

- **Rev 06.TTO INTERVIEW FLOW**

1. GENERAL WELCOME

- Objectives of project & interview
- Hypothetical nature of questions
- How data will be used
- Right to withdraw at any time
- Informed consent

2. EUROQOL EQ-5D-5L QUESTIONNAIRE

- Self-reported health on the EQ-5D-5L
- Self-reported health on the EQ-VAS

3. TIME TRADE-OFF

- Instructions and examples of TTO task
 - i. Interviewer demonstrates living in a wheelchair TTO exercise
 - ii. Interviewer repeats living in a wheelchair TTO exercise to introduce valuation of states worse than death
- Practice/ warm up exercise
 - i. EQ-5D-5L health state 15411 valued (against EQ-5D-5L 11111)
- Main TTO exercises
 - i. 6 health states introduced
 - ii. Participant rank orders all six health states according to preference
 - iii. TTO 1 participant values own current health against EQ-5D-5L 11111
 - iv. TTO 2 participant values base case (HS2) against EQ-5D-5L 11111
 - v. TTO 3-6 random order valuation against EQ-5D-5L 11111 of
 - 1. HS3 (no exacerbations)
 - 2. HS4 (3x exacerbations/year)
 - 3. HS5 (4x inhaled medications)
 - 4. HS6 (3x physio sessions)
 - vi. Participant shown values given for all six health states & asked if they agree with these scores, or if they would make changes

4. WRAP-UP

- Semi- structured feedback
 - i. 7-point Likert scale "How difficult did you find the trade-off tasks?"
 - ii. Open-ended questions:
 - What was difficult about the task?
 - What do you consider to be treatment burden (or how would you define treatment burden)?
 - What element of your treatment do you struggle with the most?
 - What other aspects of your treatment do you feel have a big impact on your quality of life?
 - On a typical day, how much time (in minutes) would you say you spend on:
 - Physio
 - Inhaled medicines
 - Other aspects of treatment
 - Is there any further feedback on the tasks that you would like to add?

eTable 1: Response to question “would you make changes to these scores if you were to repeat the exercises?”

	All (n=51) No. (%)	Consistent responders (n=34) No. (%)	Inconsistent responders (n=17) No. (%)
Would not change scores	40 (78)	30 (88)	10 (59)
Would change scores	11 (22)	4 (12)	7 (41)
p=0.02 (X ² test)			

eTable 2: Ease of completion of the TTO tasks

	All (n=51) No. (%)	Consistent responders (n=34) No. (%)	Inconsistent responders (n=17) No. (%)
Extremely easy	7 (14)	6 (18)	1 (6)
Moderately easy	11 (22)	9 (26)	2 (12)
Slightly easy	3 (6)	2 (6)	1 (6)
Total easy	21 (41)	17 (50)	4 (24)
Neither difficult nor easy	6 (12)	5 (15)	1 (6)
Slightly difficult	14 (27)	7 (21)	7 (41)
Moderately difficult	10 (20)	5 (15)	5 (29)
Extremely difficult	0 (0)	0 (0)	0 (0)
Total difficult	24 (47)	12 (35)	12 (71)
p=0.06 (X ² test for three-category table [Total easy, Neither difficult nor easy, Total difficult])			

eTable 3: Summary of inconsistent responses

	Inconsistent responders (n=17) No. (%)
Number of inconsistent responses	
1	9 (53)
2	6 (35)
3	2 (12)
Base case with no exacerbations requiring IV abx (HS3)	5 (29)
Base case with 3 exacerbations requiring IV abx (HS4)	5 (29)
Base case with additional nebulised medication (HS5)	9 (53)
Base case with additional physiotherapy (HS6)	8 (47)

eTable 4: Comparison of characteristics of consistent responders and inconsistent responders

