

Is any type of surgery worth doing pleural mesothelioma?

No

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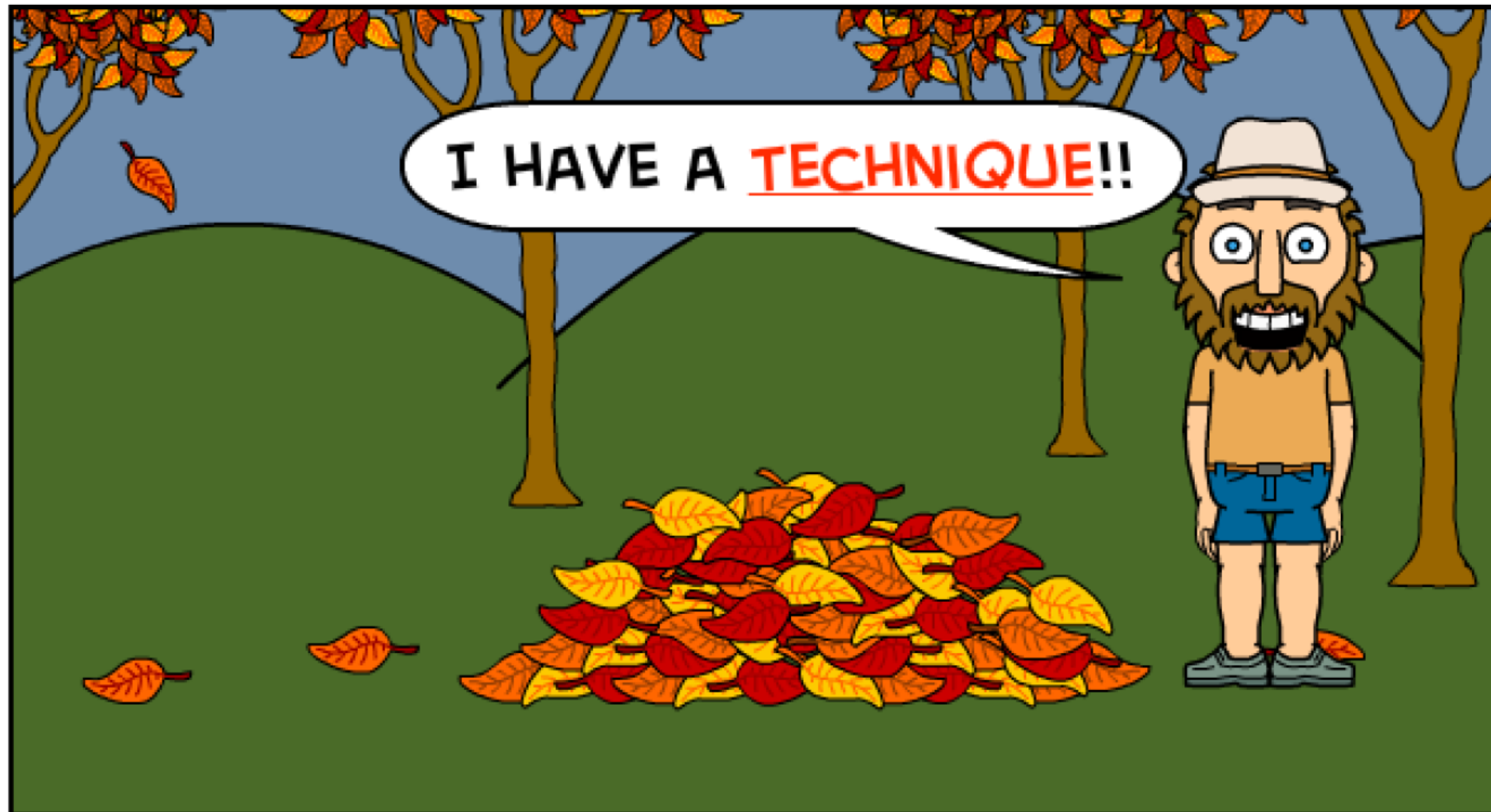
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Disclosures

