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Comparing 3L and 5L EQ-5D

Contributions

3L to 5L mapping methods:
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Case studies:
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Dr Manuel Gomes, Dr Zia Sadique – LSHTM, London.
Dr David Meads, John O'Dwyer – University of Leeds
Model based case studies:
Contributors to NICE TA and HST programme
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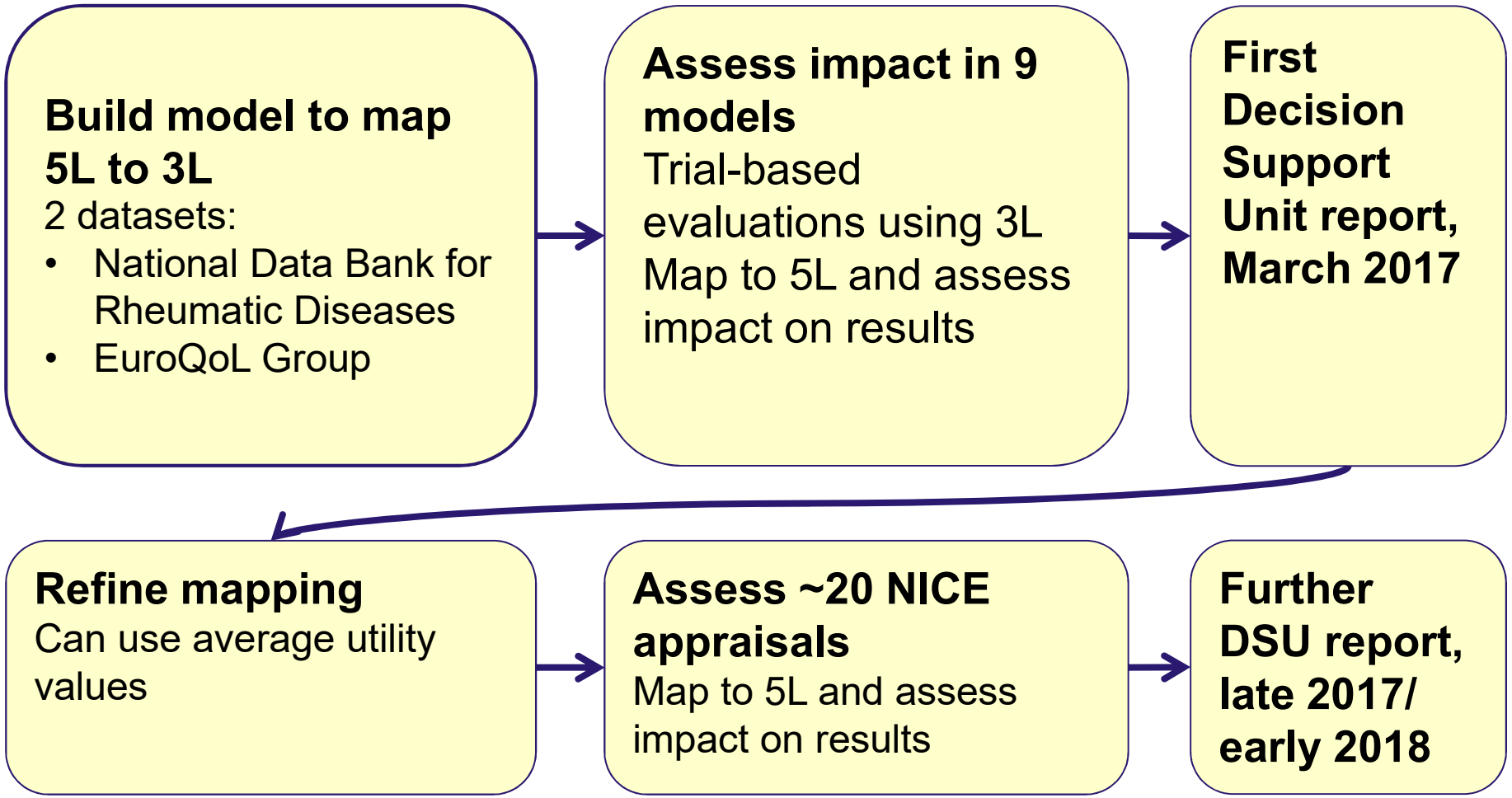
Comparing 3L and 5L EQ-5D

