Economic Evaluation alongside Clinical Trials

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Outline

- Introduction of economic evaluation
- Type of economic evaluation
- Economic evaluation alongside clinical trial
- Economic evaluation on the REDUCE Trial

Definition of Economic Evaluation

- Definition: The comparative analysis of the alternative courses of actions in terms of their costing and their consequences. (Drummond, 19997).

- Requirements:

  - The comparison of two or more alternatives.
  - Estimation of both costs and consequences

Introduction of An Economic Evaluation

- Premise of an economic evaluation: Scarce health care resource, such as NHS.
- Aim of an economic evaluation: to maximise health gain with a limited resource use
- Method: to estimate the cost and consequence of the interventions compared with alternatives
- Balance: cost and consequence, available input and output.

Types of Economic Evaluations

Based on good evidence of effectiveness of interventions compared with alternatives

- Costing analysis if effectiveness is not considered.
- Cost minimisation analysis if effectiveness is equal between intervention and alternatives
- Cost effectiveness analysis if effectiveness is measured by single outcome.
- Cost consequence analysis if effectiveness is measured by multiple outcome
- Cost utility analysis if effectiveness is measured by quality of life
- Cost benefit analysis if effectiveness is valued in monetary (willingness to pay)

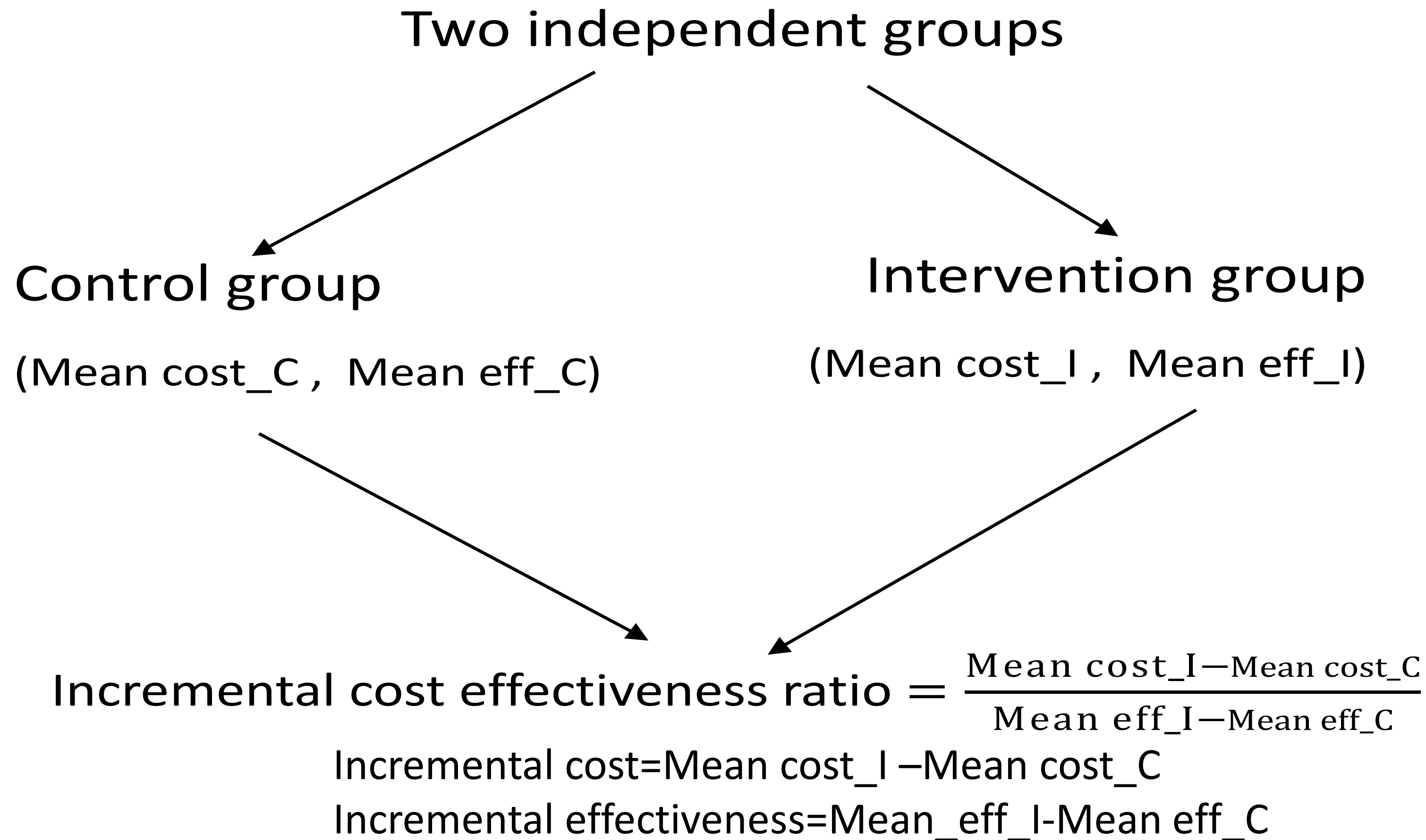
Vehicle for Economic Evaluations

- Data based economic evaluation
  - Perspective collection of data alongside randomised clinical trials.
  - Perspective collection of data alongside non-randomised study, such as perspective cohort comparative study.
- Modelling based economic evaluation: data from different sources, combined in decision analytic modelling. Such as systematic review.

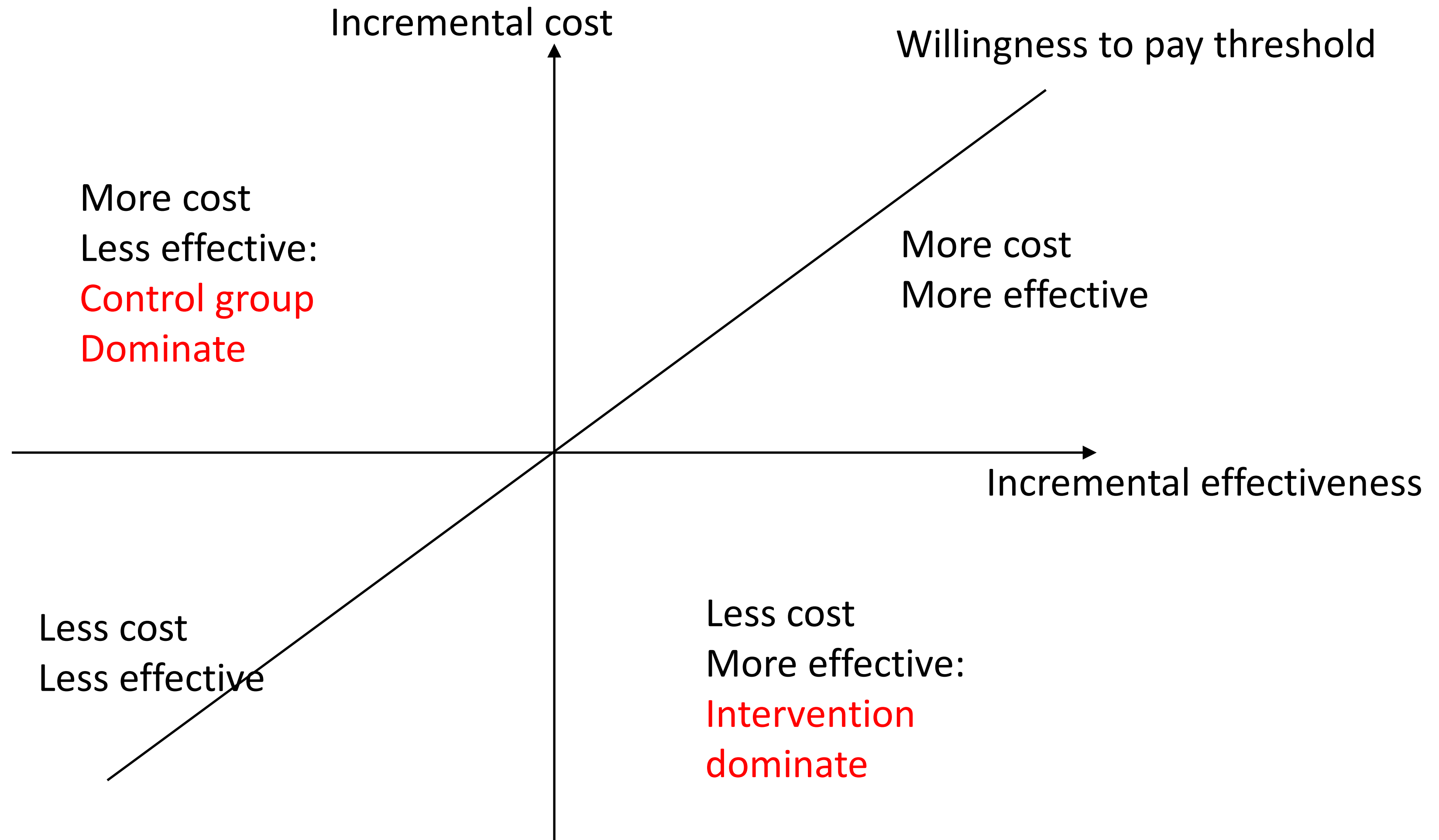
Economic Evaluation alongside Clinical Trials