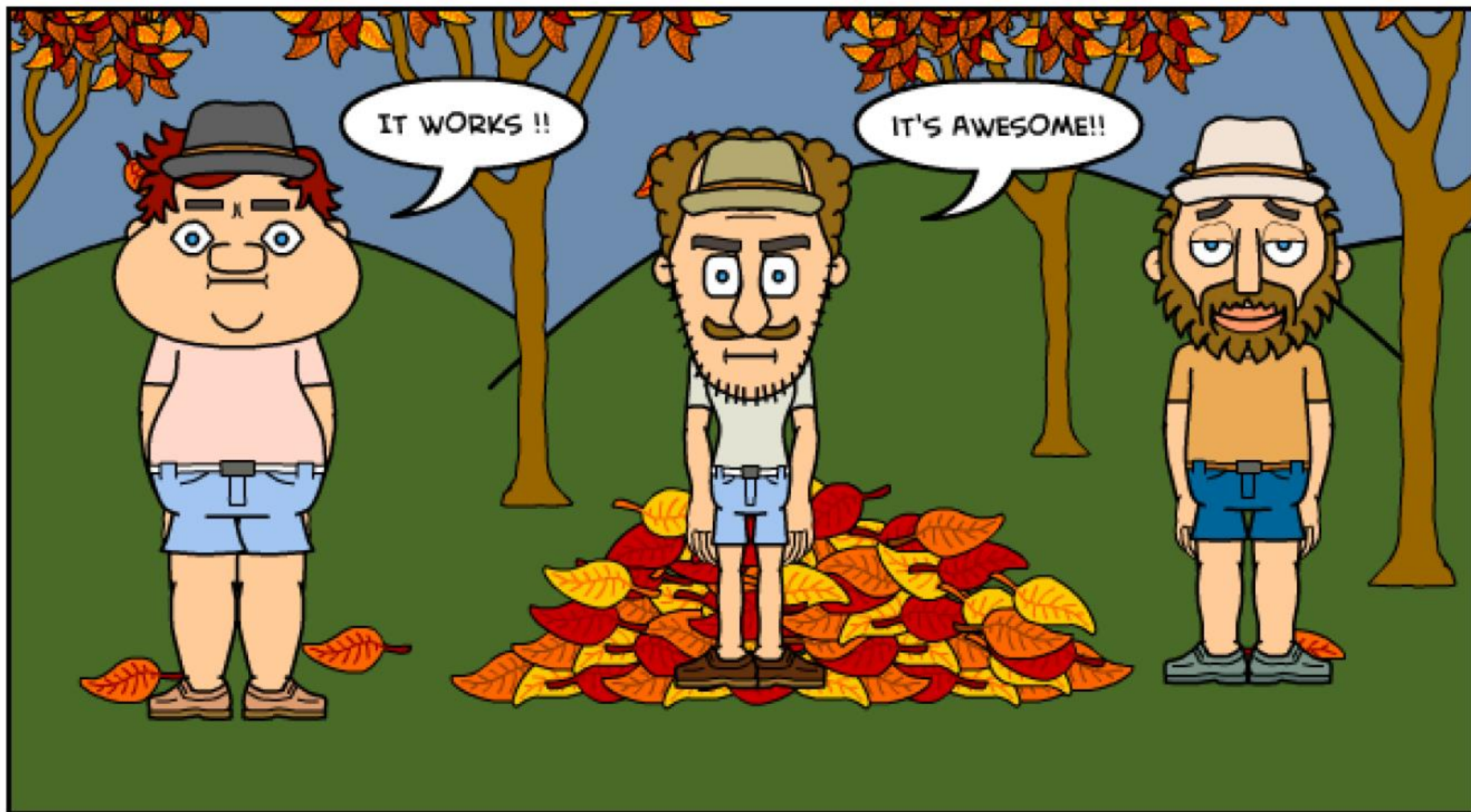
- Consultancy / Advisory Board
 - Strategen, Abbott Molecular, Glaxo Smith Klein, Pfizer, Novartis, Covidien, Ethicon
- Educational presentations / speaker
 - Roche, Immedex, Glaxo Smith Klein, Lilly, Pfizer, Medela, Boehringer Ingelheim, Ethicon
- Travel, accommodation and course fees
 - Covidien, Medela
- Research funding
 - ScreenCell®, Meleida
- Other
 - Founder of Informative Genomics (blood based molecular diagnostics laboratory)
 - Director of the BUPA Cromwell Lung Cancer Screening Programme
 - Chief Investigator for MARS 2 – surgery versus no surgery for mesothelioma
 - Chief Investigator for VIOLET – VATS versus thoracotomy for lung cancer