- What is the impact of this likely to be in the UK?
  - How are the two related? (Mapping)
  - What is the impact on cost-effectiveness?
    - Trial-based analyses
    - Model based analyses
- (UK) Valuations are taken as given
  - EQ-5D-3L Dolan (1997)
  - EQ-5D-5L Devlin et al. (2017) - England

Assessing impact of adopting 5L valuation set in UK



Modelling method

Simple mapping methods suffer from bias

DSU developed methods to overcome this:

1. Need to map from 3L to 5L, and the other way round
   - joint model - 10 equation model (5 domains x 2 instruments)
2. Avoid making unnecessary/unwarranted assumptions:
   - 5L is simply more detailed categorisation of 3L
   - Influence of covariates the same
3. Capture strong association between 3L and 5L domains without assuming same strength across distribution
   - Different copulas joining each pair
4. Flexible models to fit " odd" distributions (use mixture models)
5. Allow dependencies across domains capturing
   - Common underlying causes
   - Individual specific response styles

- See Hernandez and Pudney, JHE 2017
- Results tested and validated in DSU report (July 2017)

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Datasets

Datasource	**National Data Bank for Rheumatic Diseases**	**EuroQoL Group**
N (estimation)	5,311 (5,205)	3,691 (3,551)
Patient characteristics	Rheumatoid Arthritis	8 broad patient groups and students.
Setting	United States and Canada	Denmark, England, Italy, the Netherlands, Poland, and Scotland
Method	Postal and web. 5L first then 3L. Substantial separation.	Paper and pencil. England online. 5L first then 3L, little separation.
Year	January 2011	August 2009 to September 2010
Descriptive stats. Median age % females	 64 81%	 54 53%

Impact on cost-effectiveness

- 9 case studies provide 12 pairwise comparisons between technologies
- Trial based economic evaluations conducted using 3L
- Re-analysis using identical methods, substituting in 5L estimates

CARDERA	Combination of Anti-Rheumatic Drugs in **Early Rheumatoid Arthritis**
CACTUS	**Aphasia** Computer Treatment after stroke
RAIN	Risk Adjustment in Neurocritical care for acute **Traumatic Brain Injury**
IMPROVE	Endovascular repair vs open repair for **ruptured abdominal aortic aneurysm**
COUGAR-02	Docetaxel chemotherapy in **oesophagogastric cancer**
ARCTIC	Rituximab for **Chronic Lymphocytic Leukaemia**
SHARPISH	Self help booklets for **smoking cessation**
WRAP	**Weight loss** programmes
CvLPRIT	Complete vs Lesion only revascularisation for **ST-segment elevation Myocardial Infarction**

Effect on ICERS (inc QALYs) [7]

Title	3L	5L EuroQoL	5L NDB
CARDERA1	4648 (0.145)	5940 (0.113)	6054 (0.111)
CARDERA2	13,666 (0.084)	15,252 (0.075)	14,846 (0.077)
CARDERA3	15929 (0.082)	23940 (0.054)	30418 (0.043)
CACTUS	3,058 (0.15)	9,481 (0.05)	23,022 (0.02)
RAIN a)	184,700 (0.02)	738,800 (0.005)	1,231,333 (0.003)
RAIN b)	294,137 (0.051)	714,333 (0.021)	714,333 (0.021)
IMPROVE	-44,617 (0.052)	-48,113 (0.046)	-54,742 (0.042)
COUGAR II	27,180 (0.115)	26,434 (0.119)	26,484 (0.118)
ARCTIC	112,193 (0.058)	162,744 (0.043)	152,130 (0.046)
Sharpish	(0.000)	(-0.003)	(-0.003)
WRAP - CP12	1812 (0.062)	2373 (0.047)	2840 (0.039)
WRAP - CP52	4305 (0.044)	4312 (0.044)	5316 (0.036)
CvLPRIT	21496 (0.020)	46761 (0.010)	47521 (0.009)

Effect on ICERS (inc QALYs) [8]

