PET and decision making for the surgical management of Non-Small Cell Lung Cancer.

Professor Frank Kee*
Dr Karen Cairns $
*UKCRC Centre of Excellence for Public Health Research
$ Centre for Statistics and Operational Research, QUB

Overview

- framework for diagnostic test evaluation
- background to the evaluation of PET for NSCLC
- extending the HTBS model
- results
- broader messages

Hierarchy of HTA evaluation

- Technical efficacy
- Diagnostic accuracy
- Diagnostic thinking
- Therapeutic efficacy
- Patient outcome
- Societal efficacy

Efficacy

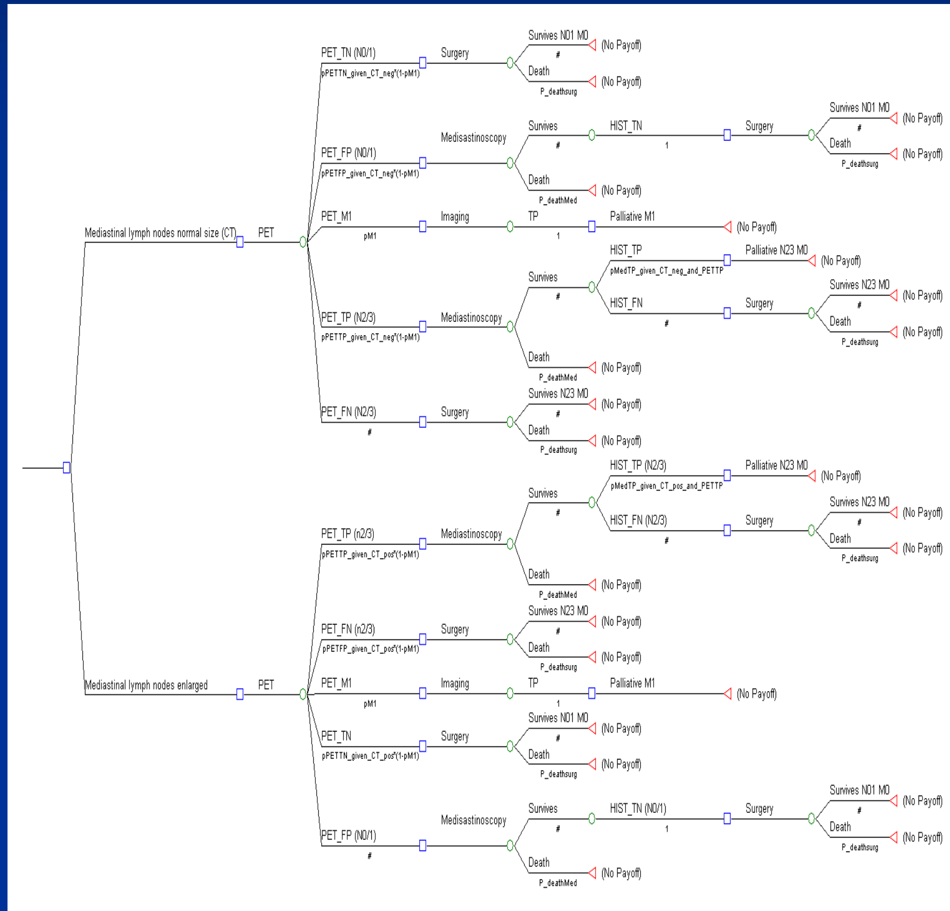
↓

Effectiveness

Frybeck D, Thornbury J, Med Decis Making 1991; 11: 88-94

Main findings and recommendations of HTBS report (2002)

- Cost effectiveness depends on location of PET in clinical pathway
- PET more cost-effective in CT -ve patients than CT +ve patients and than in a "PET for all" strategy
- More information required on patient-related utilities.



Other studies

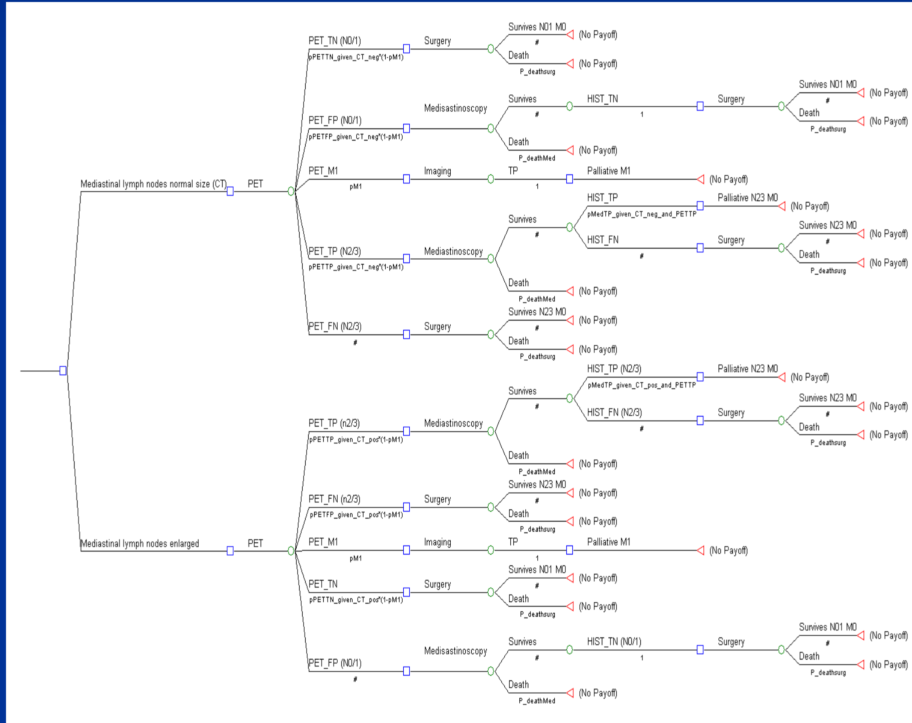
- Probably ≈ 8-10 CE studies published
  - deterministic decision trees
- Key features of CE studies:
  - Benefit depends on the number of avoided futile thoracotomies
  - 60-65 year old man
  - Assumptions
    - LE following surgery 4.5 years
    - LE following chemo-radiation for N2/3 disease: 1.8 years
  - Utilities derived from oncologists
- Only two RCTs (conflicting results)
- A fresh meta-analysis of test performance (Gould et al, 2003)

Main objectives

- To document the PET pathway today and the effect on clinical management decision making
  (including the rate of "futile thoracotomy")
- To estimate patients' utilities for PET-determined treatment states
- To help inform future research and practice priorities

Some issues

- Survivorship after "curative" thoracotomy depends on age
- Utility "weighting" for FP and FN
- Non independence of CT and PET results

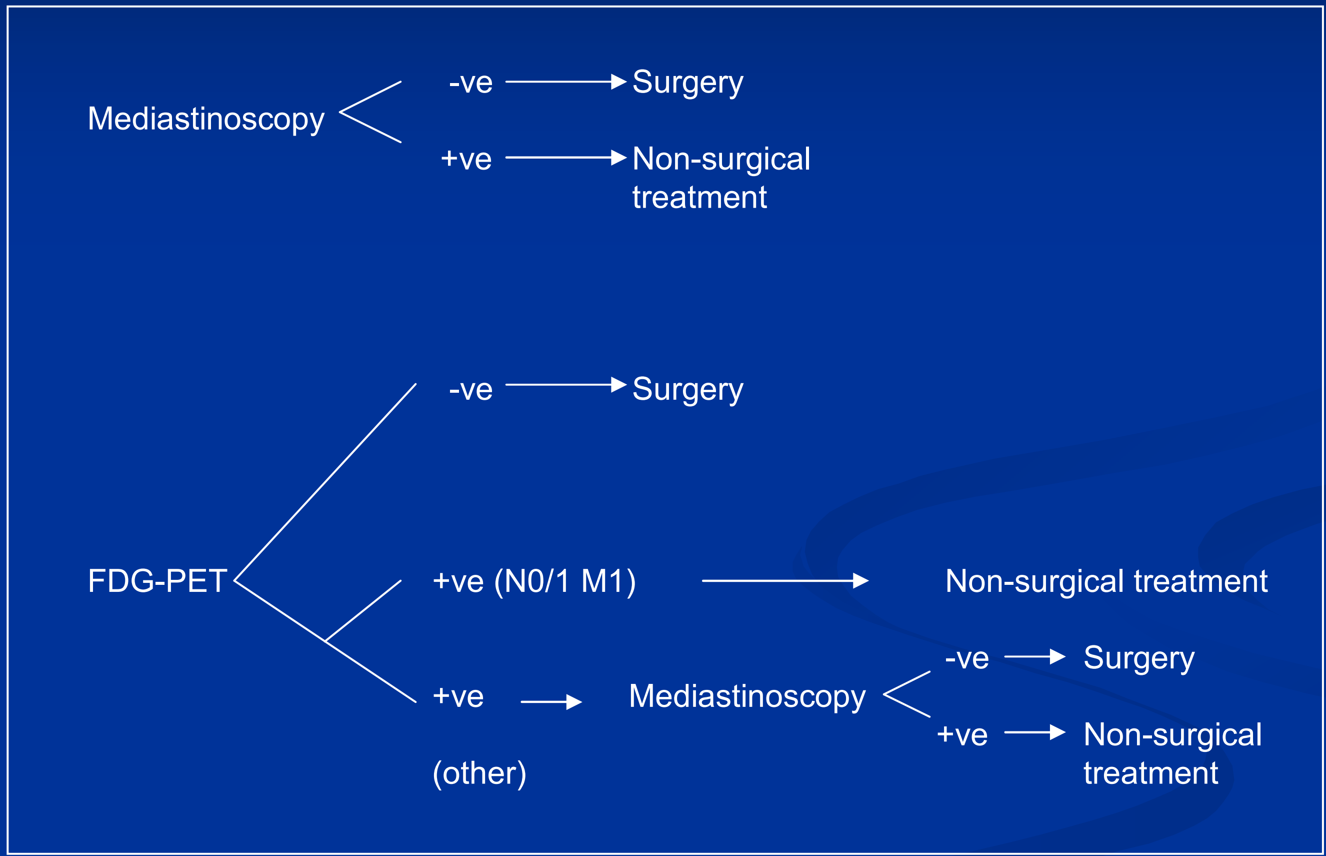


Randomised controlled trial of the role of PET in the management of Stage I and II non small cell lung cancer

Thus the value of FDG PET for management of patients with clinical Stage I-II NSCLC is dependent on the management strategy for Stage IIA disease…….