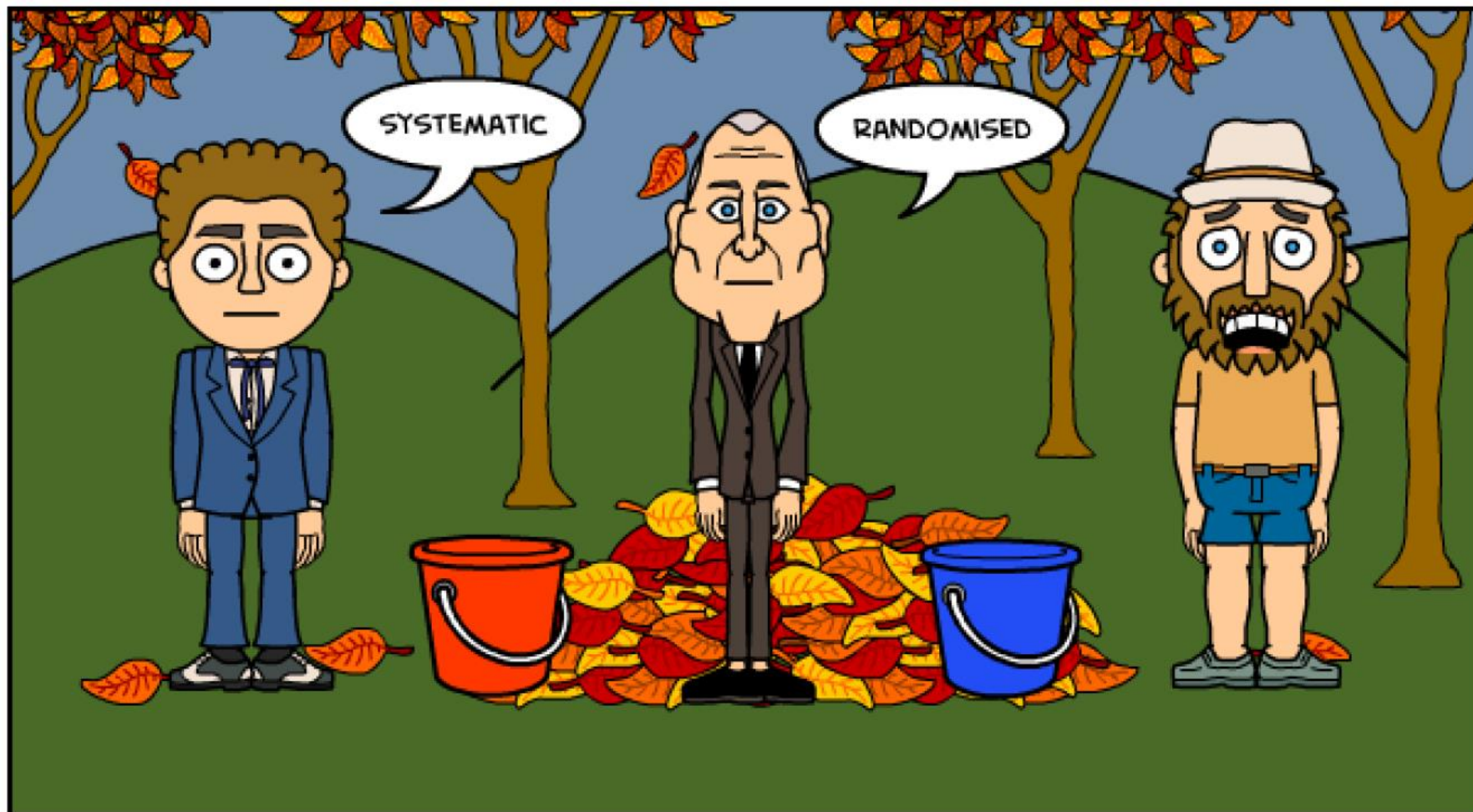


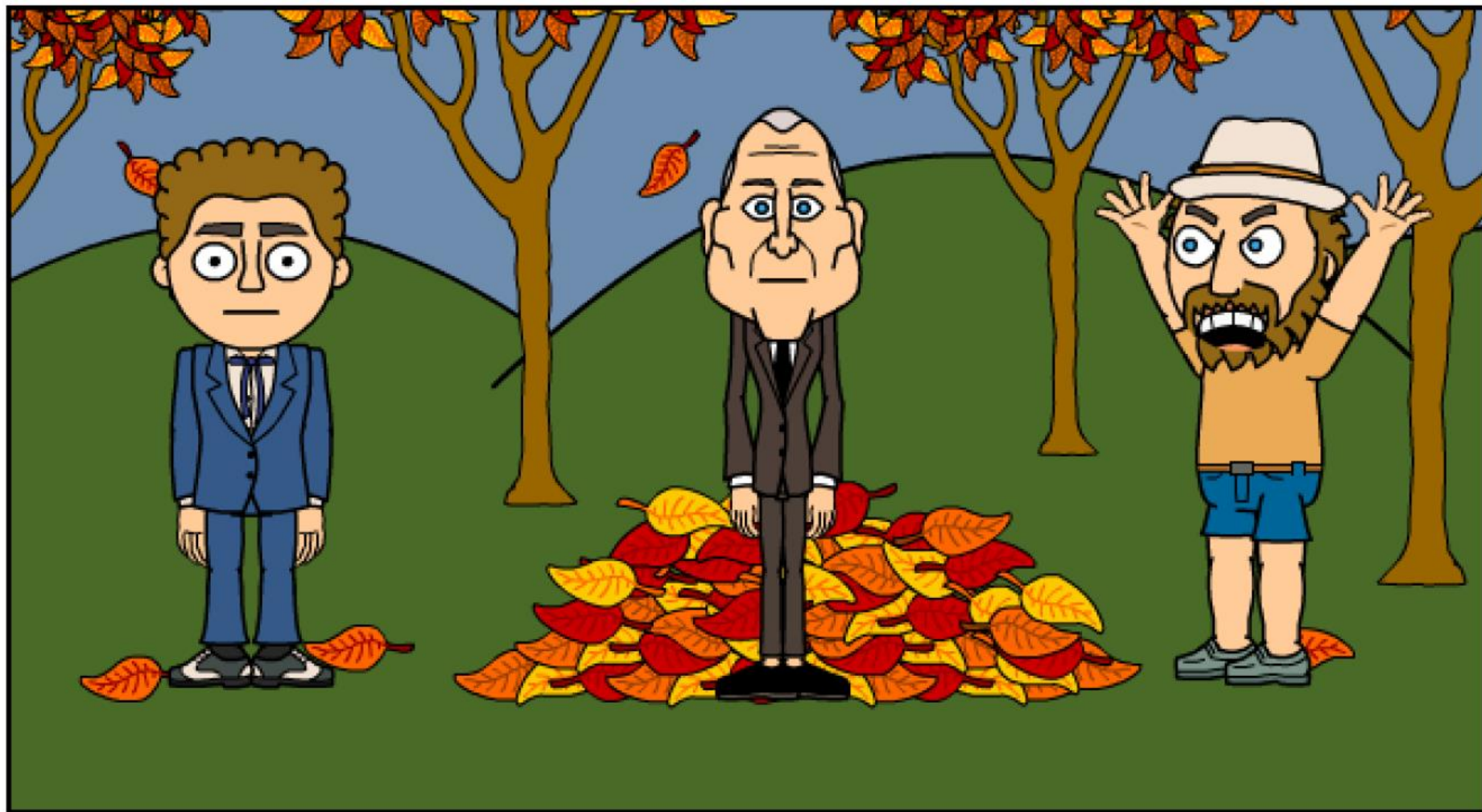












Why do we offer surgery for mesothelioma?

- Improve length of life
- Improve quality of life
- I will summarise ALL the randomised controlled trials to date covering all the major surgical procedures for mesothelioma
 - Of which there are only 3
 - Extra-pleural pneumonectomy
 - Pleurectomy decortication
 - Partial pleurectomy
 - All of them conducted in the UK

What do we offer?

- Extra-pleural pneumonectomy
 - removal of the lining of the chest wall, lining of the lung, the lung itself with the sac of the heart and / or diaphragm (as required to achieve complete tumour removal)
- Pleurectomy decortication
 - removal of the lining of the chest wall, lining of the lung, with the sac of the heart and / or diaphragm (as required to achieve complete tumour removal) but leaving the lung in-situ
- Partial pleurectomy
 - removal of part of the lining of the chest wall and lining of the lung only