Title	3L	5L EuroQoL	5L NDB
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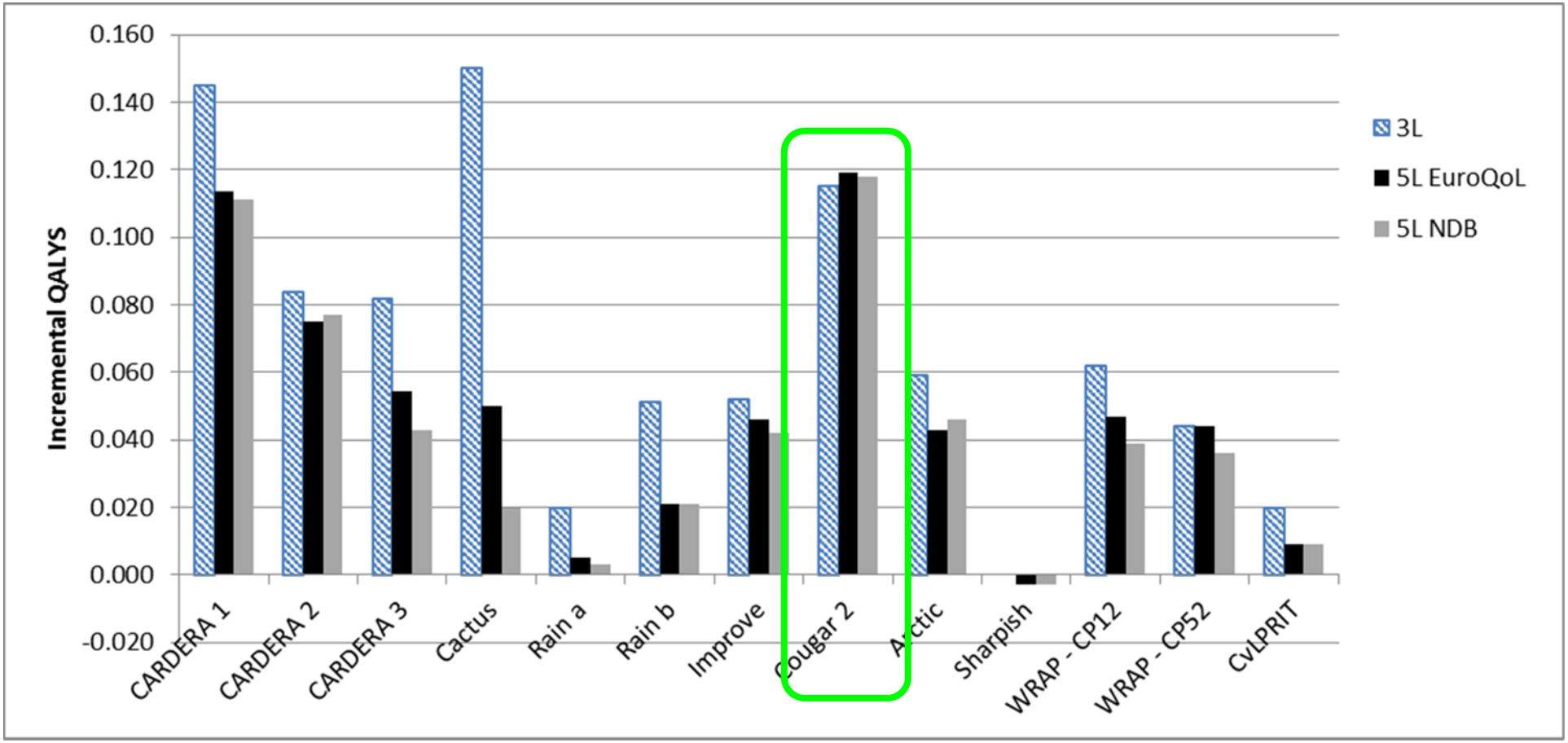
Marginal health gain lower with 5L ICERs ↑

Except COUGAR II (advanced cancer trial): Mortality gains important!