Viney R, Boyer M, King M et al.
J Clin Oncol 2004; 22: 2357-62.

The two clinical strategies dominating others in HTBS: (Each preceded by CT scan)



Stage distribution used in the HTBS model

	N0/1, M0	N0/1, M1	N2/3, M0	N2/3, M1
Normal lymph nodes	48.4	5.4	10.7	1.2
Enlarged lymph nodes	14.6	1.6	16.3	1.8

Utilities assigned in base case

Stage of disease	Treatment	Utility*	Based on
N0/N1, M0	Surgery	0.88	Earle's figure for local disease
N2/N3, M0	Surgery	0.65	Berthelot's figure for advanced disease which responds to treatment
N0-3, M1	Surgery	0.65	Berthelot's figure for advanced disease which responds to treatment
N0/N1, M0	Non-surgical treatment	0.65	Berthelot's figure for advanced disease which responds to treatment
N2/N3, M0	Non-surgical treatment	0.65	Berthelot's figure for advanced disease which responds to treatment
N0-3, M1	Non-surgical treatment	0.65	Berthelot's figure for advanced disease which responds to treatment

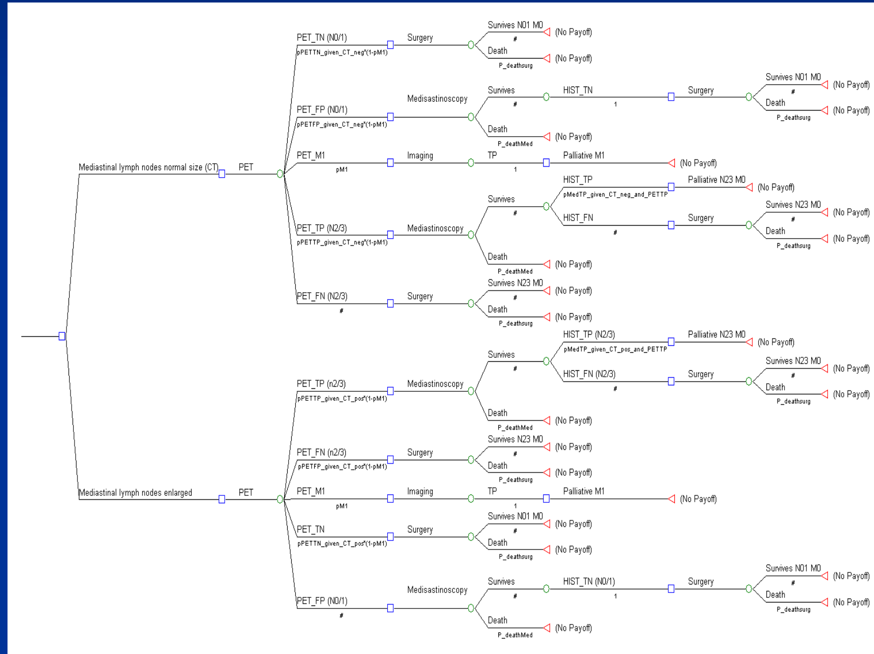
Inputs to the HTBS economic model: base case

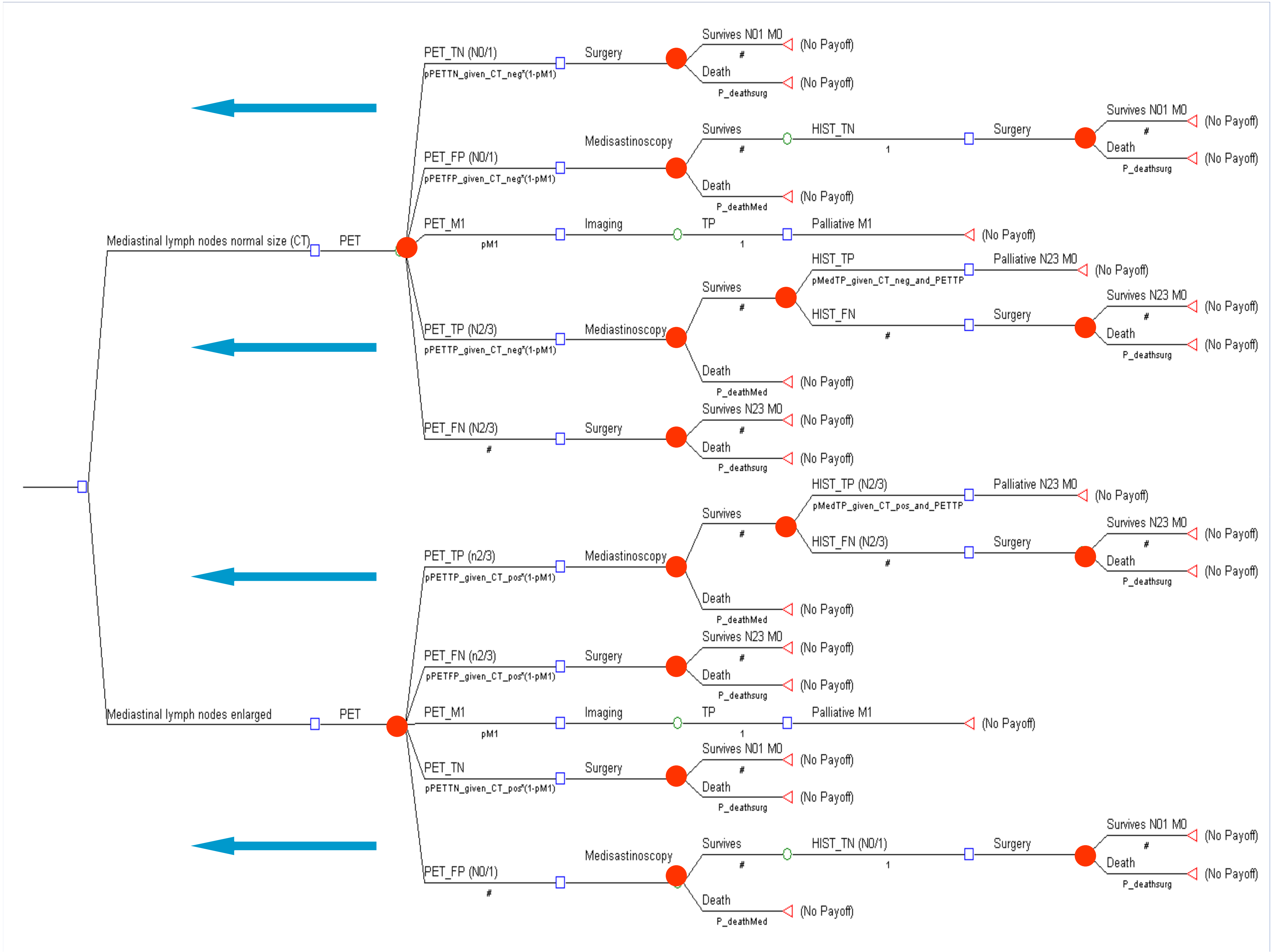
Variable	Input / assumption
Base case patient	62-year-old fit for surgery or non-surgical treatment
Prevalence of N2/N3	30%
FDG-PET sensitivity	CT-negative 86%; CT-positive 92%
FDG-PET specificity	CT-negative 90%; CT-positive 76%
Mediastinoscopy: Specificity Sensitivity	100% 72%
CT and PET mortality	0%
Mediastinoscopy mortality	0.5%
Surgery mortality	3.7%
Life expectancy (LE) after surgery	N0/1, M0 4.5 years N2/3, M0 1.8 years M1 0.5 years
LE after palliation	N0/1, M0 2.6 years N2/3, M0 1.8 years M1 0.5 years
Cost of thoracic FDG-PET	£677
Cost of mediastinoscopy	£375
Cost of surgery	£3,419
Non-surgical treatment: Radical radiotherapy Chemotherapy Best supportive care	£2,102 £4,003 £3,371

		DISEASE	
		Present	Absent
TEST	Positive	True positive a	False positive b
	Negative	False negative c	d True negative

