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Patient-Reported Outcomes & Patient Preference Research
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W4: COMBINING TWO TYPES OF VALUATION DATA TO ESTIMATE HEALTH STATE UTILITIES: THE HYBRID REGRESSION MODEL

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Conflict of interest & disclaimer

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- The views of the discussion leaders expressed in the workshop do not necessarily reflect the views of the EuroQol Group

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Health-State Valuation & Data Collection



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Health-state utility

- Value of a health state to a stakeholder such as the general public
- Measured on a cardinal scale anchored by 0 (death) and 1 (full health)
- Quality-of-life weights for calculating quality-adjusted life years (QALYs) in cost-utility analysis
- Determination of utility values
 - Direct method: eliciting the utility value of a health state from a respondent using a valuation technique such as standard gamble
 - Indirect method: preference-based instrument

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The EQ-5D-5L instrument

- The questionnaire
 - A new version of the EQ-5D instrument
 - Consist of a descriptive system and a visual analog scale for measuring health related quality of life
 - Defines 3,125 unique health states with 5 dimensions (mobility, self-care, usual activities, pain/discomfort, anxiety/depression) and 5 levels of problems for each dimension (no/slight/moderate/severe/extreme)
- The value set
 - Consist of utility values for all 3,125 EQ-5D-5L health states
 - Values anchored by 0 (dead) and 1 (full health)
 - Reflecting the average values of the health states to the general public
 - Country-specific value set

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Deriving utility values using EQ-5D-5L

Under each heading, please tick the ONE box that best describes your health today.

MOBILITY

I have no problems walking about

I have slight problems walking about

I have moderate problems walking about

I have severe problems walking about

I am unable to walk about

SELF-CARE

I have no problems washing or dressing myself

I have slight problems washing or dressing myself

I have moderate problems washing or dressing myself

I have severe problems washing or dressing myself

I am unable to wash or dress myself

USUAL ACTIVITIES (e.g. work, study, housework, family or leisure activities)

I have no problems doing my usual activities

I have slight problems doing my usual activities

I have moderate problems doing my usual activities

I have severe problems doing my usual activities

I am unable to do my usual activities

PAIN / DISCOMFORT

I have no pain or discomfort

I have slight pain or discomfort

I have moderate pain or discomfort

I have severe pain or discomfort

I have extremely severe pain or discomfort

ANXIETY / DEPRESSION

I am not anxious or depressed

I am slightly anxious or depressed

I am moderately anxious or depressed

I am severely anxious or depressed

I am extremely anxious or depressed

→ “12345” →

Coding:
 No = 1
 Slight = 2
 Moderate = 3
 Severe = 4
 Extreme = 5

Value Set

| State | Value |
|-------|-------|
| 11111 | 1.00 |
| | |
| 12344 | 0.13 |
| 12345 | 0.10 |
| 12351 | 0.05 |
| 12352 | 0.07 |
| 12353 | 0.03 |
| ... | |
| 55555 | -0.60 |

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Estimating an EQ-5D utility value set

- A 2-step procedure is used:
 - First, the values for a subset of health states are derived from stakeholders using the direct valuation approach
 - Second, a function is estimated by modeling the directly measured values to predict values for all health states

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EQ-5D-5L Valuation Study

- To establish EQ-5D-5L value sets using a standardized data collection protocol
- The data collection protocol has been used in many countries including 8 Asian countries
- Main features:
 - Face-to-face personal interview using a computer program called EuroQol Valuation Technology (EQ-VT)
 - Interviewer training and monitoring
 - Use of two valuation methods: time trade-off (TTO) & discrete choice experiment (DCE)

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The EQ-VT interview

1. Introduction
 - a. Self-reported health on the EQ-5D-5L descriptive system
 - b. Self-reported health on the EQ-VAS
 - c. Background questions
2. Composite Time Trade-Off (TTO)
 - a. Instructions and example
 - b. Three practices
 - c. Valuation of 10 EQ-5D-5L states
 - d. Feedback module
 - e. Debriefing questions
3. Discrete Choice Experiment
 - a. Instructions
 - b. Valuation of 7 pairs of EQ-5D-5L states
 - c. Debriefing questions
4. Demographic/additional questions

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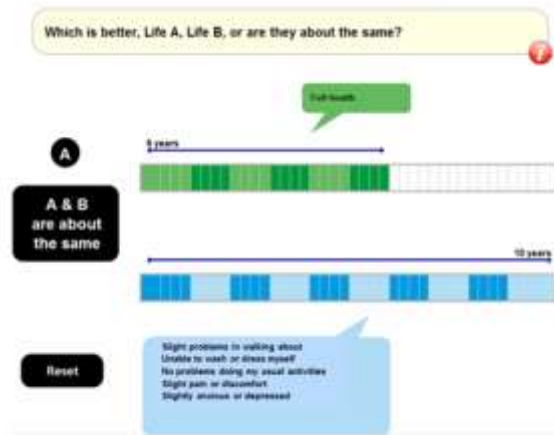


Composite TTO

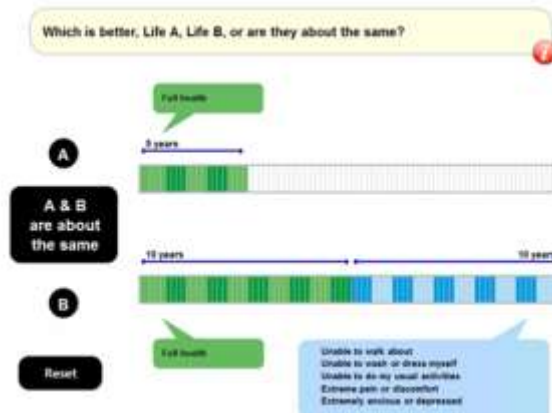
- Conventional or lead-time TTO procedure is used contingent on the value of a health state to the respondent
- If the health state is considered as better than dead, the procedure used in the EQ-5D-3L valuation studies is used
- If the health state is considered as worse than dead, a new, lead-time procedure is used