0.160
0.140
0.120
0.100
0.080
0.060
0.040
0.020
0.000
-0.020
Incremental QALYS
3L
5L EuroQoL
5L NDB
CARDERA 1
CARDERA 2
CARDERA 3
Cactus
Rain a
Rain b
Improve
Cougar 2
Arctic
Sharpish
WRAP - CP12
WRAP - CP52
CvLPRIT

Effect on ICERS (inc QALYs)[10]

Title	3L	5L EuroQoL	5L NDB
CARDERA1	4648 (0.145)	5940 (0.113)	6054 (0.111)
CARDERA2	13,666 (0.084)	15,252 (0.075)	14,846 (0.077)
CARDERA3	15929 (0.082)	23940 (0.054)	30418 (0.043)
CACTUS	3,058 (0.15)	9,481 (0.05)	23,022 (0.02)
RAIN a)	184,700 (0.02)	738,800 (0.005)	1,231,333 (0.003)
RAIN b)	294,137 (0.051)	714,333 (0.021)	714,333 (0.021)
IMPROVE	-44,617 (0.052)	-48,113 (0.046)	-54,742 (0.042)
COUGAR II	27,180 (0.115)	26,434 (0.119)	26,484 (0.118)
ARCTIC	112,193 (0.058)	162,744 (0.043)	152,130 (0.046)
Sharpish	(0.000)	(-0.003)	(-0.003)
WRAP - CP12	1812 (0.062)	2373 (0.047)	2840 (0.039)
WRAP - CP52	4305 (0.044)	4312 (0.044)	5316 (0.036)
CvLPRIT	21496 (0.020)	46761 (0.010)	47521 (0.009)

Marginal health gain is usually lower when using NDB mapping compared to EuroQoL dataset

Effect on ICERS (inc QALYs) [11]

Title	3L	5L EuroQoL	5L NDB
CARDERA1	4648 (0.145)	5940 (0.113) 22%	6054 (0.111) 23%
CARDERA2	13,666 (0.084)	15,252 (0.075) 10%	14,846 (0.077) 8%
CARDERA3	15929 (0.082)	23940 (0.054) 34%	30418 (0.043) 48%
CACTUS	3,058 (0.15)	9,481 (0.05) 67%	23,022 (0.02) 87%
RAIN a)	184,700 (0.02)	738,800 (0.005) 75%	1,231,333 (0.003) 85%
RAIN b)	294,137 (0.051)	714,333 (0.021) 59%	714,333 (0.021) 59%
IMPROVE	-44,617 (0.052)	-48,113 (0.046) 12%	-54,742 (0.042) 19%
COUGAR II	27,180 (0.115)	26,434 (0.119) +4%	26,484 (0.118) +3%
ARCTIC	112,193 (0.058)	162,744 (0.043) 27%	152,130 (0.046) 22%
Sharpish	(0.000)	(-0.003)	(-0.003)
WRAP - CP12	1812 (0.062)	2373 (0.047) 24%	2840 (0.039) 36%
WRAP - CP52	4305 (0.044)	4312 (0.044) 0%	5316 (0.036) 19%
CvLPRIT	21496 (0.020)	46761 (0.010) 53%	47521 (0.009) 53%

Impact is particularly pronounced in CACTUS (aphasia in stroke), RAIN (traumatic brain injury) and CvLPRIT (MI) studies