RCT evidence remains gold standard

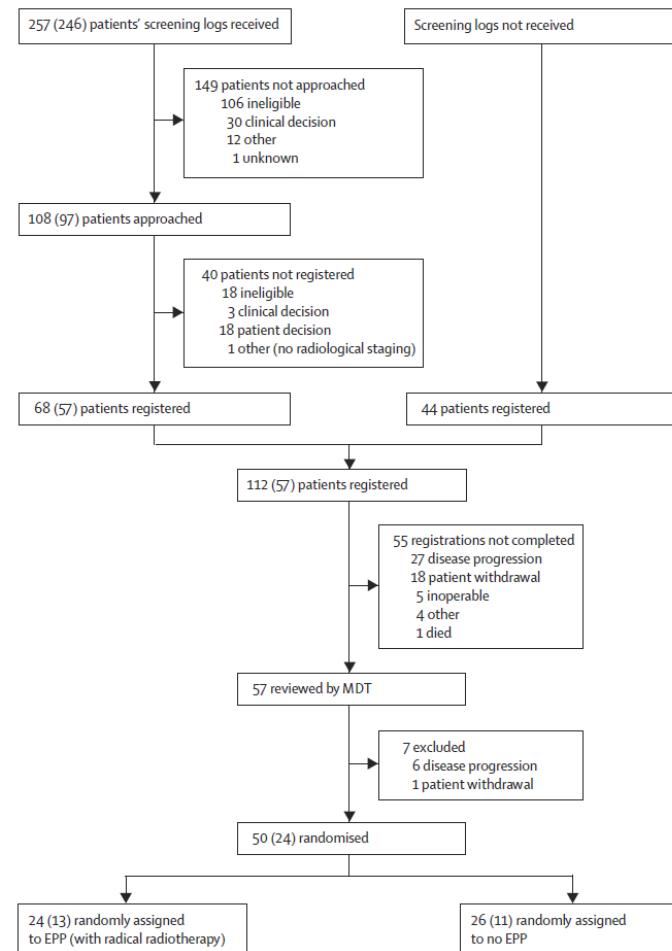
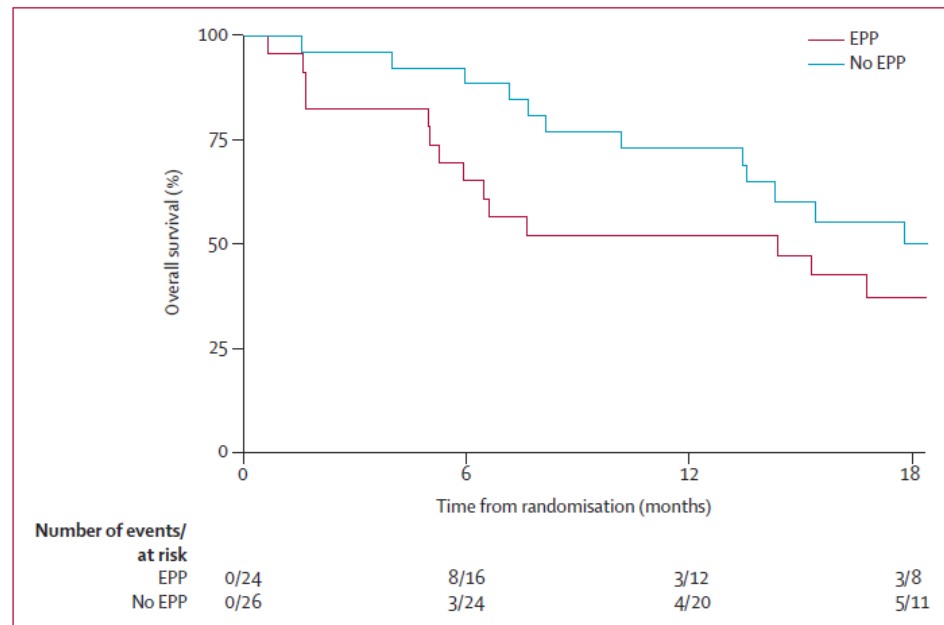
- Data is collected **prospectively**
 - Outcomes are defined
 - Serious adverse events are reported real time to CI and DMEC
- Patients are **randomised**
 - Groups are equal in disease extent and co-morbidities
- **Controlled trial**
 - Treatment allocations according to protocol
 - Analysed by intention to treat



Improve length of life

Extra-pleural pneumonectomy versus no extra-pleural pneumonectomy for patients with malignant pleural mesothelioma: clinical outcomes of the Mesothelioma and Radical Surgery (MARS) randomised feasibility study

Tom Treasure, Loic Lang-Lazdunski, David Waller, Judith M Bliss, Carol Tan, James Entwisle, Michael Snee, Mary O'Brien, Gill Thomas, Suresh Senan, Ken O'Byrne, Lucy SKilburn, James Spicer, David Landau, John Edwards, Gill Coombes, Liz Darlison, Julian Peto, for the MARS trialists*