Two independent groups					
Patient	Control group		Patient	Intervention group	
	Cost	Effectiveness		Cost	Effectiveness
1	Cost_C1	Eff_C1	1	Cost_I1	Eff_I1
2	Cost_C2	Eff_C2	2	Cost_I2	Eff_I1
3	Cost_C3	Eff_C3	3	Cost_I3	Eff_I3
.			.		
.			.		
.			.		
n	Cost_Cn	Eff_Cn	m	Cost_Im	Eff_Im
	Mean_cost_C	Mean_eff_C		Mean_cost_I	Mean_eff_I

Economic Evaluation alongside Clinical Trials



Cost Effectiveness Plane



NICE Guided Method

- Outcome: preferred measure of cost effective
  - Cost per Quality of adjusted life year gained (QALY)
  - Alternatively, cost per life year gained (LY)
- The willingness to pay (WTP) threshold accepted by NICE for the new treatment is £20,000-£30,000 per quality adjusted life year (QALY).

Why QALYs as Measure of Outcome

- Guide the decision making by using the cost effectiveness
- Outcome measured the cost effectiveness can be used in the wide ranges:
    - Life year gained if survival is the primary outcome in the trial
    - Quality adjusted life years (QALYs) gained: common use in the trial, composite of the survival and quality of life

Quality of Life Measurement

- Generic quality of life instruments are commonly used to measure quality of life
- EuroEQ 5D is a generic quality of life widely used in the Europe and other countries.
- SF36 and SF12 are also generic quality of life. They also commonly used.
- The other generic quality life: HUI in children population and ICECAP in older population

EuroEQ5D-3L

By placing a tick in one box in each group below, please indicate which statements best describe your own health state TODAY.

Mobility

- I have no problems in walking about ❑
- I have some problems in walking about ❑
- I am confined to bed ❑

Self-Care

- I have no problems with self-care ❑
- I have some 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 with performing my usual activities ❑
- I have some problems with performing my usual activities ❑
- I am unable to perform my usual activities ❑

Pain / Discomfort

I have no pain or discomfort ❑
I have moderate pain or discomfort ❑
I have extreme pain or discomfort ❑

Anxiety / Depression

I am not anxious or depressed ❑
I am moderately anxious or depressed ❑
I am extremely anxious or depressed ❑