$$Se = \frac{a}{a + c}$$

$$Sp = \frac{d}{b + d}$$





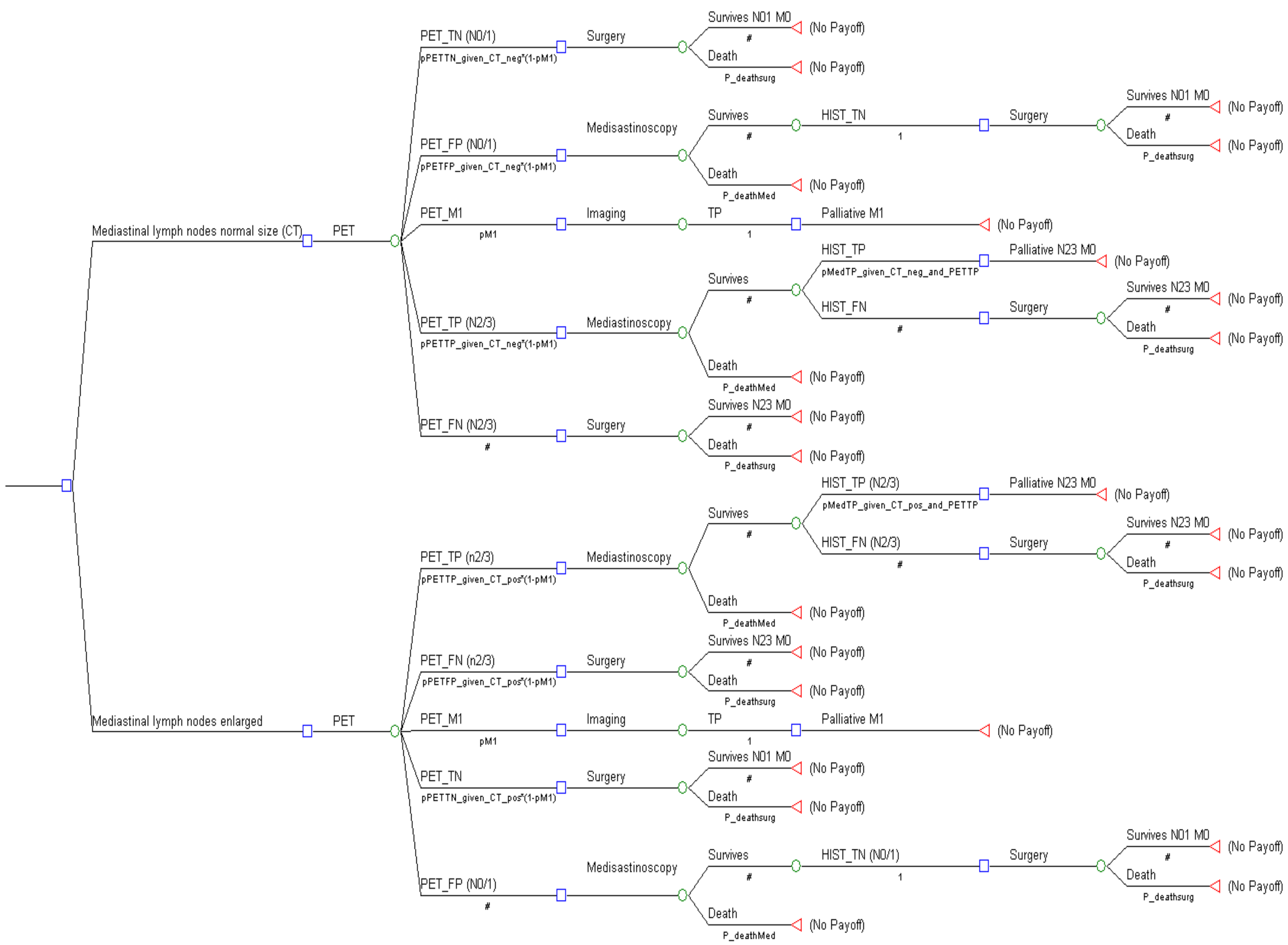
Mediastinal lymph nodes normal size (CT)
PET
PET_TN (N0/1)
pPETTN_given_CT_neg*(1-pM1)
Surgery
Survives N01 M0
#
Death
P_deathsurg
(No Payoff)
PET_FP (N0/1)
pPETFP_given_CT_neg*(1-pM1)
Medisastinoscopy
Survives
HIST_TN
1
Death
P_deathMed
PET_M1
pM1
Imaging
TP
Palliative M1
PET_TP (N2/3)
pPETTP_given_CT_neg*(1-pM1)
Mediastinoscopy
HIST_TP
pMedTP_given_CT_neg_and_PETTP
Palliative N23 M0
HIST_FN
Survives N23 M0
PET_FN (N2/3)
Mediastinal lymph nodes enlarged
PET_TP (n2/3)
pPETTP_given_CT_pos*(1-pM1)
HIST_TP (N2/3)
pMedTP_given_CT_pos_and_PETTP
HIST_FN (N2/3)
PET_FN (n2/3)
pPETFP_given_CT_pos*(1-pM1)
PET_TN
pPETTN_given_CT_pos*(1-pM1)
PET_FP (N0/1)
HIST_TN (N0/1)

		DISEASE	
		Present	Absent
TEST	Positive	True positive a	b False positive
	Negative	False negative c	d True negative

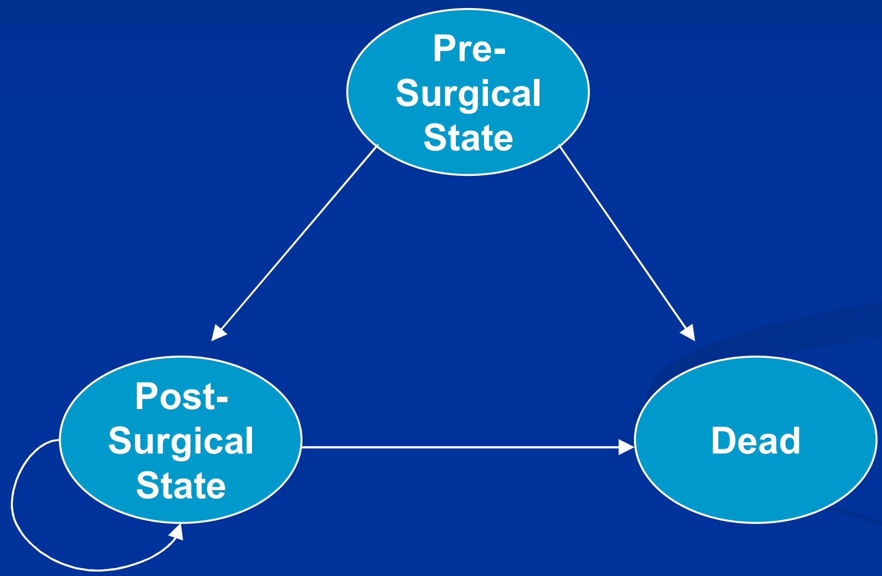
$$Se = \frac{a}{a + c} \qquad Sp = \frac{d}{b + d}$$

p(PET TP / CT –ve) = [**p** (CT-ve / PET TP) . **p**(PET TP)] / **p(**CT –ve)

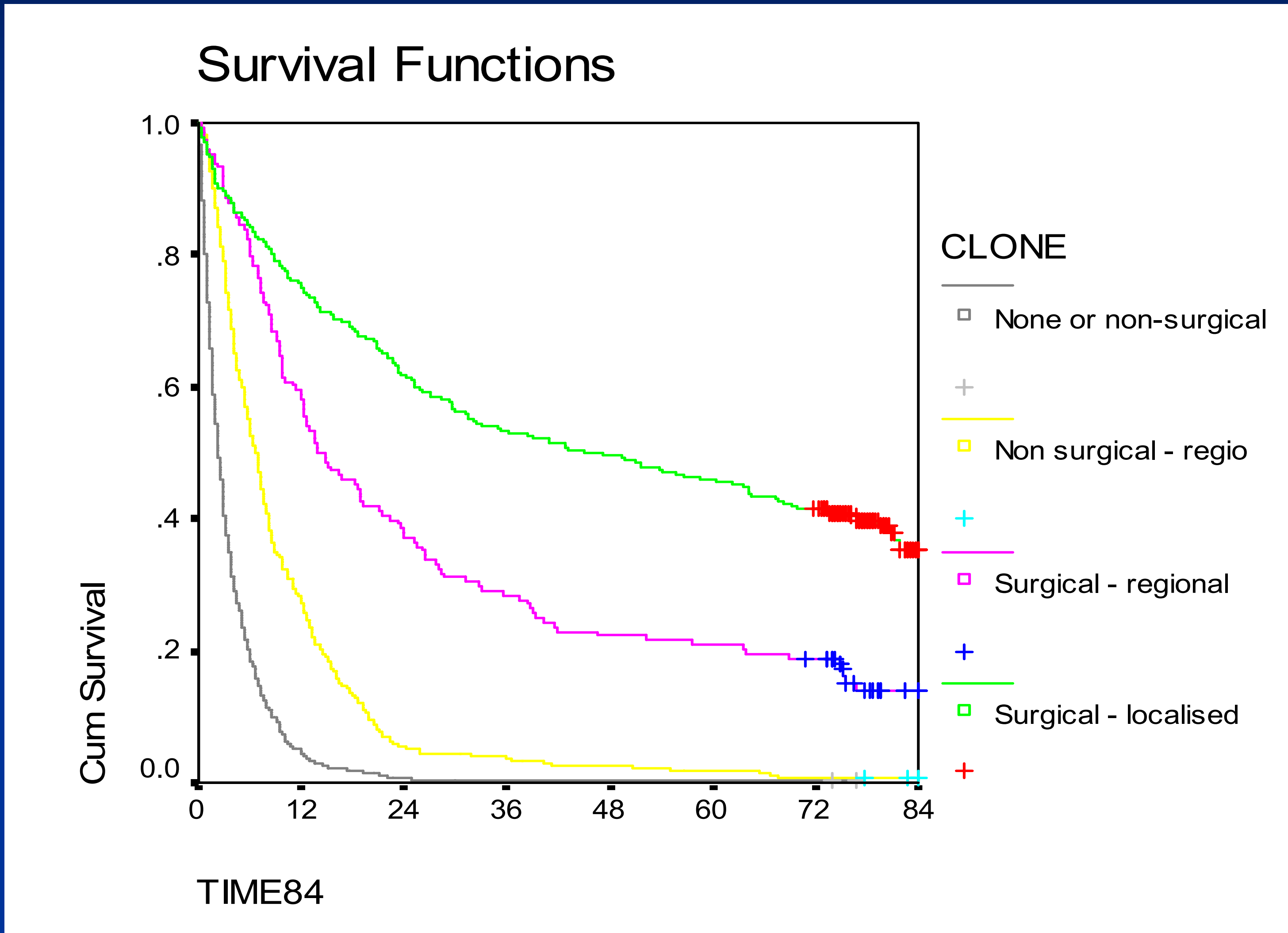
p(CT –ve) = [**p**(CT –ve /N0/1) . **p**(N0/1)] + [**p**(CT –ve / N2/3) . **p**(N2/3)]