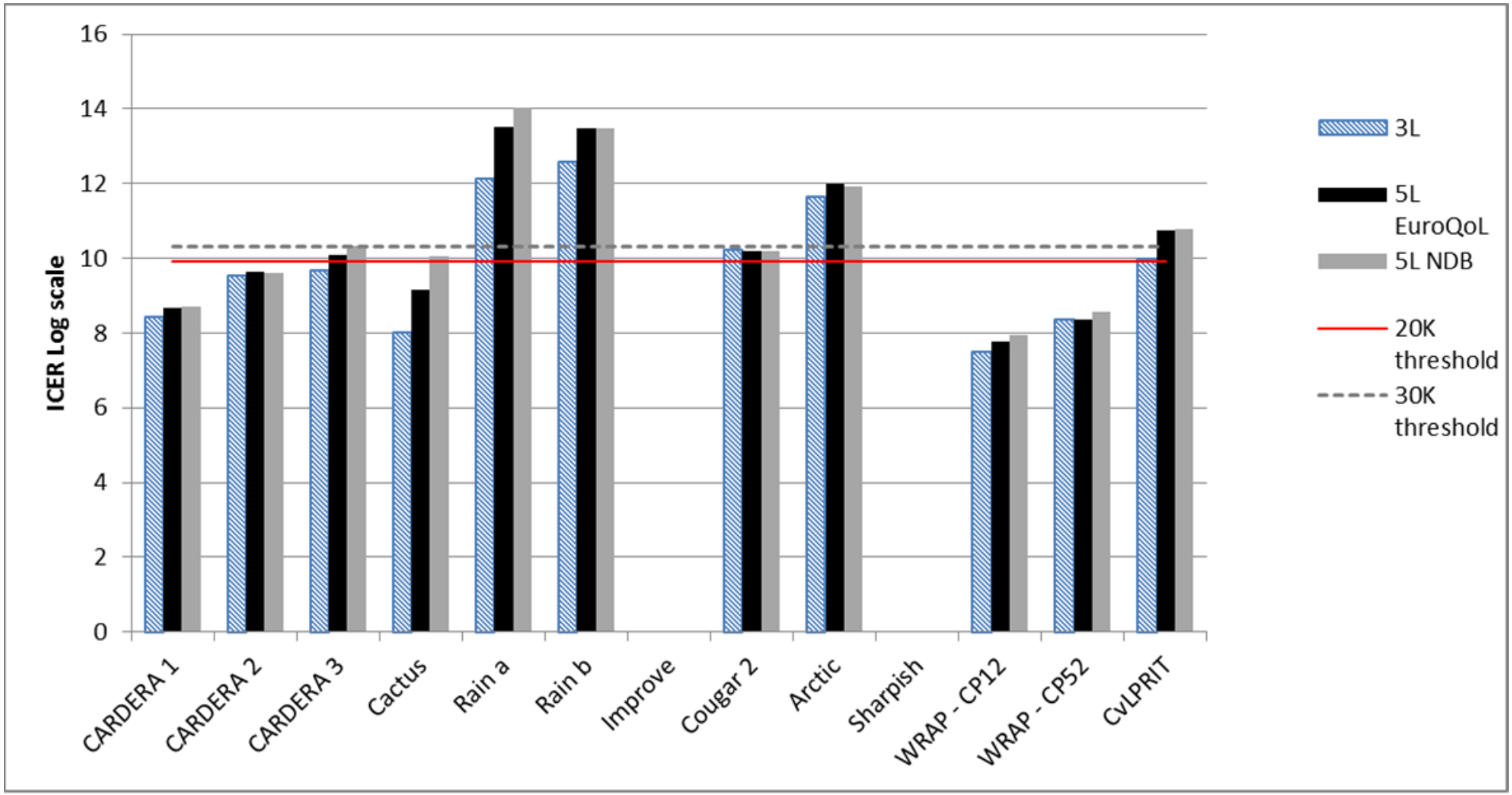
Severity of patients?
- RAIN 0.3 at baseline
- CACTUS 0.55
- But CARDERA only 0.4
- And CvLPRIT 0.8

Effect on ICERS (inc QALYs)[12]

Title	3L	5L EuroQoL	5L NDB
CARDERA1	4648 (0.145)	5940 (0.113)	6054 (0.111)
CARDERA2	13,666 (0.084)	15,252 (0.075)	14,846 (0.077)
CARDERA3	15929 (0.082)	23940 (0.054)	30418 (0.043)
CACTUS	3,058 (0.15)	9,481 (0.05)	23,022 (0.02)
RAIN a)	184,700 (0.02)	738,800 (0.005)	1,231,333 (0.003)
RAIN b)	294,137 (0.051)	714,333 (0.021)	714,333 (0.021)
IMPROVE	-44,617 (0.052)	-48,113 (0.046)	-54,742 (0.042)
COUGAR II	27,180 (0.115)	26,434 (0.119)	26,484 (0.118)
ARCTIC	112,193 (0.058)	162,744 (0.043)	152,130 (0.046)
Sharpish	(0.000)	(-0.003)	(-0.003)
WRAP - CP12	1812 (0.062)	2373 (0.047)	2840 (0.039)
WRAP - CP52	4305 (0.044)	4312 (0.044)	5316 (0.036)
CvLPRIT	21496 (0.020)	46761 (0.010)	47521 (0.009)

5L NDB *
6,941
(0.097)
17,627
(0.065)
20,304
(0.064)

Better mapping model uses HAQ and pain as covariates. Lowers marginal QALY still further in 2 comparisons


ICER Log scale
16
14
12
10
8
6
4
2
0
CARDERA 1
CARDERA 2
CARDERA 3
Cactus
Rain a
Rain b
Improve
Cougar 2
Arctic
Sharpish
WRAP - CP12
WRAP - CP52
CvLPRIT
3L
5L EuroQoL
5L NDB
20K threshold
30K threshold

Impact on cost-effectiveness

- 16 model-based analyses from NICE Technology Appraisals programme
- Extensions of mapping model allows estimation of 5L utility from 3L utility score (and vice versa)
- Utility score does not need to be unique to a health state. Can be a mean score (for example).
- Rounded for anonymity and divided into oncology technologies, others with and without mortality gains.