EuroEQ5D-5L

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

MOBILITY

- I have no problems in walking about ❑
- I have slight problems in walking about ❑
- I have moderate problems in walking about ❑
- I have severe problems in 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 extreme pain or discomfort ❑

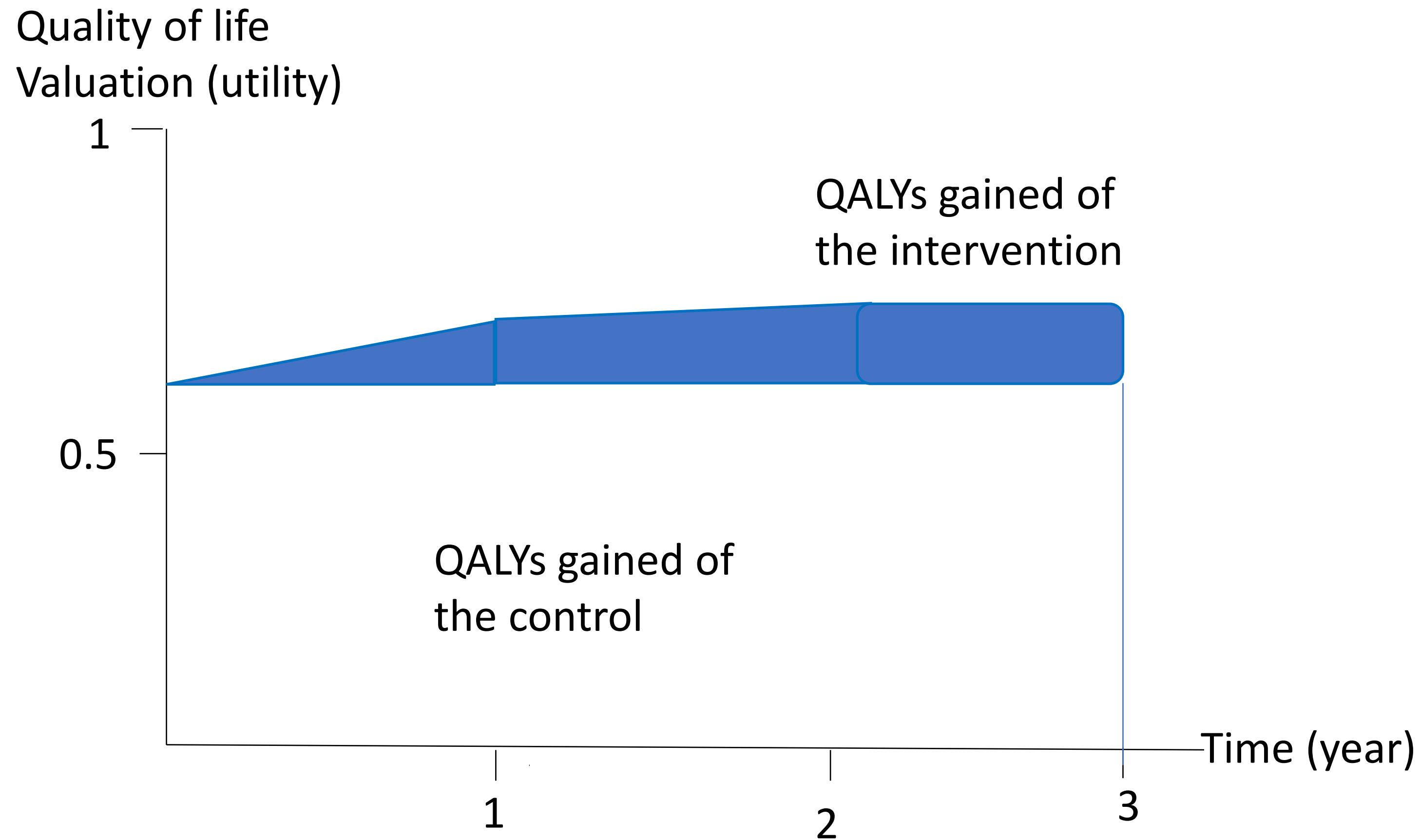
ANXIETY / DEPRESSION

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 ❑

Tariff (Utility) of EQ5D-3L

	Coefficient
Constant	0.081
Mobility	
some problems	0.069
confined to bed	0.314
Self care	
some problems	0.104
Unable to wahs/dress	0.214
Usual activity	
some problems	0.036
Unable to perform	0.094
Pain/discomfort	
moderate	0.123
Extreme	0.386
Anxiety/depression	
moderate	0.071
Extreme	0.236
N3 (level at least once)	0.269

Calculation of Quality Adjusted Life Years



REDUCE Trial

- Internet and telephone support for discontinuing long-term antidepressants: cluster randomized trial.
- Pragmatic RCT
- Recruited 330 Participants were adults on antidepressants for more than one year for a first episode of depression, or two years for recurrent depression, at low risk of relapse, and willing to discontinue
- Randomisation: 131 general practices were randomised-(178 in intervention practices and 152 in controls).
- Outcome: PHQ-9 scores and discontinued antidepressants

Design and Analysis of Economic Evaluation on REDUCE Trial

- Cost measurement and valuation
- Quality of life measurement and valuation
  - EQ5D-5L questionnaire
  - SF12 questionnaire
  - Patient self-report
- Economic analysis within trial data and extrapolating beyond trial

Measurement of Resource Use

- Perspective NHS and personal social services
- Resources
  - medication,
  - Primary care: GP, nurse, out of hours, working in
  - Second care: out-patient, A&E, hospitalisation
  - Community:
  - Out of pocket
  - Off work, loss of productivity
- Data collected by designed online questionnaire and GP records.

Valuation of Costing

- Resource use (cost generating event)
- Unit cost: cost/per event. Such as cost/ GP consultation, cost/per day of inpatient.
  - Medication: British National Formulary (BNF)
  - Primary care: Personal Social Service Research Unit (PSSRU)
  - Secondary care: National Reference Cost
  - Unit cost based on 2022/2023 prices
- Costing: the product of resource use and related unit cost

Unit Cost on the Trial

Services	Sources	Year	Comments	Unit cost (£)	Adjusted to 2023 (£)
GP face to face at surgery	PSSRU	2022		42	43.70
GP telephone	PSSRU	2022		15.8	16.44
GP out of hour service	PSSRU	2022		82.32	85.65
GP online and Video	PSSRU	2022		41.13	42.80
Nurse at GP	PSSRU	2022	£46 /hour, 13.5mins assumed the same time in PROMDEP	10.35	10.77
Nurse out of hour service	Thorm 2020	2019	Average OOH hourly evening rate was £58.36 in 2005 compared with £36.75 for normal hours. Same differential applied to current GP nurse in hour costs.	20.29	21.11
CMHN	PSSRU	2022	£46 /hour assumed 23 mins as the same time in PROMDEP	17.63	18.35
Community doctor	PSSRU	2022	£66/hour band 7 , assumed 30 mins	33	34.34
Counsellor	PSSRU	2022	£66/hour band 7 assumed 30 mins	33	34.34
Psychiatrist	PSSRU	2022	£66/hour band 7 , 60 mins in RPOMDEP	66	68.67
Psychologist	PSSRU	2022	£66/hour band 7 , 37.5 mins in PROMDEP	41.25	42.92
Walk in	Reference cost	2021/2022	type 4 non-admitted,	55.34	57.45
NHS_111	Thorm 2020	2019	NHS 111 phone call 8.06 Maximum call cost of £7.80 in May 2013	11.4	12.34
Outpatient	Reference cost	2021/2022		203	210.76
Day case	Reference cost	2021/2022		1038	1077.66
A&E	Reference cost	2021/2022		242	251.25
Inpatient (bed day)	Reference cost	2021/2022		406	421.51
Medication	BNF	2023	BNF (British National Formulary) | NICE		