Mediastinal lymph nodes normal size (CT)
PET
PET_TN (N0/1)
pPETTN_given_CT_neg*(1-pM1)
Surgery
Survives N01 M0
#
Death
P_deathsurg
(No Payoff)
PET_FP (N0/1)
pPETFP_given_CT_neg*(1-pM1)
Medisastinoscopy
Survives
HIST_TN
1
Surgery
P_deathMed
PET_M1
pM1
Imaging
TP
Palliative M1
HIST_TP
pMedTP_given_CT_neg_and_PETTP
Palliative N23 M0
HIST_FN
Survives N23 M0
PET_TP (N2/3)
pPETTP_given_CT_neg*(1-pM1)
Mediastinoscopy
PET_FN (N2/3)
HIST_TP (N2/3)
pMedTP_given_CT_pos_and_PETTP
HIST_FN (N2/3)
PET_TP (n2/3)
pPETTP_given_CT_pos*(1-pM1)
PET_FN (n2/3)
pPETFP_given_CT_pos*(1-pM1)
Mediastinal lymph nodes enlarged
PET_TN
pPETTN_given_CT_pos*(1-pM1)
PET_FP (N0/1)
HIST_TN (N0/1)

Markov states

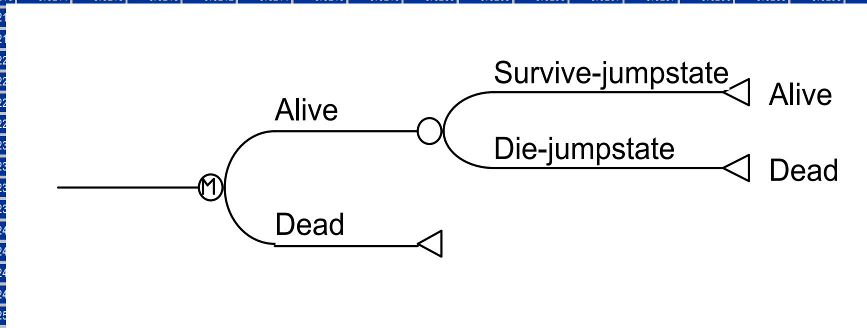


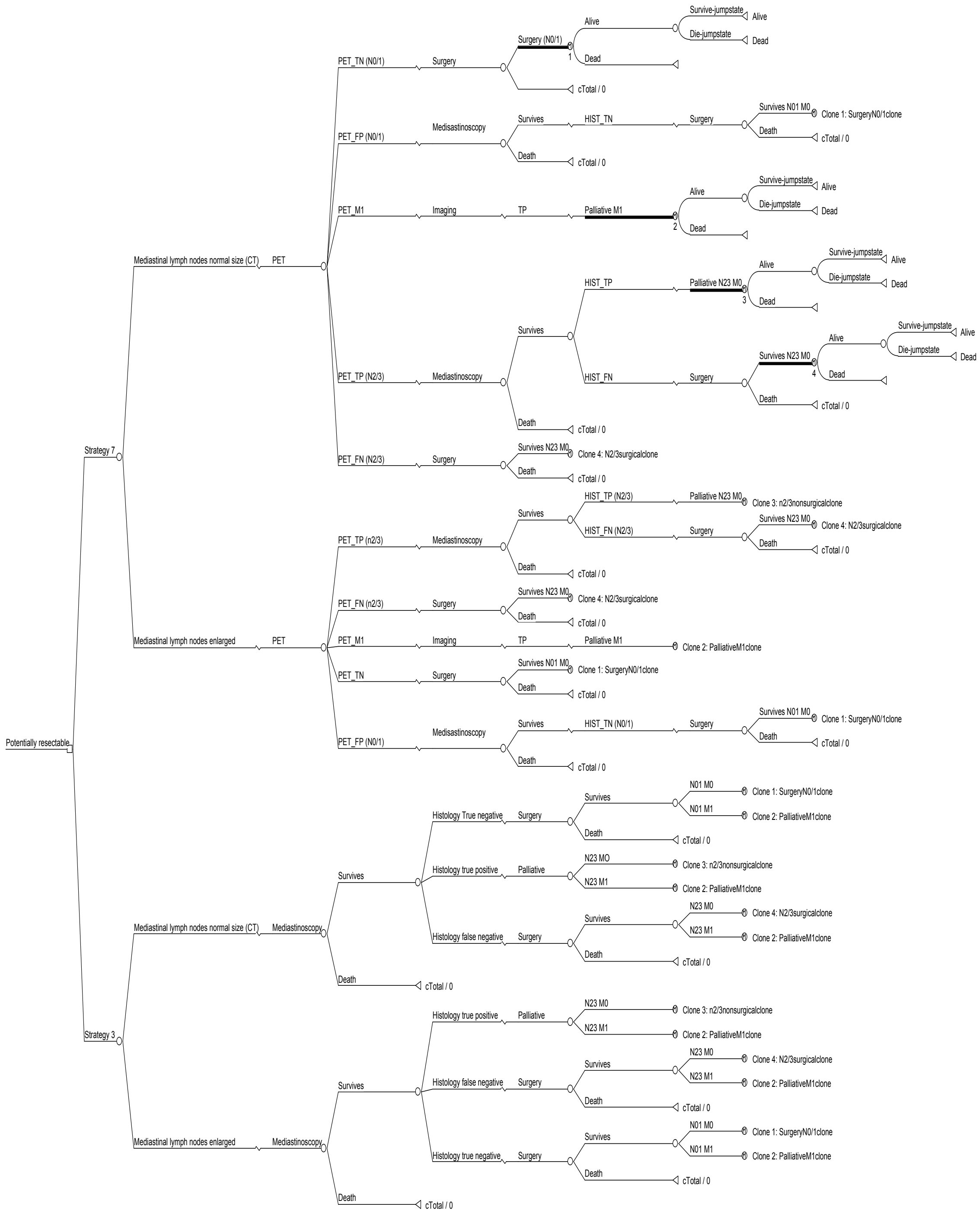
Cumulative survival for four clones used in the model