Effect on ICERS

Area	3L	5L EuroQoL	5L NDB
Intervention in oncology	33,000	33,000	36,000
	44,000	40,000	39,000
	45,000	39,000	39,000
	45,000	40,000	40,000
	46,000	44,000	45,000
	47,000	44,000	46,000
Intervention improves survival and quality of life	Dominant	Dominant	Dominant
	5,000	6,000	7,000
	6,000	6,000	6,000
	7,000	7,000	7,000
	18,000	29,000	38,000
	23,000	23,000	27,000
Intervention improves quality of life only	Dominant	Dominant	Dominant
	19,000	33,000	42,000
	21,000	25,000	38,000
	22,000	36,000	48,000

If intervention increases LYs in pre-progression but not post-progression, QALY gain decreases as difference in utilities is less, so ICER increases.

Most oncology ICERs decrease, as there are more QALYs gained from increasing survival.

Effect on ICERS

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	44,000	40,000	39,000
	45,000	39,000	39,000
	45,000	40,000	40,000
	46,000	44,000	45,000
	47,000	44,000	46,000
Intervention improves survival and quality of life	Dominant	Dominant	Dominant
	5,000	6,000	7,000
	6,000	6,000	6,000
	7,000	7,000	7,000
	18,000	29,000	38,000
	23,000	23,000	27,000
Intervention improves quality of life only	Dominant	Dominant	Dominant
	19,000	33,000	42,000
	21,000	25,000	38,000
	22,000	36,000	48,000

If there is a survival benefit, change in ICER depends on size of survival benefit and change in utility.

If there is no survival benefit, ICERs increase as difference in utilities is less.

