioma



Bovolato, Journal of Thoracic Oncology, March 2014

Surgery in mesothelioma



Number at risk							
No surgery	58	44	20	13	7	2	1
EPP	169	125	65	39	22	14	8
PD	86	69	41	19	10	6	4

- *<70 years*
- *Chemotherapy*
- *Epithelial subtype*

Bovolato, Journal of Thoracic Oncology, March 2014

Surgery

- No curative treatment for early stage mesothelioma

Currently, there is no consensus regarding the optimal multimodality approach to patients with resectable MPM.[17] As complete surgical resection (R0 resection) remains elusive in most patients with MPM, local recurrence represents the most common form of disease relapse. To

Current and Future Management of Malignant Mesothelioma: A Consensus Report from the National Cancer Institute Thoracic Malignancy Steering Committee, International Association for the Study of Lung Cancer, and Mesothelioma Applied Research Foundation

Conclusion:

SCREENING FOR EARLY STAGE MESOTHELIOMA IS POINTLESS

Future perspective

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- We need better treatment !

Combining immunotherapy with surgery

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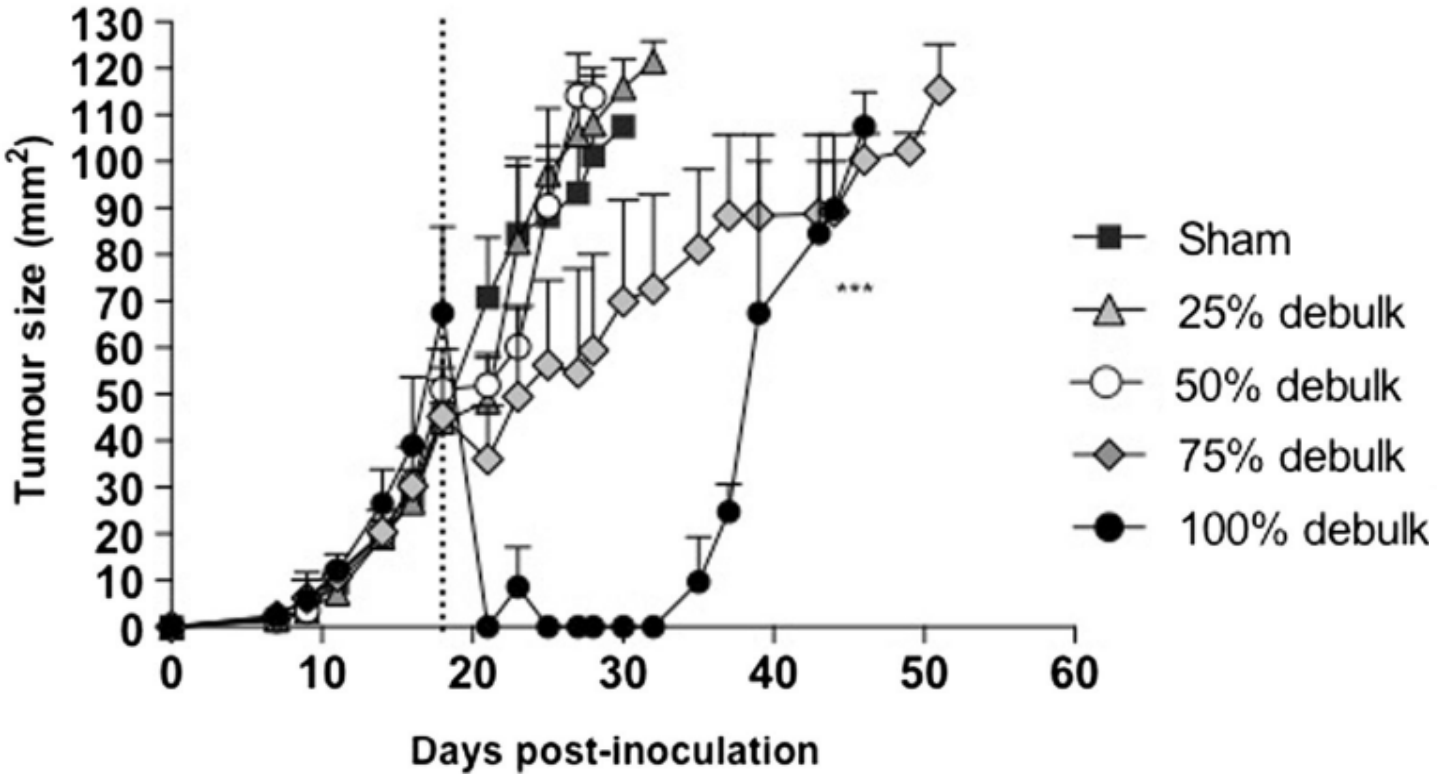
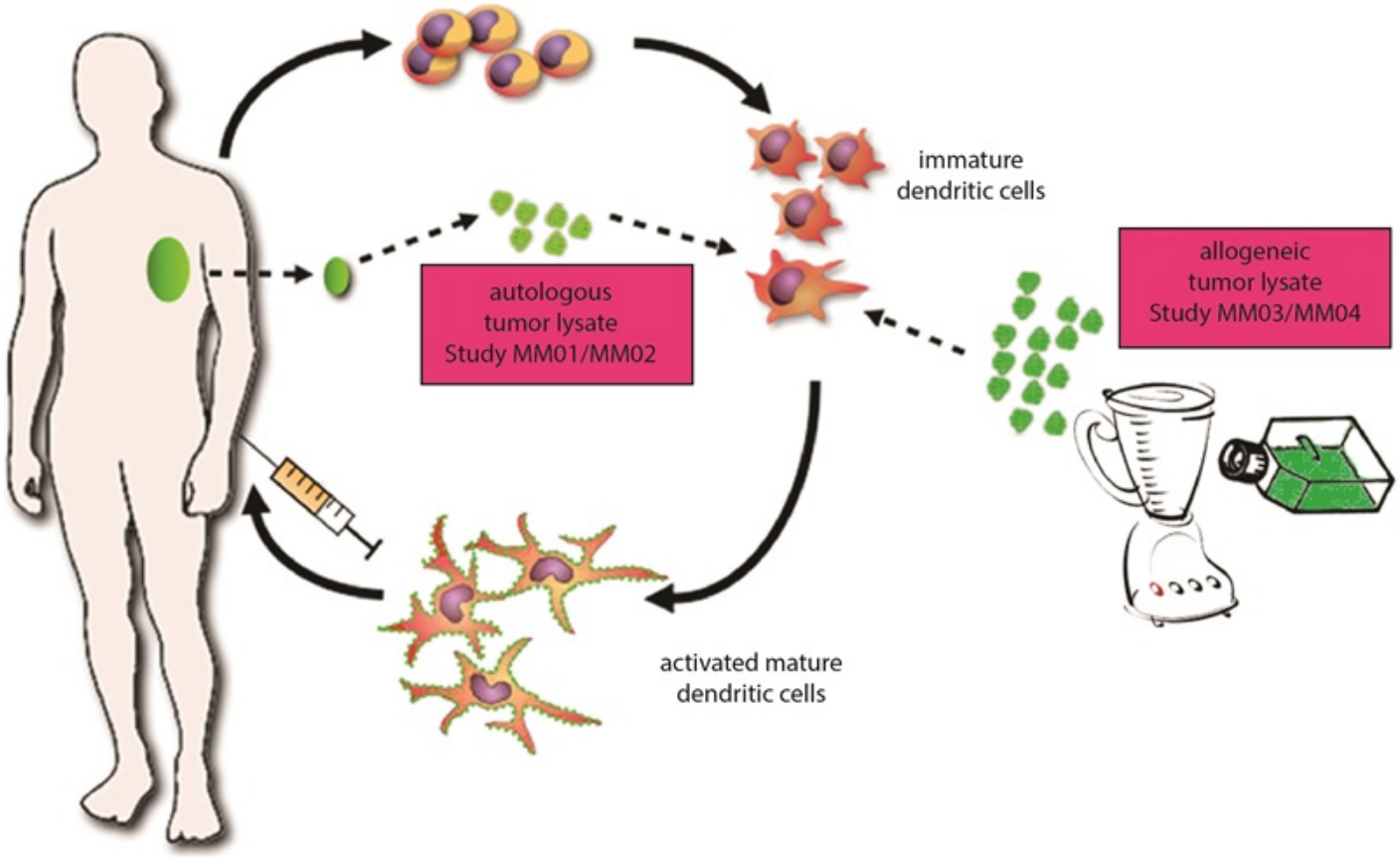