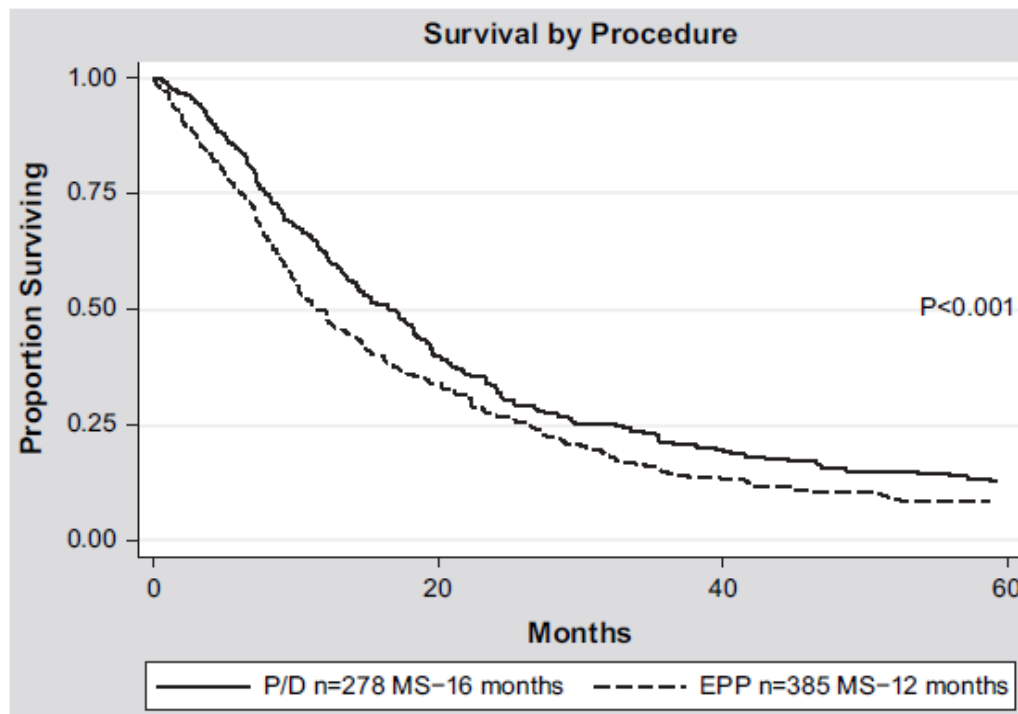
Lancet Oncol 2011; 12: 763-72

Royal Brompton & Harefield NHS Foundation Trust

HR was 2.75 (1.21-6.26; $p=0.016$)

Extrapleural pneumonectomy versus pleurectomy/decortication in the surgical management of malignant pleural mesothelioma: Results in 663 patients

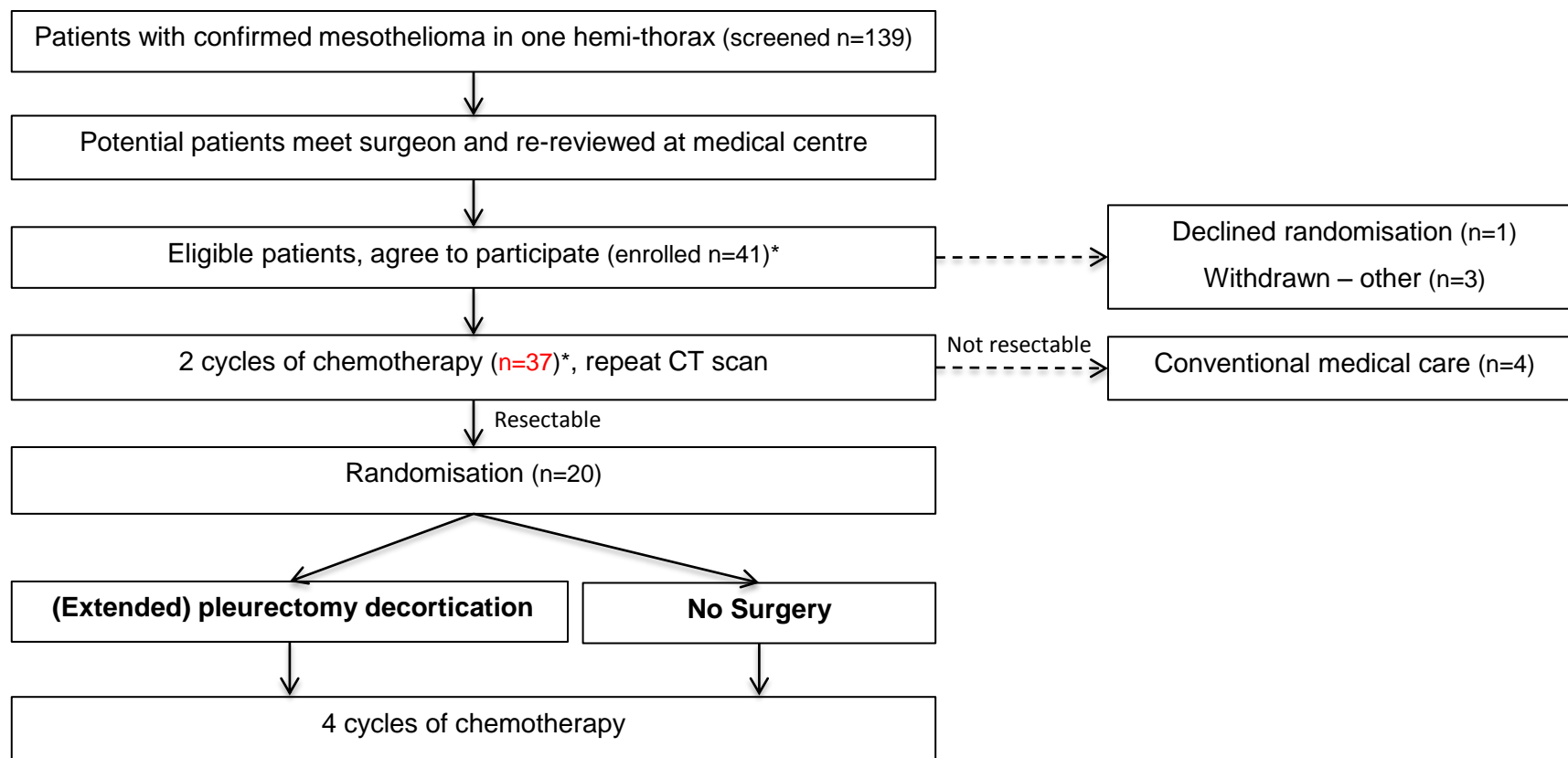
Raja M. Flores, MD,^a Harvey I. Pass, MD,^d Venkatraman E. Seshan, PhD,^b Joseph Dycoco, BA,^a Maureen Zakowski, MD,^c Michele Carbone, MD,^e Manjit S. Bains, MD,^a and Valerie W. Rusch, MD^a