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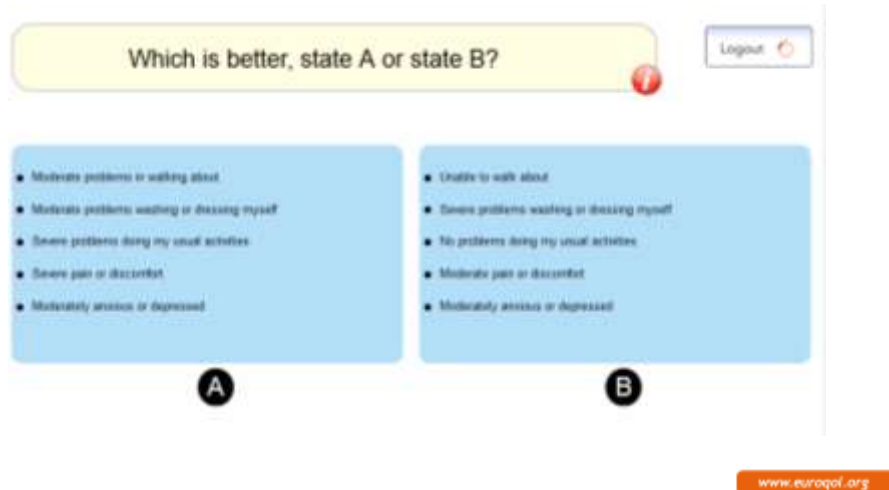
Conventional TTO



Lead-Time TTO



DCE task



Which is better, state A or state B?

Logout

A

- Moderate problems in walking about
- Moderate problems washing or dressing myself
- Severe problems doing my usual activities
- Severe pain or discomfort
- Moderately anxious or depressed

B

- Unable to walk about
- Severe problems washing or dressing myself
- No problems doing my usual activities
- Moderate pain or discomfort
- Moderately anxious or depressed

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Health states for direct valuation

TTO

- 86 states were divided into 10 blocks, with each block containing 10 states
 - 1 mildest state
 - 55555 (all-worst)
 - 8 other states
- Each respondent was randomized to value one block

DCE

- 196 pairs were randomly divided into 28 blocks, with each block containing 7 pairs of states
- Each respondent was randomized to value one block

Overview of modelling analysis

| Data | Model function form | Model parameter estimator | Model prediction evaluation | Model validation |
|-----------|------------------------------------|--|-----------------------------|-----------------------------|
| TTO | Linear models Non-linear models | OLS; GLS; etc. | MAE | Out-of-sample health states |
| DCE | | Conditional logit; Conditional probit | MAE | |
| TTO + DCE | | "Hybrid" estimator | ??? | Out-of-sample respondents |

OLS – ordinary least square; GLS – generalized least square; MAE – mean absolute error

The 20-parameter main-effects model

$$y = \alpha +$$

$$\beta_{MO2}x_{MO2} + \beta_{SC2}x_{SC2} + \beta_{UA2}x_{UA2} + \beta_{PD2}x_{PD2} + \beta_{AD2}x_{AD2} +$$

$$\beta_{MO3}x_{MO3} + \beta_{SC3}x_{SC3} + \beta_{UA3}x_{UA3} + \beta_{PD3}x_{PD3} + \beta_{AD3}x_{AD3} +$$

$$\beta_{MO4}x_{MO4} + \beta_{SC4}x_{SC4} + \beta_{UA4}x_{UA4} + \beta_{PD4}x_{PD4} + \beta_{AD4}x_{AD4} +$$

$$\beta_{MO5}x_{MO5} + \beta_{SC5}x_{SC5} + \beta_{UA5}x_{UA5} + \beta_{PD5}x_{PD5} + \beta_{AD5}x_{AD5}$$



DCE models and non-linear (constrained) models



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University of Oslo

Singapore, September 2016

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DCE task - reminder

Which is better, state A or state B?

Logout

| | |
|---|---|
| <ul style="list-style-type: none">Moderate problems in walking aboutModerate problems washing or dressing myselfSevere problems doing my usual activitiesSevere pain or discomfortModerately anxious or depressed | <ul style="list-style-type: none">Unable to walk aboutSevere problems washing or dressing myselfNo problems doing my usual activitiesModerate pain or discomfortModerately anxious or depressed |
| A | B |

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DCE models (rationale)

- We assume that respondents will select the alternative that maximizes their utility, with some degree of random error.
- If $u(A)$ is the utility of alternative A, and $u(B)$ is the utility of state B, the probability of selecting A is
- Since both $u(A)$ and $u(B)$ are subject to random variance, $u(X) = v(X) + \epsilon_X$

$$P(Y_i = A) = P(U_{iA} > U_{iB}) = P(V_{iA} + \epsilon_{iA} > V_{iB} + \epsilon_{iB}) = P(V_{iA} - V_{iB} > \epsilon_{iB} - \epsilon_{iA})$$

$$P(Y_i = A) = \frac{e^{V_{iA}}}{e^{V_{iA}} + e^{V_{iB}}}$$

$$V_i = \sum_{j=1}^J X_{i,j} \beta_j$$

- Conditional logistic model
- Specific conditional logit/probit model for pair comparisons
- GLS random intercept logit/probit model

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DCE Conditional logistic model

| STATE_ID | RESP_ID | MC | DC | UA | PO | AC | PROBABILIST_CHOICE | Value | MPROD | TIME_TIME_MIN | Probit | Power |
|----------|---------|----|----|----|----|----|--------------------|-------|-------|---------------|--------|-------|
| 18 | 4 | 1 | 4 | 5 | 3 | 3 | 0 | DCE_A | 19.6 | 14533 | 16 | |
| 18 | 4 | 2 | 1 | 5 | 4 | 2 | 1 | DCE_B | 19.6 | 21542 | 14 | |
| 42 | 6 | 2 | 3 | 1 | 3 | 4 | 1 | DCE_A | 18.2 | 23134 | 13 | |
| 42 | 6 | 1 | 4 | 3 | 1 | 4 | 0 | DCE_B | 18.2 | 14314 | 13 | |
| 75 | 5 | 5 | 3 | 4 | 3 | 1 | 0 | DCE_A | 9.4 | 53431 | 16 | |
| 75 | 5 | 5 | 2 | 2 | 5 | 5 | 1 | DCE_B | 9.4 | 52255 | 19 | |
| 76 | 2 | 5 | 1 | 5 | 2 | 2 | 0 | DCE_A | 21.4 | 51522 | 15 | |
| 76 | 2 | 4 | 5 | 2 | 4 | 4 | 1 | DCE_B | 21.4 | 45244 | 19 | |
| 127 | 7 | 1 | 4 | 2 | 2 | 4 | 1 | DCE_A | 33.2 | 14224 | 13 | |
| 127 | 7 | 3 | 2 | 3 | 2 | 2 | 0 | DCE_B | 33.2 | 32322 | 12 | |
| 180 | 3 | 4 | 4 | 1 | 4 | 5 | 1 | DCE_A | 7.2 | 44145 | 18 | |
| 180 | 3 | 4 | 5 | 4 | 3 | 2 | 0 | DCE_B | 7.2 | 45432 | 18 | |
| 196 | 1 | 1 | 1 | 2 | 2 | 1 | 1 | DCE_A | 52.1 | 11221 | 7 | |
| 196 | 1 | 2 | 2 | 1 | 2 | 2 | 0 | DCE_B | 52.1 | 22122 | 9 | |