Khong BMC Cancer 2014

Dendritic Cell Immunotherapy



This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 668769

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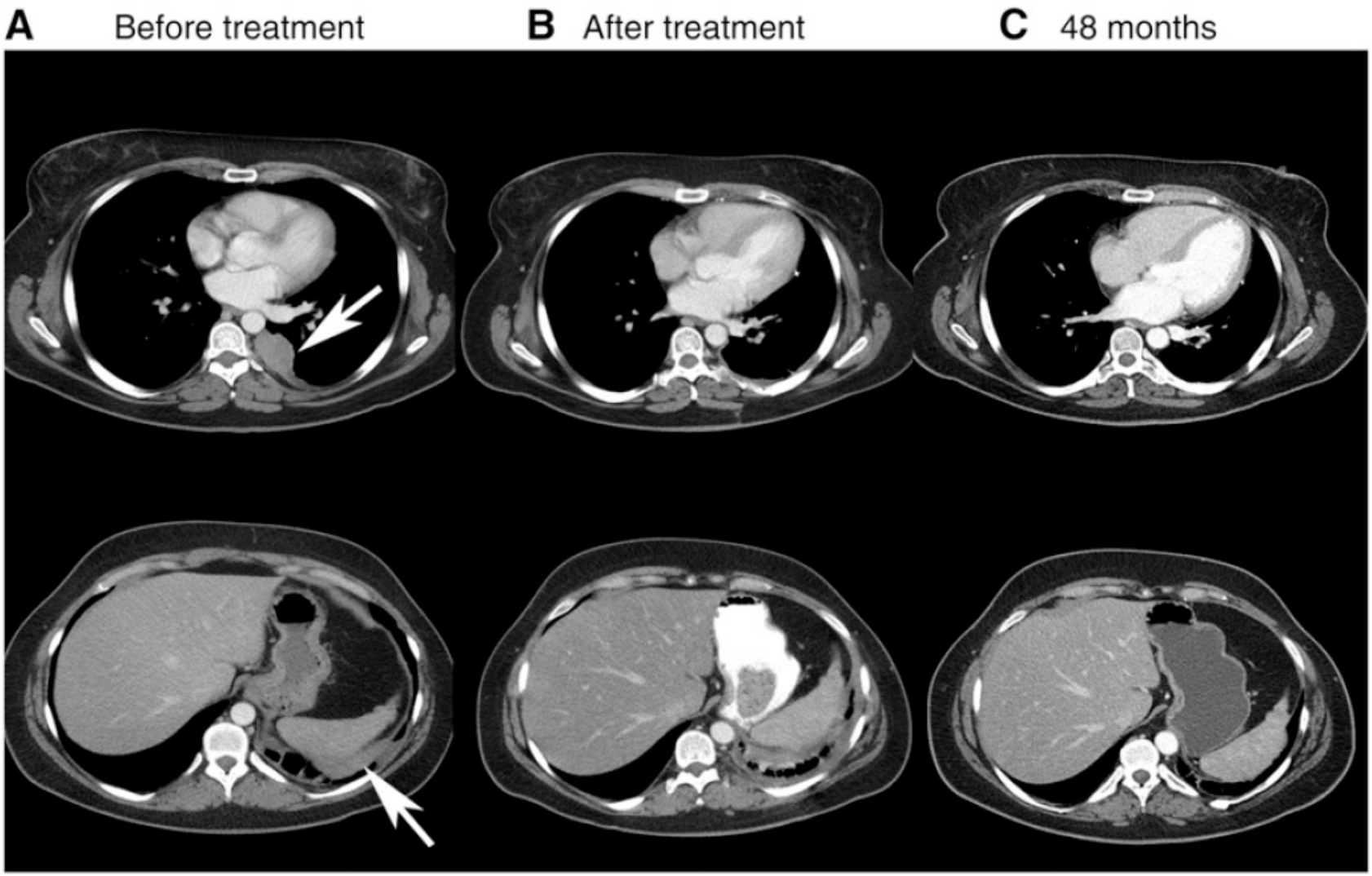
University Medical Center Rotterdam