J Thorac Cardiovasc Surg 2008;135:620-6

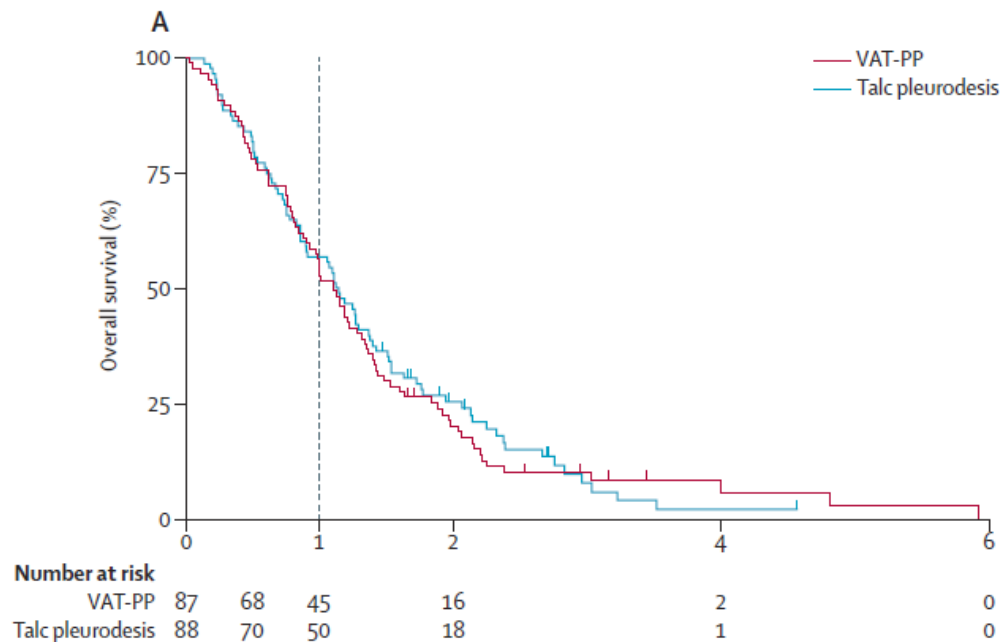
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MARS 2 a UK multicentre RCT of (e) P/D



Efficacy and cost of video-assisted thoracoscopic partial pleurectomy versus talc pleurodesis in patients with malignant pleural mesothelioma (MesoVATS): an open-label, randomised, controlled trial