Stata code:

```
generate dce_group = concat(respondent_id state_id)
clogit choice dummy_variables, group(dce_group)
```

R code:

```
df$dce_group <- interaction(df$respondent_id, df$state_id)
Clogit(Value ~ [dummy_variables] + strata(dce_group))
```

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```

- logit choice model fit method="TTC" & state_16 clrt, group( dce_group)

Iteration 0: log likelihood = -4009.8238
Iteration 1: log likelihood = -3797.2972
Iteration 2: log likelihood = -3794.7752
Iteration 3: log likelihood = -3794.7752
Iteration 4: log likelihood = -3794.7752

Conditional (FIML-EFEM) logit-like regression      Number of obs   =   14224
                                                    LR chi2(10)     =   2415.34
                                                    Prob > chi2     =   0.0000
log likelihood = -3794.7752                        Pseudo R2       =   0.2414

```

| varname | Coeff. | Std. Err. | z | P> z | [95% Conf. Interval] | |
|---------|----------|-----------|------|-------|----------------------|-----------|
| no1 | .4127326 | .0378989 | 7.19 | 0.000 | -.298232 | -.0241333 |
| no2 | 1.022228 | .0542377 | 5.96 | 0.000 | -.0268847 | 1.2688505 |
| no3 | .922523 | .0423833 | 8.49 | 0.000 | .4697522 | 1.182804 |
| no4 | .822489 | .0466246 | 8.24 | 0.000 | .4198053 | .6888956 |
| no5 | .130481 | .0413851 | 2.45 | 0.014 | -.021693 | .2707839 |
| no6 | 1.822482 | .0483989 | 2.82 | 0.005 | .7546597 | .3094299 |
| no7 | .848123 | .0499205 | 8.21 | 0.000 | .2112218 | .8814229 |
| no8 | .3482482 | .0442272 | 5.39 | 0.000 | .1381883 | .4723872 |
| no9 | .2342737 | .0466688 | 5.07 | 0.000 | .119887 | .2499204 |
| no10 | .0482232 | .0426889 | 0.96 | 0.337 | -.0431384 | 1.041832 |
| no11 | .4118889 | .0474011 | 6.49 | 0.000 | .287537 | .5362428 |
| no12 | .3218364 | .0484207 | 4.81 | 0.000 | .1912837 | .4521732 |
| no13 | .2818592 | .0488909 | 4.84 | 0.000 | .1427072 | .4004111 |
| no14 | 1.341248 | .0446124 | 5.92 | 0.000 | .0203914 | .2507449 |
| no15 | .1133224 | .0497241 | 0.90 | 0.369 | -.048139 | 1.242147 |
| no16 | .3751377 | .0494619 | 5.44 | 0.000 | .239791 | .5103993 |
| no17 | .2247386 | .0426243 | 5.29 | 0.000 | .1313938 | .2473237 |
| no18 | .2471128 | .0458841 | 4.07 | 0.000 | .1384272 | .3579445 |
| no19 | .0442468 | .0420222 | 1.00 | 0.319 | .4166889 | .6914443 |
| no20 | .4628682 | .0470387 | 6.91 | 0.000 | -.033148 | .5943317 |

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Specific conditional logit/probit model for DCE pair comparisons

| no1 | no2 | no3 | no4 | no5 | no6 | no7 | no8 | no9 | no10 | no11 | no12 | no13 | no14 | no15 | no16 | no17 | no18 | no19 | no20 |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|------|------|------|------|-------|------|-------|------|-------|------|------|
| 18 | 4 | 1 | 4 | 5 | 3 | 3 | 2 | 1 | 5 | 4 | 2 | 0 | DCE_A | 19.6 | 14533 | 16 | 21542 | 14 | |
| 42 | 6 | 2 | 3 | 1 | 3 | 4 | 1 | 4 | 3 | 1 | 4 | 1 | DCE_A | 18.2 | 23134 | 13 | 14314 | 13 | |
| 75 | 5 | 5 | 3 | 4 | 3 | 1 | 5 | 2 | 2 | 5 | 5 | 0 | DCE_A | 9.4 | 53431 | 16 | 52255 | 19 | |
| 76 | 2 | 5 | 1 | 5 | 2 | 2 | 4 | 5 | 2 | 4 | 4 | 0 | DCE_A | 21.4 | 51522 | 15 | 45244 | 19 | |
| 127 | 7 | 1 | 4 | 2 | 2 | 4 | 3 | 2 | 3 | 2 | 2 | 1 | DCE_A | 33.2 | 14224 | 13 | 32322 | 12 | |
| 180 | 3 | 4 | 4 | 1 | 4 | 5 | 4 | 5 | 4 | 3 | 2 | 1 | DCE_A | 7.2 | 44145 | 18 | 45432 | 18 | |
| 196 | 1 | 1 | 1 | 2 | 2 | 1 | 2 | 2 | 1 | 2 | 2 | 1 | DCE_A | 52.1 | 11221 | 7 | 22122 | 9 | |

- Generate "A-B"
- **logit** choice dummy_variables, nocons
- **probit** choice dummy_variables, nocons
- **hetprobit** choice dummy_variables, nocons het(dummy_variables)

- Random intercept/random slope logistic models can be fitted in STATA:
 - **xtlogit** choice dummy_variables
 - **xtprobit** choice dummy_variables
 - **melogit** choice dummy_variables
 - **meprobit** choice dummy_variables

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Stata output

```

logit value _mo2_5d IF method="DCE_2" & stata_18 <137, covars>.