Resource Use and Costing

	Intervention group (N=178)			Control group (N=147)		
Item of service	Recorded Number	Mean no. per patient (SD)	Mean costs (£) (SD)	Recorded Number	Mean no. per patient (SD)	Mean costs (£) (SD)
Medications	125	4.3 (3.3)	23.7 (30.8)	107	3.9 (3.2)	20.6 (40.9)
GP face to face contact	115	2.1 (2.1)	91.2 (90.1)	105	2.5 (2.4)	107.4 (105)
GP telephone contact	125	4.1 (2.5)	66.7 (41.6)	101	3.6 (2.7)	58.6 (44.4)
GP online contact	36	2.1 (2.1)	90.4 (88.5)	13	2.5 (2.6)	108.6 (111.4)
GP out of hour contact	8	1.1 (0.4)	96.4 (30.3)	8	1 (0)	85.7 (0)
Practice nurse face to face contact	84	2.8 (2.5)	30.5 (26.9)	65	2.2 (1.5)	23.5 (15.8)
Practice nurse out of hours contact	4	1.8 (1.5)	36.9 (31.7)	2	1 (0)	21.1 (0)
Community Mental Health Nurse	1	3 (.)	55.1 (.)	1	1 (.)	18.4 (.)
Other Nurse contacts	35	2.2 (2)	39.8 (36)	10	1.6 (1)	29.4 (17.7)
Community doctor contacts	5	1.8 (1.3)	61.8 (44.8)	9	1.8 (1)	61 (33.4)
Counsellor contacts	4	2.3 (2.5)	77.3 (85.9)	4	2.3 (2.5)	77.3 (85.9)
Psychiatrist contacts	2	2.5 (2.1)	171.7 (145.7)	1	1 (.)	68.7 (.)
Psychologist contacts	2	1 (0)	42.9 (0)	0	. (.)	. (.)
Other therapist contacts	15	2.3 (1.7)	97.3 (71.6)	16	2.1 (1.9)	91.2 (79.7)
Walk-in service contacts	6	1 (0)	57.5 (0)	5	1 (0)	57.5 (0)
NHS 111 contacts	5	1 (0)	12.3 (0)	9	1.2 (0.4)	15.1 (5.4)
Outpatient appointments	64	2 (1.1)	421.5 (237.5)	54	1.9 (1.1)	402 (221.5)
Day case attendances	10	1 (0)	1077.7 (0)	15	1.3 (0.5)	1365 (493.3)
A&E attendance	16	1.2 (0.4)	298.4 (101.3)	20	1.2 (0.5)	301.5 (131.4)
Inpatient stay	6	2 (0)	4355.6 (7802.7)	6	2 (0)	1756.3 (1012.2)
Intervention	178		25 (0)			. (.)
Total	178		595.5 (1662.5)	147		668.9 (921.5)