Deriving conditional survivorship tables for the Markov clones

Age \ Month	43	44	45	46	47	48	49	50	51	52	53	54	55	56	57	58	59	60	61	62	63	64	65	66	67	68	69	70	71	72	73	74	75
35	0.0183	0.0183	0.0182	0.0181	0.0180	0.0180	0.0179	0.0178	0.0178	0.0177	0.0176	0.0176	0.0175	0.0175	0.0174	0.0174	0.0173	0.0173	0.0172	0.0172	0.0171	0.0171	0.0170	0.0170	0.0169	0.0169	0.0168	0.0168	0.0167	0.0167	0.0167	0.0166	0.0166
36	0.0185	0.0184	0.0184	0.0183	0.0182	0.0182	0.0181	0.0180	0.0180	0.0179	0.0178	0.0178	0.0177	0.0177	0.0176	0.0175	0.0175	0.0174	0.0174	0.0173	0.0173	0.0172	0.0172	0.0171	0.0171	0.0171	0.0170	0.0170	0.0169	0.0169	0.0168	0.0168	0.0168
37	0.0187	0.0186	0.0186	0.0185	0.0184	0.0183	0.0183	0.0182	0.0181	0.0181	0.0180	0.0180	0.0179	0.0178	0.0178	0.0177	0.0177	0.0176	0.0176	0.0175	0.0175	0.0174	0.0174	0.0173	0.0173	0.0172	0.0172	0.0171	0.0171	0.0171	0.0170	0.0170	0.0169
38	0.0189	0.0188	0.0187	0.0187	0.0186	0.0185	0.0185	0.0184	0.0183	0.0183	0.0182	0.0181	0.0181	0.0180	0.0180	0.0179	0.0179	0.0178	0.0178	0.0177	0.0176	0.0176	0.0175	0.0175	0.0175	0.0174	0.0174	0.0173	0.0173	0.0172	0.0172	0.0171	0.0171
39	0.0191	0.0190	0.0189	0.0189	0.0188	0.0187	0.0187	0.0186	0.0185	0.0185	0.0184	0.0183	0.0183	0.0182	0.0182	0.0181	0.0180	0.0180	0.0179	0.0179	0.0178	0.0178	0.0177	0.0177	0.0176	0.0176	0.0175	0.0175	0.0175	0.0174	0.0174	0.0173	0.0173
40	0.0193	0.0192	0.0191	0.0191	0.0190	0.0189	0.0188	0.0188	0.0187	0.0186	0.0186	0.0185	0.0185	0.0184	0.0183	0.0183	0.0182	0.0182	0.0181	0.0181	0.0180	0.0180	0.0179	0.0179	0.0178	0.0178	0.0177	0.0177	0.0176	0.0176	0.0175	0.0175	0.0175
41	0.0195	0.0194	0.0193	0.0193	0.0192	0.0191	0.0190	0.0190	0.0189	0.0188	0.0188	0.0187	0.0187	0.0186	0.0185	0.0185	0.0184	0.0184	0.0183	0.0183	0.0182	0.0182	0.0181	0.0181	0.0180	0.0180	0.0179	0.0179	0.0178	0.0178	0.0177	0.0177	0.0176
42	0.0197	0.0196	0.0195	0.0195	0.0194	0.0193	0.0192	0.0192	0.0191	0.0190	0.0190	0.0189	0.0188	0.0188	0.0187	0.0187	0.0186	0.0186	0.0185	0.0184	0.0184	0.0183	0.0183	0.0182	0.0182	0.0181	0.0181	0.0180	0.0180	0.0180	0.0179	0.0179	0.0178
43	0.0199	0.0198	0.0197	0.0197	0.0196	0.0195	0.0194	0.0194	0.0193	0.0192	0.0192	0.0191	0.0190	0.0190	0.0189	0.0189	0.0188	0.0187	0.0187	0.0186	0.0186	0.0185	0.0185	0.0184	0.0184	0.0183	0.0183	0.0182	0.0182	0.0181	0.0181	0.0181	0.0180
44	0.0201	0.0200	0.0199	0.0199	0.0198	0.0197	0.0196	0.0196	0.0195	0.0194	0.0194	0.0193	0.0192	0.0192	0.0191	0.0191	0.0190	0.0189	0.0189	0.0188	0.0188	0.0187	0.0187	0.0186	0.0186	0.0185	0.0185	0.0184	0.0184	0.0183	0.0183	0.0182	0.0182
45	0.0203	0.0202	0.0202	0.0201	0.0200	0.0199	0.0198	0.0198	0.0197	0.0196	0.0196	0.0195	0.0194	0.0194	0.0193	0.0193	0.0192	0.0191	0.0191	0.0190	0.0190	0.0189	0.0189	0.0188	0.0188	0.0187	0.0187	0.0186	0.0186	0.0185	0.0185	0.0184	0.0184
46	0.0205	0.0204	0.0204	0.0203	0.0202	0.0201	0.0201	0.0200	0.0199	0.0198	0.0198	0.0197	0.0196	0.0196	0.0195	0.0195	0.0194	0.0193	0.0193	0.0192	0.0192	0.0191	0.0191	0.0190	0.0190	0.0189	0.0189	0.0188	0.0188	0.0187	0.0187	0.0186	0.0186
47	0.0207	0.0207	0.0206	0.0205	0.0204	0.0203	0.0203	0.0202	0.0201	0.0200	0.0200	0.0199	0.0198	0.0198	0.0197	0.0197	0.0196	0.0195	0.0195	0.0194	0.0194	0.0193	0.0193	0.0192	0.0192	0.0191	0.0191	0.0190	0.0190	0.0189	0.0189	0.0188	0.0188
48	0.0210	0.0209	0.0208	0.0207	0.0206	0.0205	0.0205	0.0204	0.0203	0.0203	0.0202	0.0201	0.0201	0.0200	0.0199	0.0199	0.0198	0.0197	0.0197	0.0196	0.0196	0.0195	0.0195	0.0194	0.0194	0.0193	0.0193	0.0192	0.0192	0.0191	0.0191	0.0190	0.0190
49	0.0212	0.0211	0.0210	0.0209	0.0208	0.0208	0.0207	0.0206	0.0205	0.0205	0.0204	0.0203	0.0203	0.0202	0.0201	0.0201	0.0200	0.0199	0.0199	0.0198	0.0198	0.0197	0.0197	0.0196	0.0196	0.0195	0.0195	0.0194	0.0194	0.0193	0.0193	0.0192	0.0192
50	0.0214	0.0213	0.0212	0.0211	0.0211	0.0210	0.0209	0.0208	0.0208	0.0207	0.0206	0.0205	0.0205	0.0204	0.0203	0.0203	0.0202	0.0202	0.0201	0.0200	0.0200	0.0199	0.0199	0.0198	0.0198	0.0197	0.0197	0.0196	0.0196	0.0195	0.0195	0.0194	0.0194
51	0.0216	0.0215	0.0214	0.0214	0.0213	0.0212	0.0211	0.0210	0.0210	0.0209	0.0208	0.0208	0.0207	0.0206	0.0206	0.0205	0.0204	0.0204	0.0203	0.0202	0.0202	0.0201	0.0201	0.0200	0.0200	0.0199	0.0199	0.0198	0.0198	0.0197	0.0197	0.0196	0.0196
52	0.0218	0.0218	0.0217	0.0216	0.0215	0.0214	0.0213	0.0213	0.0212	0.0211	0.0210	0.0210	0.0209	0.0208	0.0208	0.0207	0.0206	0.0206	0.0205	0.0205	0.0204	0.0203	0.0203	0.0202	0.0202	0.0201	0.0201	0.0200	0.0200	0.0199	0.0199	0.0198	0.0198
53	0.0221	0.0220	0.0219	0.0218	0.0217	0.0216	0.0216	0.0215	0.0214	0.0213	0.0213	0.0212	0.0211	0.0210	0.0210	0.0209	0.0209	0.0208	0.0207	0.0207	0.0206	0.0205	0.0205	0.0204	0.0204	0.0203	0.0203	0.0202	0.0202	0.0201	0.0201	0.0200	0.0200
54	0.0223	0.0222	0.0221	0.0220	0.0219	0.0219	0.0218	0.021																.0206	0.0206	0.0205	0.0205	0.0204	0.0204	0.0203	0.0203	0.0202	0.0202
55	0.0225	0.0224	0.0223	0.0223	0.0222	0.0221	0.0220	0.021																.0209	0.0208	0.0207	0.0207	0.0206	0.0206	0.0205	0.0205	0.0204	0.0204
56	0.0228	0.0227	0.0226	0.0225	0.0224	0.0223	0.0222	0.022																.0211	0.0210	0.0210	0.0209	0.0209	0.0208	0.0208	0.0207	0.0206	0.0206
57	0.0230	0.0229	0.0228	0.0227	0.0226	0.0225	0.0225	0.022																.0213	0.0212	0.0212	0.0211	0.0211	0.0210	0.0210	0.0209	0.0209	0.0208
58	0.0232	0.0231	0.0230	0.0230	0.0229	0.0228	0.0227	0.022																.0215	0.0215	0.0214	0.0213	0.0213	0.0212	0.0212	0.0211	0.0211	0.0210
59	0.0235	0.0234	0.0233	0.0232	0.0231	0.0230	0.0229	0.022																.0217	0.0217	0.0216	0.0216	0.0215	0.0215	0.0214	0.0214	0.0213	0.0212
60	0.0237	0.0236	0.0235	0.0234	0.0233	0.0233	0.0232	0.023																.0220	0.0219	0.0218	0.0218	0.0217	0.0217	0.0216	0.0216	0.0215	0.0215
61	0.0240	0.0239	0.0238	0.0237	0.0236	0.0235	0.0234	0.023																.0222	0.0221	0.0221	0.0220	0.0220	0.0219	0.0218	0.0218	0.0217	0.0217
62	0.0242	0.0241	0.0240	0.0239	0.0238	0.0237	0.0237	0.023																.0224	0.0224	0.0223	0.0222	0.0222	0.0221	0.0221	0.0220	0.0220	0.0219
63	0.0245	0.0244	0.0243	0.0242	0.0241	0.0240	0.0239	0.023																.0227	0.0226	0.0225	0.0225	0.0224	0.0224	0.0223	0.0223	0.0222	0.0221
64	0.0247	0.0246	0.0245	0.0244	0.0243	0.0242	0.0241	0.024																.0229	0.0228	0.0228	0.0227	0.0227	0.0226	0.0225	0.0225	0.0224	0.0224
65	0.0250	0.0249	0.0248	0.0247	0.0246	0.0245	0.0244	0.024																.0231	0.0231	0.0230	0.0229	0.0229	0.0228	0.0228	0.0227	0.0227	0.0226
66	0.0252	0.0251	0.0250	0.0249	0.0248	0.0247	0.0246	0.024																.0234	0.0233	0.0232	0.0232	0.0231	0.0231	0.0230	0.0229	0.0229	0.0228
67	0.0255	0.0254	0.0253	0.0252	0.0251	0.0250	0.0249	0.024																.0236	0.0235	0.0235	0.0234	0.0234	0.0233	0.0232	0.0232	0.0231	0.0231
68	0.0258	0.0257	0.0255	0.0254	0.0254	0.0253	0.0252	0.025																.0239	0.0238	0.0237	0.0237	0.0236	0.0235	0.0235	0.0234	0.0234	0.0233
69	0.0260	0.0259	0.0258	0.0257	0.0256	0.0255	0.0254	0.0253	0.0252	0.0252	0.0251	0.0250	0.0249	0.0248	0.0247	0.0247	0.0246	0.0245	0.0244	0.0244	0.0243	0.0242	0.0242	0.0241	0.0240	0.0240	0.0239	0.0238	0.0238	0.0237	0.0237	0.0236	0.0236
70	0.0263	0.0262	0.0261	0.0260	0.0259	0.0258	0.0257	0.0256	0.0255	0.0254	0.0253	0.0252	0.0252	0.0251	0.0250	0.0249	0.0248	0.0248	0.0247	0.0246	0.0246	0.0245	0.0244	0.0244	0.0243	0.0242	0.0242	0.0241	0.0240	0.0240	0.0239	0.0239	0.0238
71	0.0266	0.0265	0.0264	0.0262	0.0261	0.0260	0.0260	0.0259	0.0258	0.0257	0.0256	0.0255	0.0254	0.0253	0.0253	0.0252	0.0251	0.0250	0.0250	0.0249	0.0248	0.0247	0.0247	0.0246	0.0245	0.0245	0.0244	0.0243	0.0243	0.0242	0.0242	0.0241	0.0240
72	0.0268	0.0267	0.0266	0.0265	0.0264	0.0263	0.0262	0.0261	0.0260	0.0259	0.0259	0.0258	0.0257	0.0256	0.0255	0.0254	0.0254	0.0253	0.0252	0.0251	0.0251	0.0250	0.0249	0.0249	0.0248	0.0247	0.0247	0.0246	0.0245	0.0245	0.0244	0.0244	0.0243
73	0.0271	0.0270	0.0269	0.0268	0.0267	0.0266	0.0265	0.0264	0.0263	0.0262	0.0261	0.0260	0.0259	0.0259	0.0258	0.0257	0.0256	0.0255	0.0255	0.0254	0.0253	0.0253	0.0252	0.0251	0.0250	0.0250	0.0249	0.0249	0.0248	0.0247	0.0247	0.0246	0.0245
74	0.0274	0.0273	0.0272	0.0271	0.0270	0.0269	0.0268	0.0267	0.0266	0.0265	0.0264	0.0263	0.0262	0.0261	0.0260	0.0260	0.0259	0.0258	0.0257	0.0257	0.0256	0.0255	0.0254	0.0254	0.0253	0.0252	0.0252	0.0251	0.0250	0.0250	0.0249	0.0249	0.0248
75	0.0277	0.0276	0.0275	0.0273	0.0272	0.0271	0.0270	0.0269	0.0268	0.0268	0.0267	0.0266	0.0265	0.0264	0.0263	0.0262	0.0262	0.0261	0.0260	0.0259	0.0259	0.0258	0.0257	0.0256	0.0256	0.0255	0.0254	0.0254	0.0253	0.0252	0.0252	0.0251	0.0251
76	0.0280	0.0279	0.0277	0.0276	0.0275	0.0274	0.0273	0.0272	0.0271	0.0270	0.0269	0.0268	0.0268	0.0267	0.0266	0.0265	0.0264	0.0263	0.0263	0.0262	0.0261	0.0260	0.0260	0.0259	0.0258	0.0258	0.0257	0.0256	0.0256	0.0255	0.0254	0.0254	0.0253
77	0.0283	0.0281	0.0280	0.0279	0.0278	0.0277	0.0276	0.0275	0.0274	0.0273	0.0272	0.0271	0.0270	0.0270	0.0269	0.0268	0.0267	0.0266	0.0265	0.0265	0.0264	0.0263	0.0262	0.0262	0.0261	0.0260	0.0260	0.0259	0.0258	0.0258	0.0257	0.0256	0.0256
78	0.0285	0.0284	0.0283	0.0282	0.0281	0.0280	0.0279	0.0278	0.0277	0.0276	0.0275	0.0274	0.0273	0.0272	0.0271	0.0271	0.0270	0.0269	0.0268	0.0267	0.0267	0.0266	0.0265	0.0264	0.0264	0.0263	0.0262	0.0262	0.0261	0.0260	0.0260	0.0259	0.0258
79	0.0288	0.0287	0.0286	0.0285	0.0284	0.0283	0.0282	0.0281	0.0280	0.0279	0.0278	0.0277	0.0276	0.0275	0.0274	0.0273	0.0273	0.0272	0.0271	0.0270	0.0269	0.0269	0.0268	0.0267	0.0266	0.0266	0.0265	0.0264	0.0264	0.0263	0.0262	0.0262	0.0261
80	0.0291	0.0290	0.0289	0.0288	0.0287	0.0286	0.0285	0.0284	0.0283	0.0282	0.0281	0.0280	0.0279	0.0278	0.0277	0.0276	0.0275	0.0275	0.0274	0.0273	0.0272	0.0271	0.0271	0.0270	0.0269	0.0268	0.0268	0.0267	0.0266	0.0266	0.0265	0.0264	0.0264
81	0.0294	0.0293	0.0292	0.0291	0.0290	0.0289	0.0288	0.0287	0.0286	0.0285	0.0284	0.0283	0.0282	0.0281	0.0280	0.0279	0.0278	0.0277	0.0277	0.0276	0.0275	0.0274	0.0273	0.0273	0.0272	0.0271	0.0271	0.0270	0.0269	0.0268	0.0268	0.0267	0.0267
82	0.0297	0.0296	0.0295	0.0294	0.0293	0.0292	0.0291	0.0290	0.0289	0.0288	0.0287	0.0286	0.0285	0.0284	0.0283	0.0282	0.0281	0.0280	0.0279	0.0279	0.0278	0.0277	0.0276	0.0276	0.0275	0.0274	0.0273	0.0273	0.0272	0.0271	0.0271	0.0270	0.0269
83	0.0301	0.0299	0.0298	0.0297	0.0296	0.0295	0.0294	0.0293	0.0292	0.0290	0.0290	0.0289	0.0288	0.0287	0.0286	0.0285	0.0284	0.0283	0.0282	0.0281	0.0281	0.0280	0.0279	0.0278	0.0278	0.0277	0.0276	0.0275	0.0275	0.0274	0.0273	0.0273	0.0272
84	0.0304	0.0302	0.0301	0.0300	0.0299	0.0298	0.0297	0.0296	0.0295	0.0293	0.0292	0.0292	0.0291	0.0290	0.0289	0.0288	0.0287	0.0286	0.0285	0.0284	0.0284	0.0283	0.0282	0.0281	0.0280	0.0280	0.0279	0.0278	0.0278	0.0277	0.0276	0.0276	0.0275
85	0.0307	0.0306	0.0304	0.0303	0.0302	0.0301	0.0300	0.0299	0.0298	0.0297	0.0296	0.0295	0.0294	0.0293	0.0292	0.0291	0.0290	0.0289	0.0288	0.0287	0.0287	0.0286	0.0285	0.0284	0.0283	0.0283	0.0282	0.0281	0.0280	0.0280	0.0279	0.0278	0.0278
86	0.0310	0.0309	0.0307	0.0306	0.0305	0.0304	0.0303	0.0302	0.0301	0.0300	0.0299	0.0298	0.0297	0.0296	0.0295	0.0294	0.0293	0.0292	0.0291	0.0290	0.0289	0.0289	0.0288	0.0287	0.0286	0.0286	0.0285	0.0284	0.0283	0.0283	0.0282	0.0281	0.0281
87	0.0313	0.0312	0.0311	0.0309	0.0308	0.0307	0.0306	0.0305	0.0304	0.0303	0.0302	0.0301	0.0300	0.0299	0.0298	0.0297	0.0296	0.0295	0.0294	0.0293	0.0292	0.0292	0.0291	0.0290	0.0289	0.0289	0.0288	0.0287	0.0286	0.0286	0.0285	0.0284	0.0284
88	0.0316	0.0315	0.0314	0.0313	0.0311	0.0310	0.0309	0.0308	0.0307	0.0306	0.0305	0.0304	0.0303	0.0302	0.0301	0.0300	0.0299	0.0298	0.0297	0.0296	0.0295	0.0295	0.0294	0.0293	0.0292	0.0291	0.0291	0.0290	0.0289	0.0289	0.0288	0.0287	0.0286
89	0.0320	0.0318	0.0317	0.0316	0.0315	0.0313	0.0312	0.0311	0.0310	0.0309	0.0308	0.0307	0.0306	0.0305	0.0304	0.0303	0.0302	0.0301	0.0300	0.0299	0.0299	0.0298	0.0297	0.0296	0.0295	0.0294	0.0294	0.0293	0.0292	0.0292	0.0291	0.0290	0.0289