Iteration 0: log likelihood = -5002.4438
Iteration 1: log likelihood = -3800.0306
Iteration 2: log likelihood = -3794.7764
Iteration 3: log likelihood = -3794.7752
Iteration 4: log likelihood = -3794.7752

Stochastic regression              Number of obs =      7217
Log likelihood = -3794.7752        Wald chi2(100) =    1925.43
                                   Prob > chi2         =      0.0000

+-----+-----+-----+-----+-----+-----+
|       |       |       |       |       |       |
| value | coef. | Std. Err. | z     | P>|z| | [95% Conf. Intervals] |
+-----+-----+-----+-----+-----+-----+
| _mo2  | 4.127304 | .0878889 | 7.13  | 0.000 | 3.93332   4.32129 |
| _mo3  | 1.097029 | .0448377 | 2.44  | 0.014 | .9984841  1.20557 |
| _mo4  | 0.920013 | .0623932 | 1.47  | 0.143 | .7950252  1.04499 |
| _mo5  | 0.503469 | .0668544 | 0.75  | 0.452 | -.2189243  0.72582 |
| _sc2  | 1.154481 | .0413281 | 2.80  | 0.005 | 1.07188   1.23708 |
| _sc3  | 1.025462 | .0523889 | 1.96  | 0.048 | .9204587  1.13046 |
| _sc4  | .9463221 | .0499205 | 1.90  | 0.059 | .8472516  1.04539 |
| _sc5  | .8422483 | .0468272 | 1.80  | 0.073 | .7491893  0.93530 |
| _ua2  | .2842737 | .0893668 | 3.19  | 0.001 | .10587   0.46267 |
| _ua3  | 0.605232 | .0439993 | 1.38  | 0.167 | .5173489  0.69311 |
| _ua4  | .4118969 | .0534511 | 0.77  | 0.439 | .3049337  0.51886 |
| _ua5  | .3214294 | .0666257 | 0.48  | 0.630 | .1892937  0.45356 |
| _pd2  | .2814502 | .0604928 | 0.46  | 0.645 | .1567072  0.40619 |
| _pd3  | 1.241364 | .0468124 | 2.65  | 0.008 | 1.1485214  1.33420 |
| _pd4  | .9112264 | .0457141 | 2.00  | 0.046 | .8205110  1.00194 |
| _pd5  | .7351377 | .0489438 | 1.50  | 0.134 | .6389751  0.83130 |
| _ad2  | .2247088 | .0423363 | 5.31  | 0.000 | .1398388  0.31057 |
| _ad3  | .2871358 | .0485861 | 5.91  | 0.000 | .1904272  0.38394 |
| _ad4  | .5548466 | .0701222 | 7.92  | 0.000 | .4146488  0.69484 |
| _ad5  | .4838062 | .0470387 | 10.3  | 0.000 | .3913148  0.57630 |

```

DCE constant/intercept terms

| "Original" | | | Reversed | | |
|---------------|-------------|------------|---------------|-------------|------------|
| | Estimate | Std. Error | | Estimate | Std. Error |
| (Intercept) | 0.21164586 | 0.0266645 | (Intercept) | -0.21164586 | 0.0266645 |
| incr_mo2_diff | 0.44238775 | 0.0526517 | incr_mo2_diff | 0.44238775 | 0.0526517 |
| incr_mo3_diff | -0.00271168 | 0.0602873 | incr_mo3_diff | -0.00271168 | 0.0602873 |
| incr_mo4_diff | 0.77762394 | 0.0592446 | incr_mo4_diff | 0.77762394 | 0.0592446 |
| incr_mo5_diff | 1.16562366 | 0.0653388 | incr_mo5_diff | 1.16562366 | 0.0653388 |
| incr_sc2_diff | 0.35921265 | 0.0576461 | incr_sc2_diff | 0.35921265 | 0.0576461 |
| incr_sc3_diff | -0.00847681 | 0.0625683 | incr_sc3_diff | -0.00847681 | 0.0625683 |
| incr_sc4_diff | 0.67629896 | 0.0661428 | incr_sc4_diff | 0.67629896 | 0.0661428 |
| incr_sc5_diff | 0.39924359 | 0.0615881 | incr_sc5_diff | 0.39924359 | 0.0615881 |
| incr_ua2_diff | 0.27154495 | 0.0549798 | incr_ua2_diff | 0.27154495 | 0.0549798 |
| incr_ua3_diff | 0.04449129 | 0.0615065 | incr_ua3_diff | 0.04449129 | 0.0615065 |
| incr_ua4_diff | 0.53745959 | 0.0619102 | incr_ua4_diff | 0.53745959 | 0.0619102 |
| incr_ua5_diff | 0.57164557 | 0.0636063 | incr_ua5_diff | 0.57164557 | 0.0636063 |