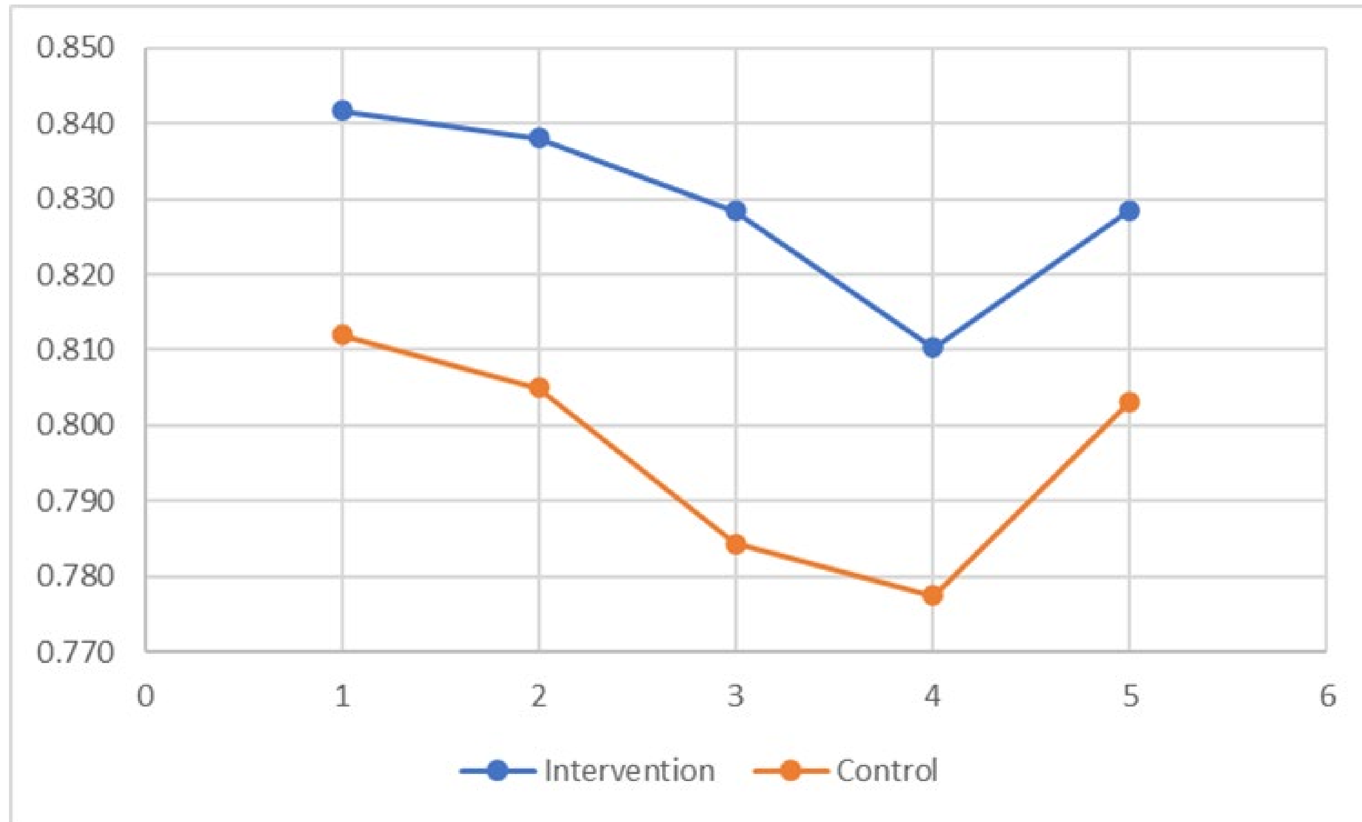
Measurement of Quality of Life

- Quality of life (QoL) was measured using both the EuroQol EQ-5D-5L and Medical Outcomes Study short form SF-12 questionnaires
- Both questionnaires were collected by online patient self-report at baseline, 3, 6, 9 and 12 months
- The validated mapping function from the existing EQ-5D-3L to the EQ-5D-5L was used to generate utility scores.
- The SF-12 scores were translated into SF-6D scores to derive patient utilities using the UK tariff.
- The SF-12 scores were translated into SF-6D scores to derive patient utilities using the UK tariff.
- Quality adjusted life years (QALYs) were calculated using the area under the curve (AUC) approach
- As the trial period was limited to 12 months no discounting rates were applied.