Patient

- Epithelial type mesothelioma
- Induction chemotherapy, 4 cycles of cisplatin – pemetrexed
  - Stable disease
- Pleurectomy/decortication
  - 90% viable tumor tissue, hardly any chemotherapy effect
  - Irradical resection allover
- Adjuvant dendritic cell immunotherapy

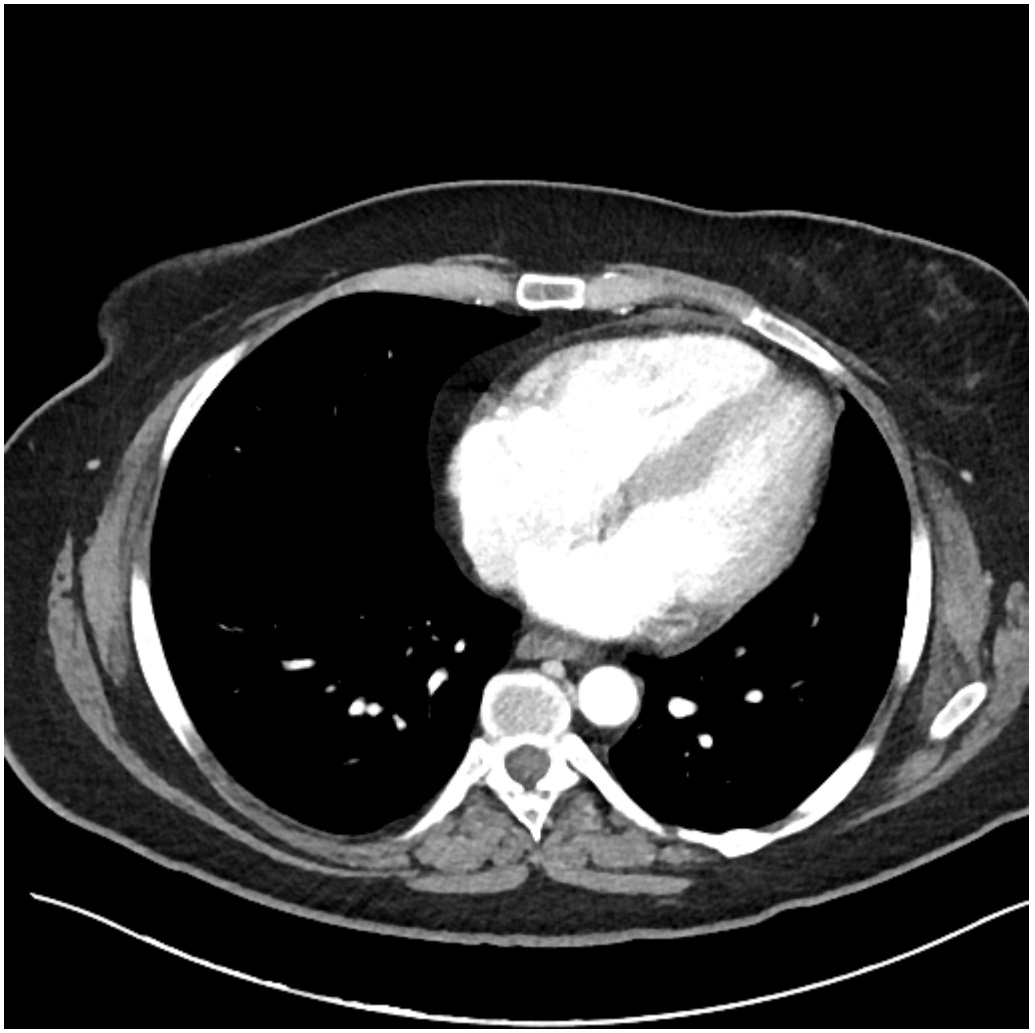
Patient



Cornelissen, AJRCCM 2015

Patient

- Treatment in 2010



January 2019

Take home messages

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- Screening for mesothelioma currently not useful
  - No proven method
  - No consequences of finding disease in early stage

- Need for improved treatment in early-stage disease
  - When available; need for better screening tools