| incr_pd2_diff | 0.25449076 | 0.0580883 | incr_pd2_diff | 0.25449076 | 0.0580883 |
| incr_pd3_diff | 0.03962988 | 0.0633029 | incr_pd3_diff | 0.03962988 | 0.0633029 |
| incr_pd4_diff | 0.80788425 | 0.0642941 | incr_pd4_diff | 0.80788425 | 0.0642941 |
| incr_pd5_diff | 0.30395110 | 0.0638620 | incr_pd5_diff | 0.30395110 | 0.0638620 |
| incr_ad2_diff | 0.27174584 | 0.0603230 | incr_ad2_diff | 0.27174584 | 0.0603230 |
| incr_ad3_diff | 0.19483877 | 0.0615435 | incr_ad3_diff | 0.19483877 | 0.0615435 |
| incr_ad4_diff | 0.88367616 | 0.0655376 | incr_ad4_diff | 0.88367616 | 0.0655376 |
| incr_ad5_diff | 0.52791784 | 0.0654440 | incr_ad5_diff | 0.52791784 | 0.0654440 |



Non-linear (constrained) models

- While the wording is somewhat different, the levels for the 5 EQ-5D dimensions correspond roughly to:
 1. No problems
 2. Slight problems
 3. Moderate problems
 4. Severe problems
 5. Extreme problems (“unable” for mobility, self-care, and usual activities)
- With the standard 20-parameter model, each decrement is considered in isolation.
- An alternative approach is to assume that the levels describe similar relative decrements across dimensions, and that the dimensions differ primarily in scale.
- The simplest such model requires only 8 parameter: one for each dimension, and one for each of levels 2, 3, and 4

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The 20-parameter model

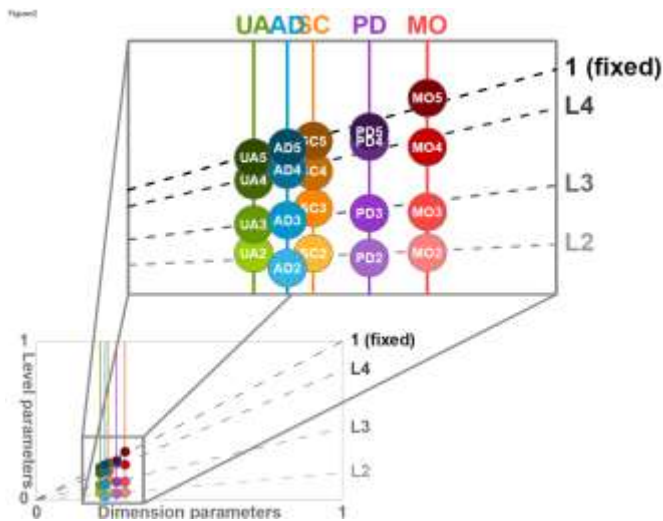
$$\begin{aligned}
 tto &= \alpha + \sum_i \sum_d \beta_{di} x_{di} + e \\
 &= \alpha + \beta_{M02} x_{M02} + \beta_{SC2} x_{SC2} + \beta_{UA2} x_{UA2} + \beta_{PD2} x_{PD2} + \beta_{AD2} x_{AD2} + \\
 &\quad \beta_{M03} x_{M03} + \beta_{SC3} x_{SC3} + \beta_{UA3} x_{UA3} + \beta_{PD3} x_{PD3} + \beta_{AD3} x_{AD3} + \\
 &\quad \beta_{M04} x_{M04} + \beta_{SC4} x_{SC4} + \beta_{UA4} x_{UA4} + \beta_{PD4} x_{PD4} + \beta_{AD4} x_{AD4} + \\
 &\quad \beta_{M05} x_{M05} + \beta_{SC5} x_{SC5} + \beta_{UA5} x_{UA5} + \beta_{PD5} x_{PD5} + \beta_{AD5} x_{AD5} + e
 \end{aligned}$$

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8-parameter model

- A single parameter per dimension (MO, SC, UA, PD, AD), and one for each of levels 2, 3, and 4 (L2, L3, L4):

$$\begin{aligned}
 tto &= \alpha + \sum_i (\sum_d \beta_d x_{di}) L_i + e \\
 &= \alpha + (\beta_{MO}x_{MO2} + \beta_{SC}x_{SC2} + \beta_{UA}x_{UA2} + \beta_{PD}x_{PD2} + \beta_{AD}x_{AD2})L_2 + \\
 &\quad (\beta_{MO}x_{MO3} + \beta_{SC}x_{SC3} + \beta_{UA}x_{UA3} + \beta_{PD}x_{PD3} + \beta_{AD}x_{AD3})L_3 + \\
 &\quad (\beta_{MO}x_{MO4} + \beta_{SC}x_{SC4} + \beta_{UA}x_{UA4} + \beta_{PD}x_{PD4} + \beta_{AD}x_{AD4})L_4 + \\
 &\quad \beta_{MO}x_{MO5} + \beta_{SC}x_{SC5} + \beta_{UA}x_{UA5} + \beta_{PD}x_{PD5} + \beta_{AD}x_{AD5} + e
 \end{aligned}$$



Extensions

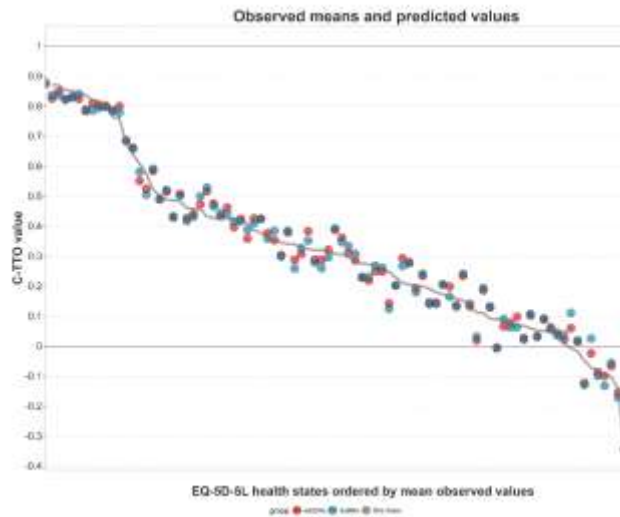
- The wording for level 5 on mobility, self-care and usual activities uses “unable to”, while pain/discomfort and anxiety/depression uses “extreme”.
- To handle this difference, a new parameter can be added for “unable to”, for a total of 9 parameters
- Alternatively, the level structure can be estimated separately for the first three and the last two dimensions, for a total of 11 parameters
- These models are non-linear, and require specialized fitting functions. In STATA:

```
nl (value = {intercept} + /*
*/ (nl_mo2*{M=0} + nl_sc2*{S=0} + nl_ua2*{U=0} + nl_pd2*{P=0} + nl_ad2*{A=0}) * {L2=0.25}) /*
*/ + (nl_mo3 * {M} + nl_sc3 * {S} + nl_ua3 * {U} + nl_pd3 * {P} + nl_ad3 * {A}) * {L3=0.5}) /*
*/ + (nl_mo4 * {M} + nl_sc4 * {S} + nl_ua4 * {U} + nl_pd4 * {P} + nl_ad4 * {A}) * {L4=1}) /*
*/ + (nl_mo5 * {M} + nl_sc5 * {S} + nl_ua5 * {U} + nl_pd5 * {P} + nl_ad5 * {A}))
*/ if .....iter(1000)
```

Non-linear models cont'd

- The code on the last slide requires the dummies to be coded such that mobility level 4 yields
mo2 = 0, mo3 = 0, mo4 = 1, mo5 = 0
- For the DCE models, the coding is generally:
mo2 = 1, mo3 = 1, mo4 = 1, mo5 = 0
- With this coding, the non-linear function previously presented will tend to become unstable and unreliable. It can be altered to accommodate this coding as follows:

```
nl (value = {intercept} + /*
*/ {MO = 0} * (_mo2 * {L2 = 0.25} + _mo3 * {L3 = 0.25} + _mo4 * {L4 = 0.25} + _mo5 * (1-L2-L3-L4)) + /*
*/ {SC = 0} * (_sc2 * L2 + _sc3 * L3 + _sc4 * L4 + _sc5 * (1-L2-L3-L4)) + /*
*/ {UA = 0} * (_ua2 * L2 + _ua3 * L3 + _ua4 * L4 + _ua5 * (1-L2-L3-L4)) + /*
*/ {PD = 0} * (_pd2 * L2 + _pd3 * L3 + _pd4 * L4 + _pd5 * (1-L2-L3-L4)) + /*
*/ {AD = 0} * (_ad2 * L2 + _ad3 * L3 + _ad4 * L4 + _ad5 * (1-L2-L3-L4)) /*
*/ if .....iter(1000)
```



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Table 2: Cross-validation results (continued)

| Country | Method | MSE | | MAE | | |
|---------------------|-------------|----------|----------|----------|----------|--------|
| | | Method 1 | Method 2 | Method 1 | Method 2 | |
| Mean absolute error | Spain | 0.0118 | 0.0118 | 0.0118 | 0.0118 | |
| | | 0.0118 | 0.0118 | 0.0118 | 0.0118 | |
| | France | 0.0118 | 0.0118 | 0.0118 | 0.0118 | |
| | | 0.0118 | 0.0118 | 0.0118 | 0.0118 | |
| | Italy | 0.0118 | 0.0118 | 0.0118 | 0.0118 | |
| | | 0.0118 | 0.0118 | 0.0118 | 0.0118 | |
| Out-of-sample | Spain | 0.0118 | 0.0118 | 0.0118 | 0.0118 | |
| | | 0.0118 | 0.0118 | 0.0118 | 0.0118 | |
| | France | 0.0118 | 0.0118 | 0.0118 | 0.0118 | |
| | | 0.0118 | 0.0118 | 0.0118 | 0.0118 | |
| | Italy | 0.0118 | 0.0118 | 0.0118 | 0.0118 | |
| | | 0.0118 | 0.0118 | 0.0118 | 0.0118 | |
| | Performance | Spain | 0.0118 | 0.0118 | 0.0118 | 0.0118 |
| | | | 0.0118 | 0.0118 | 0.0118 | 0.0118 |
| | | France | 0.0118 | 0.0118 | 0.0118 | 0.0118 |
| | | | 0.0118 | 0.0118 | 0.0118 | 0.0118 |
| | | Italy | 0.0118 | 0.0118 | 0.0118 | 0.0118 |
| | | | 0.0118 | 0.0118 | 0.0118 | 0.0118 |

- The constrained model fit than t
- In cross-validation Singapore, and out-of-sample model
- Performance fo

It in lower observed
 from Spain,
 is displayed higher
 : 20-parameter
 under investigation

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Generalization of the non-linear models

- The *hyreg* command does not presently support non-linear models
- Built-in functions in STATA and R do not support non-linear interval regression
- A package allowing non-linear hybrid models (with and without intervals) has been developed for R, but is not documented to the point where it can be made publicly available.
- We have not found STATA functions that do not allow fitting of non-linear mixed effects models (i.e. random intercept/random slope models). This is possible using the *nlme* package in R.
- The upcoming hybrid function for R currently does not support mixed effects models.

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Modelling TTO & DCE data using a hybrid model



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TTO and DCE methods

- Individuals have a utility function which determines their preferences over health states
- TTO & DCE methods both try to measure the same utility function
- TTO & DCE each have their own weaknesses
 - e.g. scale compatibility (BTD vs WTD) for C-TTO
 - e.g. no anchors for use in QALY calculations for DCE
- Which method should we choose?

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TTO, DCE or both?

- TTO: trade-off between quality of life and length of life
 - How many years are you willing to give up to avoid being in impaired health?
- DCE: trade-off between quality of life and quality of life
 - Which health state is better?
- Both questions provide relevant information
- View TTO and DCE as complementary sources of information instead of competing
 - Include both types of information in a single model (Maximum Likelihood)

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Log likelihood of basic hybrid model (OLS & clogit)

$$\ln L = -\frac{1}{2} * \sum_{j \in C} \left\{ \ln(2\pi\sigma^2) + \left(\frac{y_j - x\beta}{\sigma} \right)^2 \right\} \\ + \sum_{j \in D} \left\{ \ln \left(\frac{1}{1 + e^{(-x\beta')}} \right) * y_j + \ln \left(\frac{e^{(-x\beta')}}{1 + e^{(-x\beta')}} \right) * (1 - y_j) \right\}$$

proportional rescaling parameter θ , such that
 $\beta' = \beta * \theta$

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Log likelihood of basic hybrid model (OLS & clogit)

$$\ln L = -\frac{1}{2} * \sum_{j \in C} \left\{ \ln(2\pi\sigma^2) + \left(\frac{y_j - x\beta}{\sigma} \right)^2 \right\} \\ + \sum_{j \in D} \left\{ \ln \left(\frac{1}{1 + e^{(-x\beta * \theta)}} \right) * y_j + \ln \left(\frac{e^{(-x\beta * \theta)}}{1 + e^{(-x\beta * \theta)}} \right) * (1 - y_j) \right\}$$

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TTO data structure