Potentially resectable
Strategy 7
Strategy 3
Mediastinal lymph nodes normal size (CT)
PET
Mediastinal lymph nodes enlarged
PET_TN (N0/1)
Surgery
Surgery (N0/1)
Alive
Survive-jumpstate
Die-jumpstate
Dead
cTotal / 0
PET_FP (N0/1)
Medisastinoscopy
Survives
HIST_TN
Survives N01 M0
Clone 1: SurgeryN0/1clone
Death
PET_M1
Imaging
TP
Palliative M1
PET_TP (N2/3)
Mediastinoscopy
HIST_TP
Palliative N23 M0
HIST_FN
Survives N23 M0
PET_FN (N2/3)
Clone 4: N2/3surgicalclone
PET_TP (n2/3)
HIST_TP (N2/3)
Clone 3: n2/3nonsurgicalclone
HIST_FN (N2/3)
PET_FN (n2/3)
Clone 2: PalliativeM1clone
PET_TN
HIST_TN (N0/1)
Mediastinoscopy
Histology True negative
Histology true positive
Palliative
Histology false negative
N01 M0
N01 M1
N23 MO
N23 M1
N23 M0
Histology true negative

Scenario 1

Your pet scan indicates no significant spread of your disease and this is correct. So you will be offered surgery.

The PET got it right!

Scenario 2

Your PET scan indicates that your disease has spread, but this is not the case. On the basis of the PET result, you will not be offered the surgery that you need

The PET got it wrong!

Scenario 3

Your PET scan indicates that your disease has not spread significantly, but it actually has. You will end up getting offered surgery that cannot cure your disease.

The PET got it wrong!

Scenario 4

Your PET scan indicates that your disease has spread significantly, and this is correct. Surgery is not for you and you will get other treatments

The PET got it right!

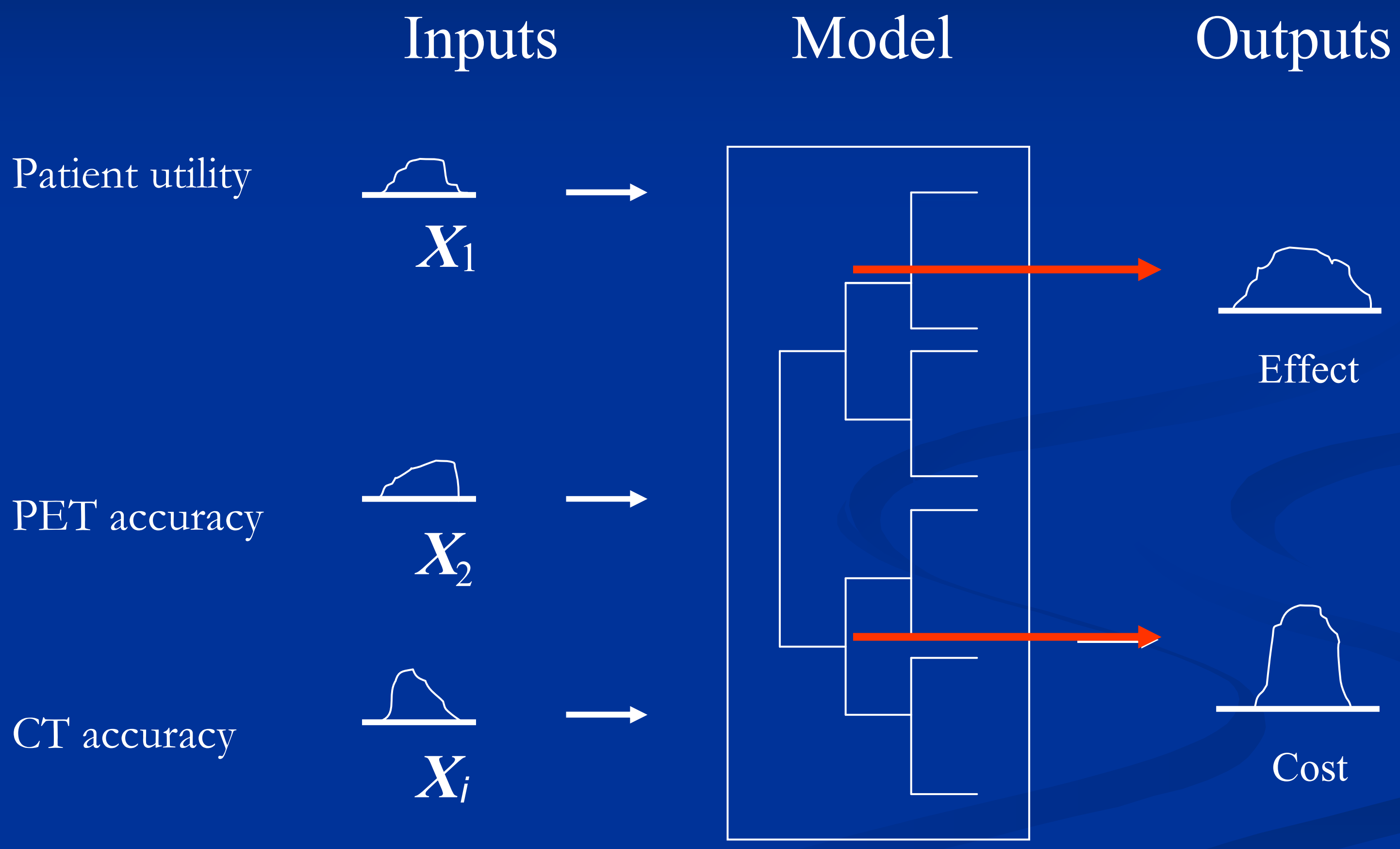
Please make a mark on the line below indicating the relative desirability of these possible outcomes, using the appropriate colour.