Effect on ICERS

Area	3L	5L EuroQoL	5L NDB
Intervention in oncology	33,000	33,000	36,000
	44,000	40,000	39,000
	45,000	39,000	39,000
	45,000	40,000	40,000
	46,000	44,000	45,000
	47,000	44,000	46,000
Intervention improves survival and quality of life	Dominant	Dominant	Dominant
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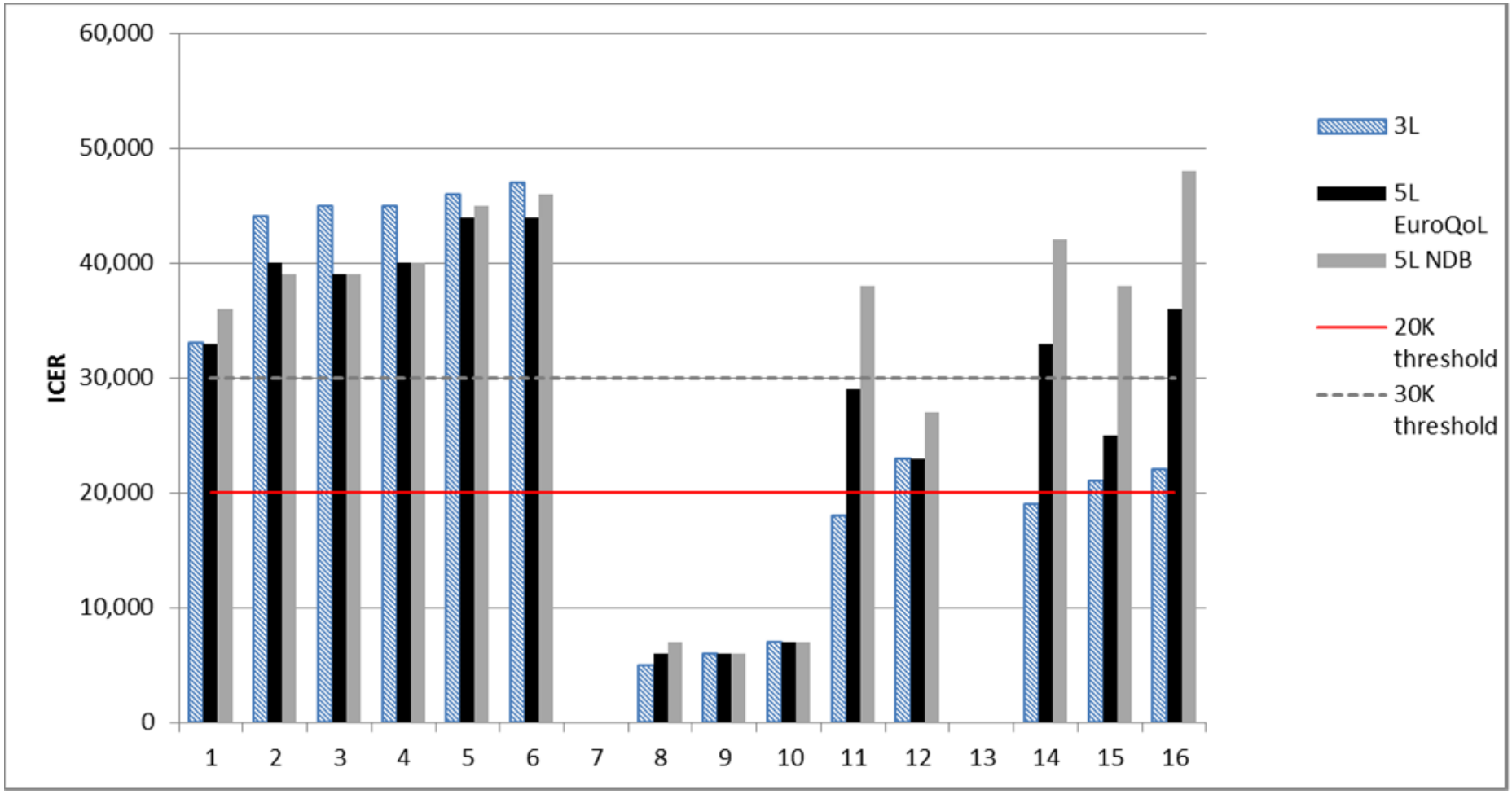
	6,000	6,000	6,000
	7,000	7,000	7,000
	18,000	29,000	38,000
	23,000	23,000	27,000
Intervention improves quality of life only	Dominant	Dominant	Dominant
	19,000	33,000	42,000
	21,000	25,000	38,000
	22,000	36,000	48,000

ICERs are higher using NDB mapping because marginal health gain is lower compared to EuroQoL dataset


60,000
50,000
40,000
30,000
20,000
10,000
0
ICER
1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
3L
5L EuroQoL
5L NDB
20K threshold
30K threshold

Discussion

Impact on ICERs

- 5L entails movement up the severity scale and compression within smaller range
- Technologies that improve QoL
  - ICERs get higher, often the change is substantial
- Technologies that improve length of life
  - ICERs can get lower, but most technologies that lengthen life also improve quality
- Impact also depends on the dataset used for mapping model
- Threshold? Should we move to 5L? Cannot use 3L and 5L interchangeably
  - Simple proportional adjustment not appropriate. Changes differ across the distribution
- Will need to link 3L and 5L for a long time…

Discussion

References:

Hernandez, M and Pudney, S (2017) “Econometric modelling of multiple self-reports of health states: The switch from EQ-5D-3L to EQ-5D-5L in evaluating drug therapies for rheumatoid arthritis.”, Journal of health Economics, Vol. 55: 139-152.

Hernandez, M., Wailoo, A., Pudney, S. (2017) “Methods for Mapping Between the EQ-5D-5L and the 3L for Technology Appraisal”, NICE DSU Report, available at: http://scharr.dept.shef.ac.uk/nicedsu/wp-content/uploads/sites/7/2017/05/Mapping-5L-to-3L-DSU-report.pdf

Wailoo, A., Hernandez, M., Grimm, S., et al. (2017) “Comparing the EQ-5D-3L and 5L Versions. What are the Implications for Cost-Effectiveness Estimates?”, NICE DSU Report, available at: http://scharr.dept.shef.ac.uk/nicedsu/wp-content/uploads/sites/7/2017/05/DSU_3L-to-5L-FINAL.pdf

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To Discover And Understand.