| ILLOC_ID | STATE_ID | ORDER_ID | MO | SC | UA | PO | AD | ORIGINAL_RESPONSE | Value | METHOD | TASK_TIME_mg | TTO_rows | TTO_realt | Profile | Severity |
|----------|----------|----------|----|----|----|----|----|-------------------|-------|--------|--------------|----------|-----------|---------|----------|
| -1 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 10.5 | 0.05 | TTO | 441.3 | 43 | 0 | 00000 | 0 |
| -1 | -1 | 2 | 2 | 1 | 1 | 2 | 1 | 14 | 0.4 | TTO | 123.0 | 4 | 0 | 21121 | 7 |
| -1 | -2 | 3 | 3 | 5 | 5 | 5 | 4 | 10.5 | 0.05 | TTO | 222.4 | 6 | 0 | 35554 | 22 |
| -1 | -3 | 4 | 1 | 5 | 4 | 1 | 1 | 2 | -0.8 | TTO | 221.4 | 7 | 0 | 15411 | 12 |
| 2 | 10 | 5 | 1 | 2 | 1 | 2 | 1 | 18.5 | 0.85 | TTO | 87.8 | 8 | 0 | 12121 | 7 |
| 2 | 12 | 6 | 3 | 4 | 1 | 5 | 5 | 10 | 0 | TTO | 46.9 | 2 | 0 | 34155 | 18 |
| 7 | 83 | 7 | 1 | 1 | 2 | 1 | 1 | 20 | 1 | TTO | 56.1 | 9 | 0 | 11211 | 6 |
| 2 | 16 | 8 | 2 | 3 | 5 | 1 | 4 | 2 | -0.8 | TTO | 63.5 | 7 | 0 | 23514 | 15 |
| 2 | 15 | 9 | 3 | 2 | 4 | 4 | 3 | 2 | -0.8 | TTO | 58.3 | 7 | 0 | 32443 | 16 |
| 2 | 13 | 10 | 5 | 2 | 2 | 1 | 5 | 10 | 0 | TTO | 27.5 | 2 | 0 | 52215 | 15 |
| 2 | 9 | 11 | 1 | 2 | 5 | 4 | 3 | 2 | -0.8 | TTO | 60.6 | 7 | 0 | 12543 | 15 |
| 2 | 11 | 12 | 4 | 3 | 5 | 4 | 2 | 1 | -0.9 | TTO | 42.3 | 8 | 0 | 43542 | 18 |
| 10 | 86 | 13 | 5 | 5 | 5 | 5 | 5 | 0 | -1 | TTO | 42.6 | 10 | 0 | 55555 | 25 |
| 2 | 14 | 14 | 4 | 5 | 1 | 3 | 3 | 14 | 0.4 | TTO | 40.6 | 4 | 0 | 45133 | 16 |

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DCE data structure

| STATE_ID | ORDER_ID | MO | SC | UA | PO | AD | ORIGINAL_RESPONSE | Value | METHOD | TASK_TIME_mg | Profile | Severity |
|----------|----------|----|----|----|----|----|-------------------|-------|--------|--------------|---------|----------|
| 18 | 4 | 1 | 4 | 5 | 3 | 3 | 0 | DCE_A | 19.6 | 14533 | 16 | |
| 18 | 4 | 2 | 1 | 5 | 4 | 2 | 1 | DCE_B | 19.6 | 21542 | 14 | |
| 42 | 6 | 2 | 3 | 1 | 3 | 4 | 1 | DCE_A | 18.2 | 23134 | 13 | |
| 42 | 6 | 1 | 4 | 3 | 1 | 4 | 0 | DCE_B | 18.2 | 14314 | 13 | |
| 75 | 5 | 5 | 3 | 4 | 3 | 1 | 0 | DCE_A | 9.4 | 53431 | 16 | |
| 75 | 5 | 5 | 2 | 2 | 5 | 5 | 1 | DCE_B | 9.4 | 52255 | 19 | |
| 76 | 2 | 5 | 1 | 5 | 2 | 2 | 0 | DCE_A | 21.4 | 51522 | 15 | |
| 76 | 2 | 4 | 5 | 2 | 4 | 4 | 1 | DCE_B | 21.4 | 45244 | 19 | |
| 127 | 7 | 1 | 4 | 2 | 2 | 4 | 1 | DCE_A | 33.2 | 14224 | 13 | |
| 127 | 7 | 3 | 2 | 3 | 2 | 2 | 0 | DCE_B | 33.2 | 32322 | 12 | |
| 180 | 3 | 4 | 4 | 1 | 4 | 5 | 1 | DCE_A | 7.2 | 44145 | 18 | |
| 180 | 3 | 4 | 5 | 4 | 3 | 2 | 0 | DCE_B | 7.2 | 45432 | 18 | |
| 196 | 1 | 1 | 1 | 2 | 2 | 1 | 1 | DCE_A | 52.1 | 11221 | 7 | |
| 196 | 1 | 2 | 2 | 1 | 2 | 2 | 0 | DCE_B | 52.1 | 22122 | 9 | |

| STATE_ID | ORDER_ID | MO | SC | UA | PO | AD | ORIGINAL_RESPONSE | Value | METHOD | TASK_TIME_mg | Profile | Severity | | | | | | |
|----------|----------|----|----|----|----|----|-------------------|-------|--------|--------------|---------|----------|-------|------|-------|----|-------|----|
| 18 | 4 | 1 | 4 | 5 | 3 | 3 | 2 | 1 | 5 | 4 | 2 | 0 | DCE_A | 19.6 | 14533 | 16 | 21542 | 14 |
| 42 | 6 | 2 | 3 | 1 | 3 | 4 | 1 | 4 | 3 | 1 | 4 | 1 | DCE_A | 18.2 | 23134 | 13 | 14314 | 13 |
| 75 | 5 | 5 | 3 | 4 | 3 | 1 | 5 | 2 | 2 | 5 | 5 | 0 | DCE_A | 9.4 | 53431 | 16 | 52255 | 19 |
| 76 | 2 | 5 | 1 | 5 | 2 | 2 | 4 | 5 | 2 | 4 | 4 | 0 | DCE_A | 21.4 | 51522 | 15 | 45244 | 19 |
| 127 | 7 | 1 | 4 | 2 | 2 | 4 | 3 | 2 | 3 | 2 | 2 | 1 | DCE_A | 33.2 | 14224 | 13 | 32322 | 12 |
| 180 | 3 | 4 | 4 | 1 | 4 | 5 | 4 | 5 | 4 | 3 | 2 | 1 | DCE_A | 7.2 | 44145 | 18 | 45432 | 18 |
| 196 | 1 | 1 | 1 | 2 | 2 | 1 | 2 | 2 | 1 | 2 | 2 | 1 | DCE_A | 52.1 | 11221 | 7 | 22122 | 9 |

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Data structure for HYREG command in Stata

| state/pair | method | datatype | EQ state | value | mo2 | mo3 | mo4 | mo5 | sc2 | sc3 | ... | ad5 |
|------------|--------|----------|----------|-------|-----|-----|-----|-----|-----|-----|-----|-----|
| 1 | TTO | 1 | 22222 | 0.75 | 1 | 0 | 0 | 0 | 1 | 0 | ... | 0 |
| 20 | DCE_A | 0 | 53121 | 0 | 0 | 0 | 0 | 1 | 0 | 1 | ... | 0 |
| 20 | DCE_B | 0 | 32122 | 1 | 0 | 1 | 0 | 0 | 1 | 0 | ... | 0 |
| 21 | DCE_A | 0 | 12345 | 1 | 0 | 0 | 0 | 0 | 1 | 0 | ... | 1 |
| 21 | DCE_B | 0 | 23435 | 0 | 1 | 0 | 0 | 0 | 0 | 1 | ... | 1 |

TTO & DCE: value* = 1- value

DCE: mo2* ... ad5* = mo2_A – mo2_B ... ad5_A – ad5_B

TTO: mo2* ... ad5* = mo2 ... ad5

| state/pair | method | datatype | EQ state | value* | mo2* | mo3* | mo4* | mo5* | sc2* | sc3* | ... | ad5* |
|------------|---------|----------|----------|--------|------|------|------|------|------|------|-----|------|
| 1 | TTO | 1 | 22222 | 0.25 | 1 | 0 | 0 | 0 | 1 | 0 | ... | 0 |
| 20 | DCE_A-B | 0 | ... | 1 | 0 | -1 | 0 | 1 | 0 | -1 | ... | 0 |
| 21 | DCE_A-B | 0 | ... | 0 | -1 | 0 | 0 | 0 | 1 | -1 | ... | 0 |

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Hybrid OLS combined with Conditional logistic model

- Model assumptions**

- Same as OLS for TTO and same as conditional logit for DCE

- Data structure**

| state/pair | method | datatype | EQ state | value* | mo2* | mo3* | mo4* | mo5* | sc2* | sc3* | ... | ad5* |
|------------|---------|----------|----------|--------|------|------|------|------|------|------|-----|------|
| 1 | TTO | 1 | 22222 | 0.25 | 1 | 0 | 0 | 0 | 1 | 0 | ... | 0 |