worst possible state — best possible state

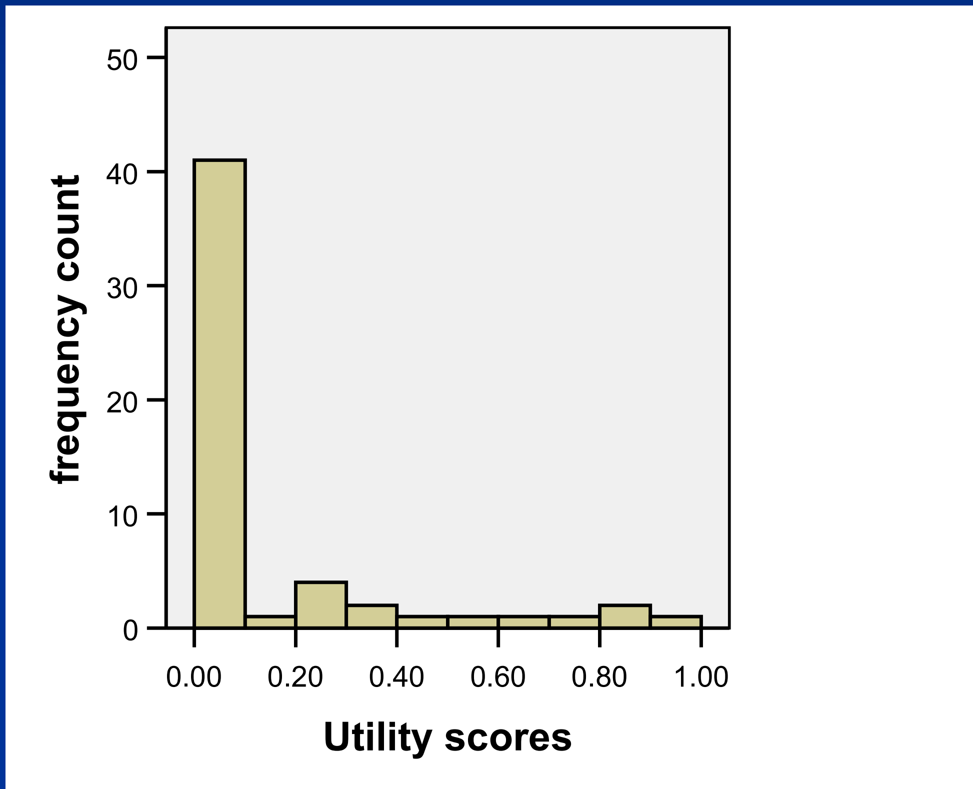
Utilities assigned in base case

Stage of disease	Treatment	Utility*	Based on
N0/N1, M0	Surgery	0.88	Earle's figure for local disease
N2/N3, M0	Surgery	0.65	Berthelot's figure for advanced disease which responds to treatment
N0-3, M1	Surgery	0.65	Berthelot's figure for advanced disease which responds to treatment
N0/N1, M0	Non-surgical treatment	0.65	Berthelot's figure for advanced disease which responds to treatment
N2/N3, M0	Non-surgical treatment	0.65	Berthelot's figure for advanced disease which responds to treatment
N0-3, M1	Non-surgical treatment	0.65	Berthelot's figure for advanced disease which responds to treatment

The concept of second-order Monte Carlo probabilistic sensitivity analysis



Distribution of utility weightings used in the Monte Carlo simulation



Results

For a 50 year old

Strategy	Cost	Incr Cost	Eff	Incr Eff	C/E	Incr C/E (ICER)
Strategy 3	£4,827		2.3129 qaly		£2,087	
Strategy 7	£4,994	£166	2.3377 qaly	0.0248 qaly	£2,136	**£6,704**

For a 60 year old

Strategy	Cost	Incr Cost	Eff	Incr Eff	C/E	Incr C/E (ICER)
Strategy 3	£4,827		2.0450 qaly		£2,361	
Strategy 7	£4,994	£166	2.0648 qaly	0.0198 qaly	£2,418	**£8,385**

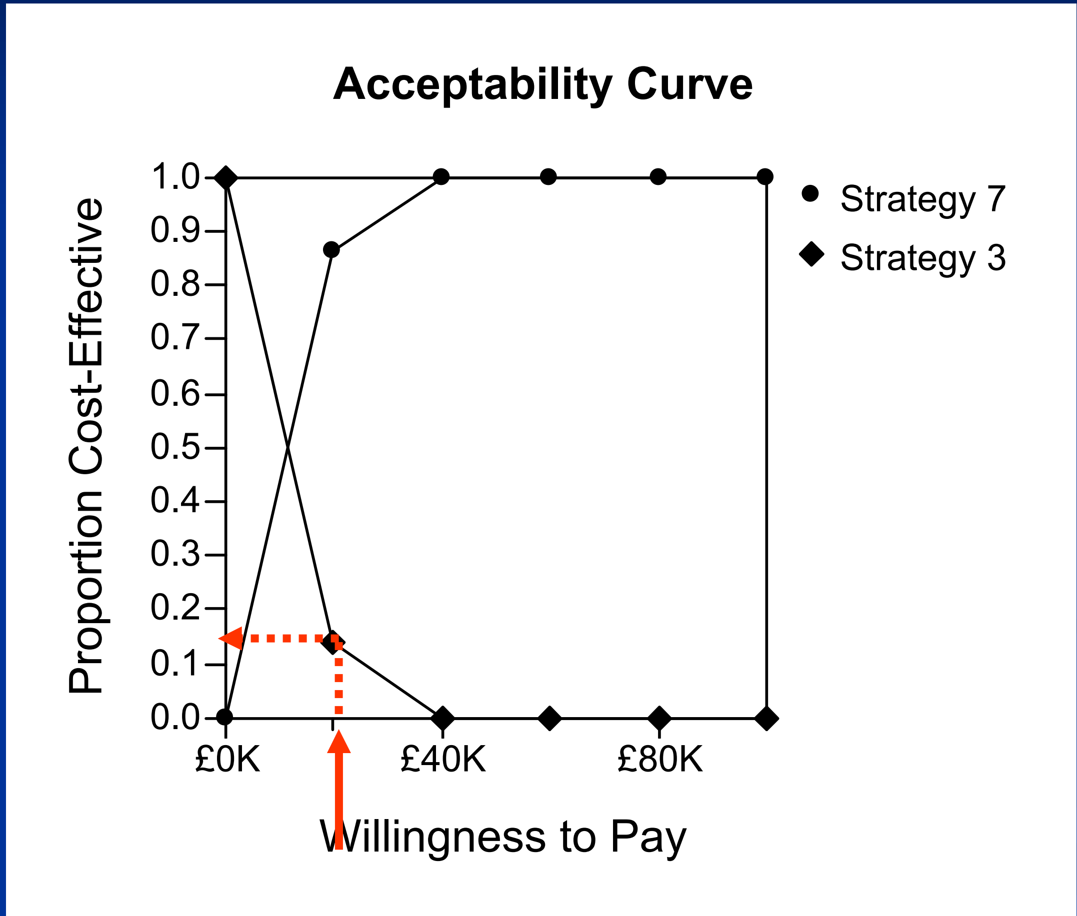
For a 70 year old

Strategy	Cost	Incr Cost	Eff	Incr Eff	C/E	Incr C/E (ICER)
Strategy 3	£4,827		1.7450 qaly		£2,766	
Strategy 7	£4,994	£166	1.7607 qaly	0.0156 qaly	£2,836	**£10,636**