Characteristics (n=51)	Sample number	Consistent responses	Inconsistent responses	p (t-test or X ²)
	(consistent, inconsistent)	Mean (SD) or No. (%)	Mean (SD) or No. (%)	
Age (years)	34, 17	34 (12)	32 (9)	0.6
Sex (female)	34, 17	16 (47%)	11 (65%)	0.2
ppFEV1 (l)	34, 17	65 (21)	67 (20)	0.7
Mild (>70%)		14 (41%)	10 (59%)	
Moderate (40-70%)		16 (47%)	5 (29%)	0.4
Severe (<40%)		4 (12%)	2 (12%)	
Required IV antibiotics in last 12 months	31, 16	17 (55%)	6 (38%)	0.3
Prescribed a CFTR modulator	34, 17	24 (71%)	11 (65%)	0.7
elexacaftor/tezacaftor/ivacaftor		20 (59%)	47 (47%)	0.6
Total treatment time (mins/day)	33, 17	126 (95)	125 (198)	0.99
EQ-5D Index score	34, 17	0.81 (22)	0.82 (16)	0.8
EQ-5D VAS score	34, 17	75 (14)	76 (10)	0.8
CFQoL treatment burden domain score	31, 16	56 (26)	62 (27)	0.4

eTable 5: Crude health state utilities for consistent responders

Health state (n=34)	Mean	95% CI	p [†]
Current health (HS1)	0.85	0.79, 0.91	0.3
Base case (HS2)	0.84	0.79, 0.9	-
Base case with no exacerbations requiring IV abx (HS3)	0.88	0.83, 0.92	0.003
Base case with 3 exacerbations requiring IV abx (HS4)	0.76	0.68, 0.84	0.0003
Base case with additional nebulised medication (HS5)	0.82	0.76, 0.88	0.02
Base case with additional physiotherapy (HS6)	0.81	0.74, 0.88	0.02

† paired t-tests: HS1 vs EQ-5D Index; HS3-6 vs HS2

eTable 6: Utility decrement estimates, with point estimates for PEx changes in HS3 & HS4

Parameter	Parameter estimate	SE	95% CI
HS3: No PEx requiring IV abx (per year)	0.044**	0.014	0.016, 0.072
HS4: Three additional PEx requiring IV abx (per year)	-0.070***	0.016	-0.10, -0.038
HS5: Additional nebulised medicine (additional 25 mins/ per day)	-0.015	0.015	-0.044, 0.013
HS6: Additional 20 minute physiotherapy session (per day)	-0.025*	0.015	-0.054, 0.005
Male	-0.031	0.053	-0.13, 0.072
Age [†]	-0.002	0.003	-0.008, 0.003
ppFEV1 [†]	0.0002	0.001	-0.002, 0.002
Intercept	0.81***	0.035	0.74, 0.88

* p <0.1 ** p<0.05 *** p<0.001

† Parameters are centred on the mean (age, 33 years; ppFEV1, 65%)

eTable 7: Utility decrement estimates for consistent responders

Parameter	Parameter estimate	SE	95% CI
HS3 & HS4: Additional PEx requiring IV abx [†] (per year)	-0.039***	0.009	-0.057, -0.020
HS5: Additional nebulised medicine (additional 25 mins/ per day)	-0.018*	0.009	-0.036, 0.0001
HS6: Additional 20 minute physiotherapy session (per day)	-0.028	0.017	-0.061, 0.005
Male	-0.088*	0.047	-0.19, 0.01
Age ^{††}	-0.002	0.003	-0.008, 0.003
ppFEV1 ^{††}	0.001	0.001	-0.001, 0.004
Intercept	0.93***	0.02	0.88, 0.97

* p <0.1 ** p<0.05 *** p<0.001

[†]PEx was specified as having a linear relationship with utility: this parameter estimate should be interpreted as the utility decrement associated with each additional PEx event

^{††}Parameters are centred on the mean (age, 33 years; ppFEV1, 65%)

eFigure 1: Bland Altman plot showing agreement between health state utility scores for the TTO and EQ-5D-5L instruments