| 20 | DCE_A-B | 0 | ... | 1 | 0 | -1 | 0 | 1 | 0 | -1 | ... | 0 |
| 21 | DCE_A-B | 0 | ... | 0 | -1 | 0 | 0 | 0 | 1 | -1 | ... | 0 |

- Stata code**

- **hyreg** value* mo2*-ad5*, datatype(datatype) contdist(normal) dichdist(logistic) noconstant

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Hybrid censored at -1 combined with conditional logistic model

- **Model assumptions**

- Same as Tobit for TTO and same as conditional logit for DCE

- **Data structure**

| state/pair | method | datatype | EQ state | value* | mo2* | mo3* | mo4* | mo5* | sc2* | sc3* | ... | ad5* |
|------------|---------|----------|----------|--------|------|------|------|------|------|------|-----|------|
| 1 | TTO | 1 | 22222 | 0.25 | 1 | 0 | 0 | 0 | 1 | 0 | ... | 0 |
| 20 | DCE_A-B | 0 | ... | 1 | 0 | -1 | 0 | 1 | 0 | -1 | ... | 0 |
| 21 | DCE_A-B | 0 | ... | 0 | -1 | 0 | 0 | 0 | 1 | -1 | ... | 0 |

- **Stata code**

- `hyreg value* mo2*-ad5*, datatype(datatype) contdist(normal) dichdist(logistic) noconstant ll(-1)`

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Apples, oranges or a fruit salad?

- TTO: trade-off between quality of life and length of life
- DCE: trade-off between quality of life and quality of life
- Hybrid:
 - Uses all available information
 - Estimates are between those of TTO and those of DCE
 - DCE can help mitigate issues present in TTO and v.v.
- Since the "true" utilities are not known, ultimately the choice is a normative one:
 - Which (imperfect) utility theory?
 - Which (imperfect) data collection technique?
- Pragmatic basis for choice: data quality; value range; performance in applications (e.g. discriminative power)

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Modelling TTO & DCE data using a advanced hybrid models



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We have seen:

Hybrid OLS combined with Conditional logistic model and censoring at -1 for all responses

Basic

- Model assumptions
 - Same as OLS for C-TTO and same as conditional logit for DCE
 - Homoscedastic variance
- Stata code:
 - **hyreg** value dummy_variables, datatype(method_dummy)

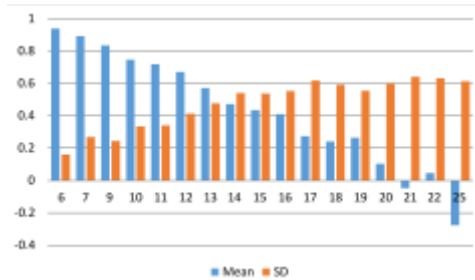
Tobit

- Model assumptions
 - Same as tobit for C-TTO and same as conditional logit for DCE
 - Homoscedastic variance
- Stata code:
 - **hyreg** value dummy_variables, datatype(method_dummy) ll(-1)

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Does the homoscedasticity assumption fit in the case of EQ-VT data?



- As more severe is a state more discrepancy about its value

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Hybrid models counting for heteroscedastic data

- In non heteroscedastic model, the variance is estimated as a single parameter. The idea behind heteroscedastic models is to model the variance as a function of the parameters which impacts on its value
- Model assumptions
 - Similar to OLS for C-TTO and similar to conditional logit for DCE
 - Heteroscedastic variance
- Stata code:
 - **hyreg** value dummy_variables, datatype(method_dummy)
 - *hetcont(dummy_variables') hetdich(dummy_variables')*

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Hybrid intervals combined with Conditional logistic model

- Model assumptions
 - Similar to interval regression for C-TTO and similar to conditional logit for DCE
 - Heteroscedastic variance
- Stata code:
 - `hyreg ll_value ul_value dummy_variables, datatype(method_dummy) intervals hetcont(dummy_variables') hetdich(dummy_variables")`

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Using intervals for censoring specific C- TTO responses on a hybrid model

- Model assumptions
 - Similar to interval regression for C-TTO and similar to conditional logit for DCE
 - Heteroscedastic variance
- Stata code:
 - `hyreg ll_value ul_value dummy_variables, datatype(method_dummy) intervals hetcont(dummy_variables') hetdich(dummy_variables")`

| Type of data | | depvar1 | depvar2 |
|---------------------|-----------|---------|---------|
| point data | a = [a,a] | a | a |
| interval data | [a,b] | a | b |
| left-censored data | (-inf,b] | . | b |
| right-censored data | [a,inf) | a | . |

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Why we may be interested in censoring/truncating specific responses

- Lack of WTD explanation by the interviewer
- Specific interviewer/respondent behaviour during the interview leading to crude preferences rather than accurate stated preferences

| state/pair | method | datatype | EQ state | value* | ll_value | ul_value |Dummies..... |
|------------|--------|----------|----------|--------|----------|----------|-------------------|
| 1 | TTO | 1 | 22222 | 0 | . | 0 | |
| 2 | TTO | 1 | ... | -1 | . | -1 | |
| 3 | TTO | 0 | ... | 0.6 | 0.5 | 0.7 | |

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Hybrid models assuming different distributions for C-TTO or DCE data

- Assumptions
 - Similar to OLS for C-TTO and similar to conditional logit for DCE
 - Heteroscedastic variance
- Stata code:
 - **hyreg** ll_value ul_value dummy_variables, datatype(method_dummy) intervals
 - contdist(normal|logistic) dichcont(normal|logistic)
 - hetcont(dummy_variables") hetdich(dummy_variables")

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Questions

Thanks for attending to this workshop

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