For an 80 year old

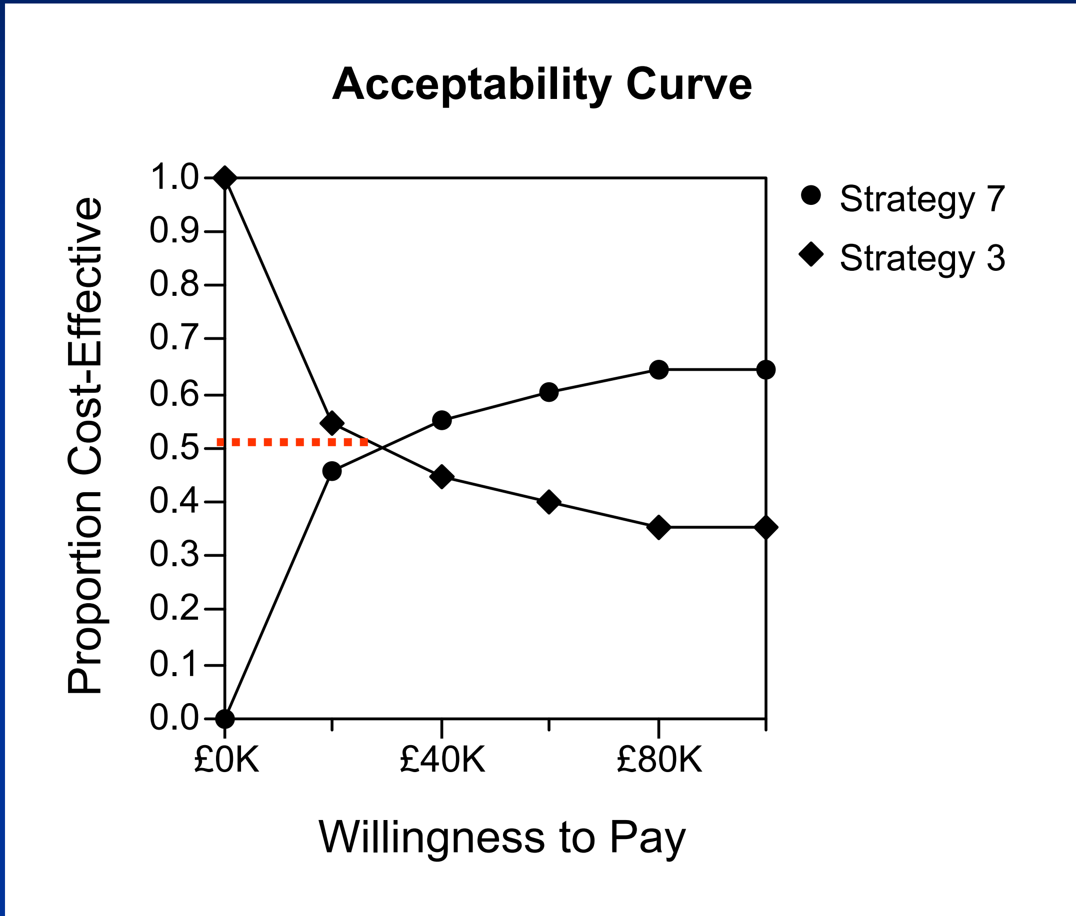
Strategy	Cost	Incr Cost	Eff	Incr Eff	C/E	Incr C/E (ICER)
Strategy 3	£4,827		1.4267 qaly		£3,384	
Strategy 7	£4,994	£166	1.4388 qaly	0.0121 qaly	£3,471	**£13,785**

Results of probabilistic sensitivity analysis: varying patient derived utility weights for futile thoracotomy



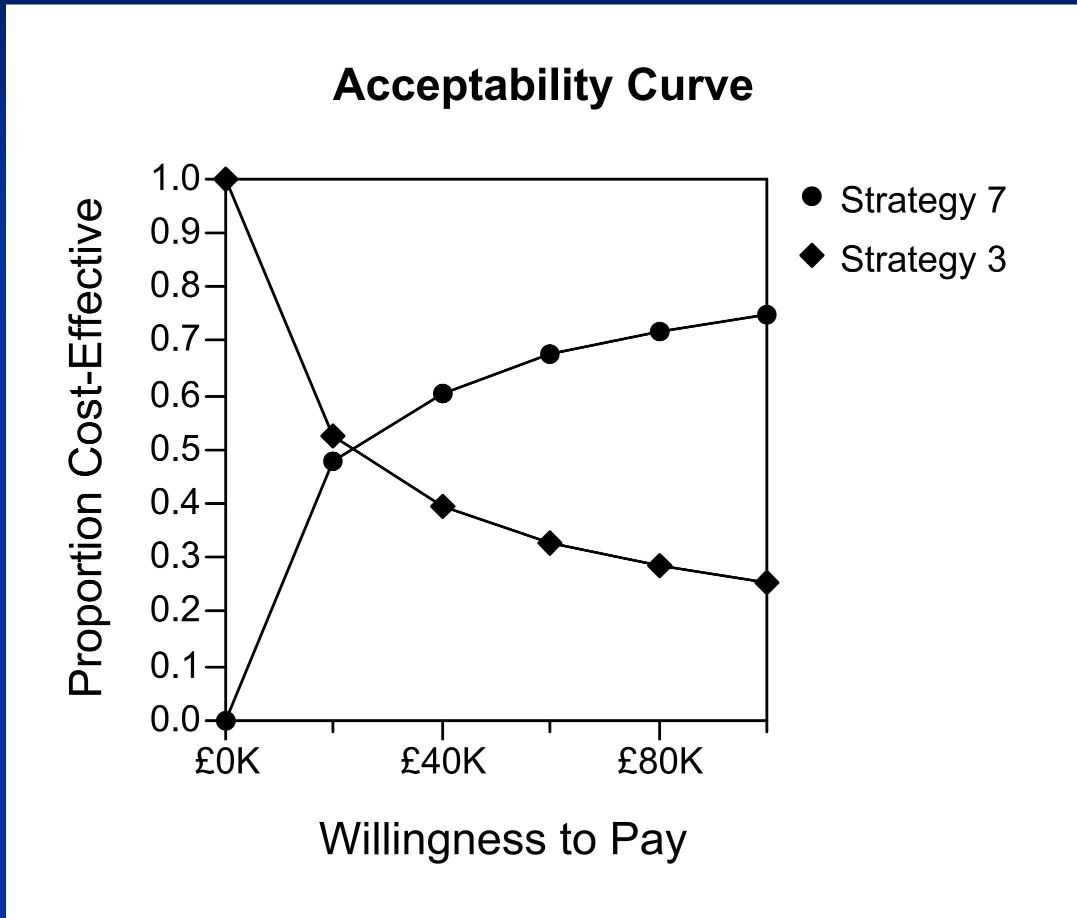
Cost effectiveness acceptability curve for 50 year old patients

Results of probabilistic sensitivity analysis: varying patient derived utility weights for futile thoracotomy



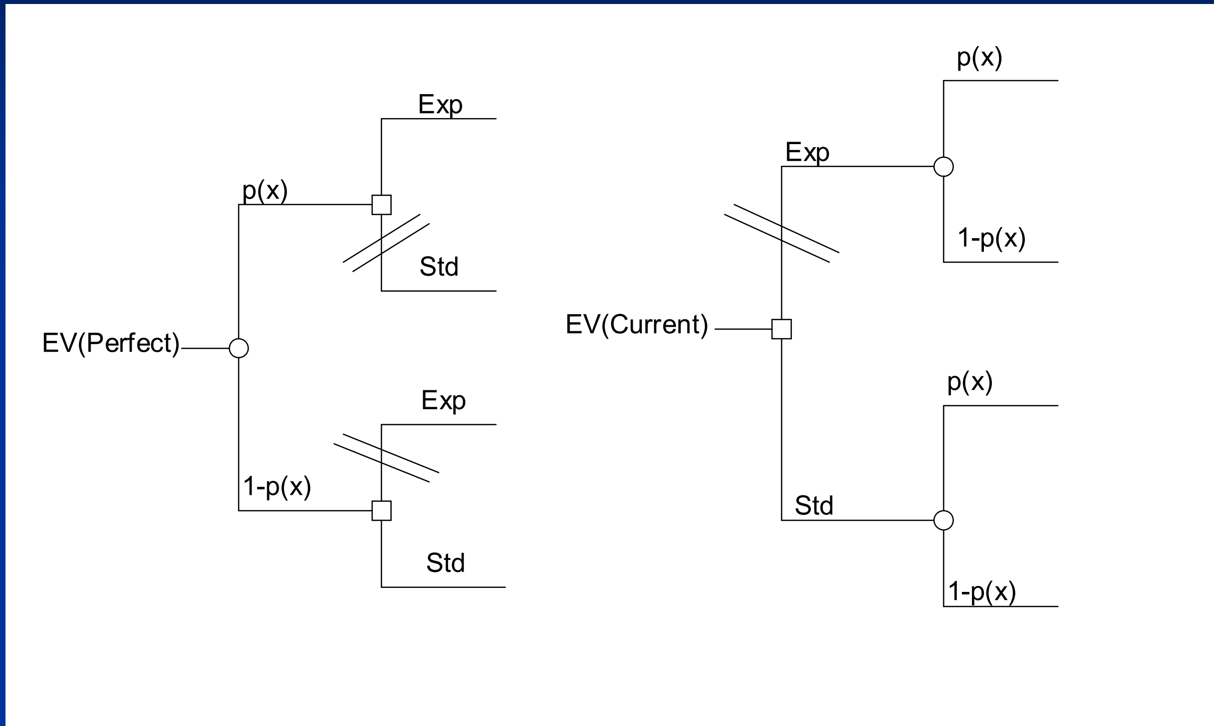
Cost effectiveness acceptability curve for 80 year old patients

Results of probabilistic sensitivity analysis: all parameters



Cost effectiveness acceptability curve for 80 year old patients

EPV1 = EV (perfect information) - EV (current information)



EVPI = { Expected value of the optimal decision under conditions of certainty } – { Expected value of the optimal decision based on prior probabilities only }

So what should have priority for future research ?

Age	Expected value of Perfect Information (for each variable and for all variables combined)			
	Utility for futile thoracotomy	Sensitivity of PET	Sensitivity of CT	All three together
50	-4.66	1.02	0	9.72
60	5.65	1.02	0	24.35
70	40.82	0	0	45.05
80	73.51	0	0	76.42

Take home messages

- Frybeck and Thornbury got it right
- Is it worth more of your time talking to your patients or fighting for an upgrade of your PET machine ?
- Whose perspective should we take when conducting a NICE technology appraisal ?

"WHAT DO YOU MEAN 'IT'S A BIT MUDDY'?"

THANKYOU

Acknowledgements

Thanks to Dr Ian Bradbury
Ruth Leathem
Angie Scott