Robert C Rintoul, Andrew J Ritchie, John G Edwards, David A Waller, Aman S Coonar, Maxine Bennett, Eleonora Lovato, Victoria Hughes, Julia A Fox-Rushby, Linda D Sharples, on behalf of the MesoVATS Collaborators*



Lancet 2014; 384: 1118-27

Improve length of life

Extra-pleural pneumonectomy – MARS 1 indicated possible harm
(extended) pleurectomy decortication – MARS 2 currently evaluating
Partial pleurectomy – MesoVATS indicated no survival difference

No role for surgery (except in a clinical trial)



Improving quality of life

Extra-pleural pneumonectomy versus no extra-pleural pneumonectomy for patients with malignant pleural mesothelioma: clinical outcomes of the Mesothelioma and Radical Surgery (MARS) randomised feasibility study

Tom Treasure, Loic Lang-Lazdunski, David Waller, Judith M Bliss, Carol Tan, James Entwisle, Michael Snee, Mary O'Brien, Gill Thomas, Suresh Senan, Ken O'Byrne, Lucy S Kilburn, James Spicer, David Landau, John Edwards, Gill Coombes, Liz Darlison, Julian Peto, for the MARS trialists*



Figure 6: Quality of life

Lancet Oncol 2011; 12: 763-72

Royal Brompton & Harefield NHS Foundation Trust

Efficacy and cost of video-assisted thoracoscopic partial pleurectomy versus talc pleurodesis in patients with malignant pleural mesothelioma (MesoVATS): an open-label, randomised, controlled trial

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Results of the analysis of some of the EORTC subscales (eg, global health, physical functioning, and role functioning) were similar to the results from the EQ-5D analysis (poorer function at 1 month and better function at 3, 6, and 12 months with VAT-PP than with talc pleurodesis), but results were not consistent between scales, nor were the differences noted between groups consistently significant (appendix).

Interpretation VAT-PP is not recommended to improve overall survival in patients with pleural effusion due to malignant pleural mesothelioma, and talc pleurodesis might be preferable considering the fewer complications and shorter hospital stay associated with this treatment.

	VAT-PP (n=78)	Talc pleurodesis (n=73)
Serious adverse events	13 (17%)	8 (11%)
Death	1 (1%)	0
Extended hospital stay		
Renal failure	1 (1%)	0
Surgical emphysema	1 (1%)	0
Repeat VAT-PP and subsequent CVA	2 (3%)	0
Fever and dyspnoea	0	1 (1%)
Re-admissions		
Leaking drain	3 (4%)	0
Persistent pleura effusion	1 (1%)	3 (4%)
Hydropneumothorax	1 (1%)	0
Empyema	1 (1%)	1 (1%)
Infected drain site	0	2 (3%)
Thoracotomy with decortication	0	1 (1%)
Symptom control	1 (1%)	0
Other		
Awareness under anaesthesia	1 (1%)	0

Data are number of events (% of patients). VAT-PP=video-assisted thoracoscopic partial pleurectomy. CVA=cerebrovascular accident.

Table 3: Deaths and serious adverse events possibly or probably related to treatment

Lancet 2014; 384: 1118-27

Improving quality of life

Extra-pleural pneumonectomy – MARS 1 indicated worse QoL

(extended) pleurectomy decortication – MARS 2 currently evaluating

Partial pleurectomy – MesoVATS indicated no consistent difference in QoL favouring talc pleurodesis (less complications and shorter stay)

No role for surgery to improve quality of life

Conclusions

- Surgery has not improved survival in any published RCT for mesothelioma
 - Good survival in surgical series merely reflects selection bias
- Given results of MARS 1 EPP should not be performed
- All things being equal, the results of EPP and (e)PD are likely to be as poor
- The role of surgery should first be defined before evaluated in the multimodality setting – MARS 2
 - Should (e)P/D be recommended at all (never mind age above 70)?

Conclusions

- There is no RCT evidence supporting radiation after radical surgery
 - PIT trial showed no benefit for tract site radiation
- RCT evidence supporting chemotherapy as standard of care
 - Given before or after surgery is not relevant
 - Advantage before surgery is to screen out non-responders
- Lymph node drainage of the pleural is not the same as lung
 - N2 involvement does not preclude surgery (MARS 2)
- MesoVATS RCT concluded talc pleurodesis is preferable (to partial pleurectomy) due to shorter hospital stay and fewer complications

Is any type of surgery is worth doing in mesothelioma?

“The only type of surgery worth doing for mesothelioma is that done in the setting of a randomised clinical trial”

Eric Lim, ELCC 2016



Thinking
is difficult,
that's why
most people
judge.
- C.G. Jung