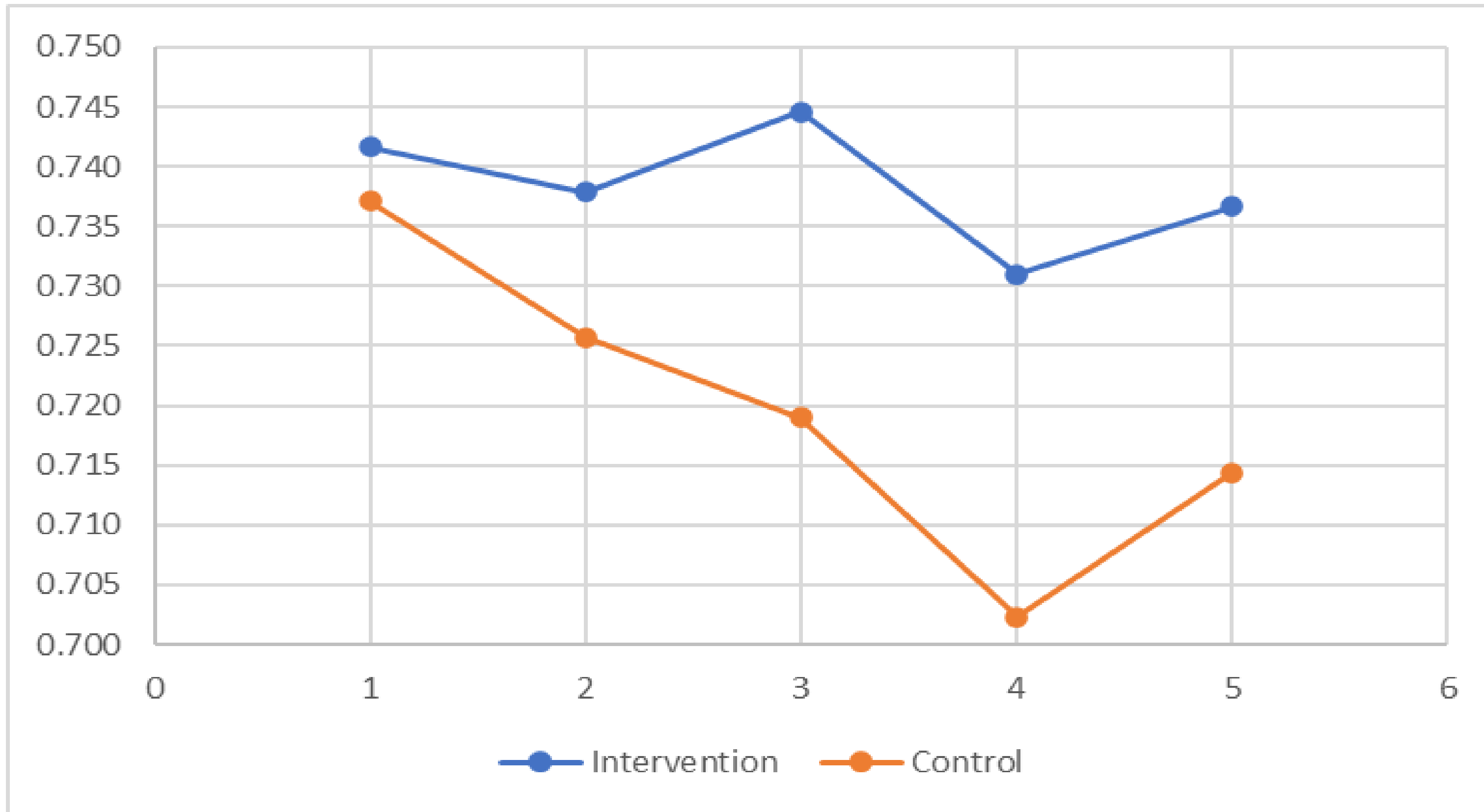
Results of Quality of Life

EQ5D (mean)	Intervention	Control
EQ5DScore_Baseline	0.842	0.812
EQ5DScore_3m	0.838	0.805
EQ5DScore_6m	0.828	0.784
EQ5DScore_9m	0.810	0.777
EQ5DScore_12m	0.829	0.803
SF12 (mean)		
SF12_baseline	0.742	0.737
SF12_ind_3m	0.738	0.726
SF12_ind_6m	0.745	0.719
SF12_ind_9m	0.731	0.702
SF12_ind_12m	0.737	0.714

EQ5D Score



SF12 Score



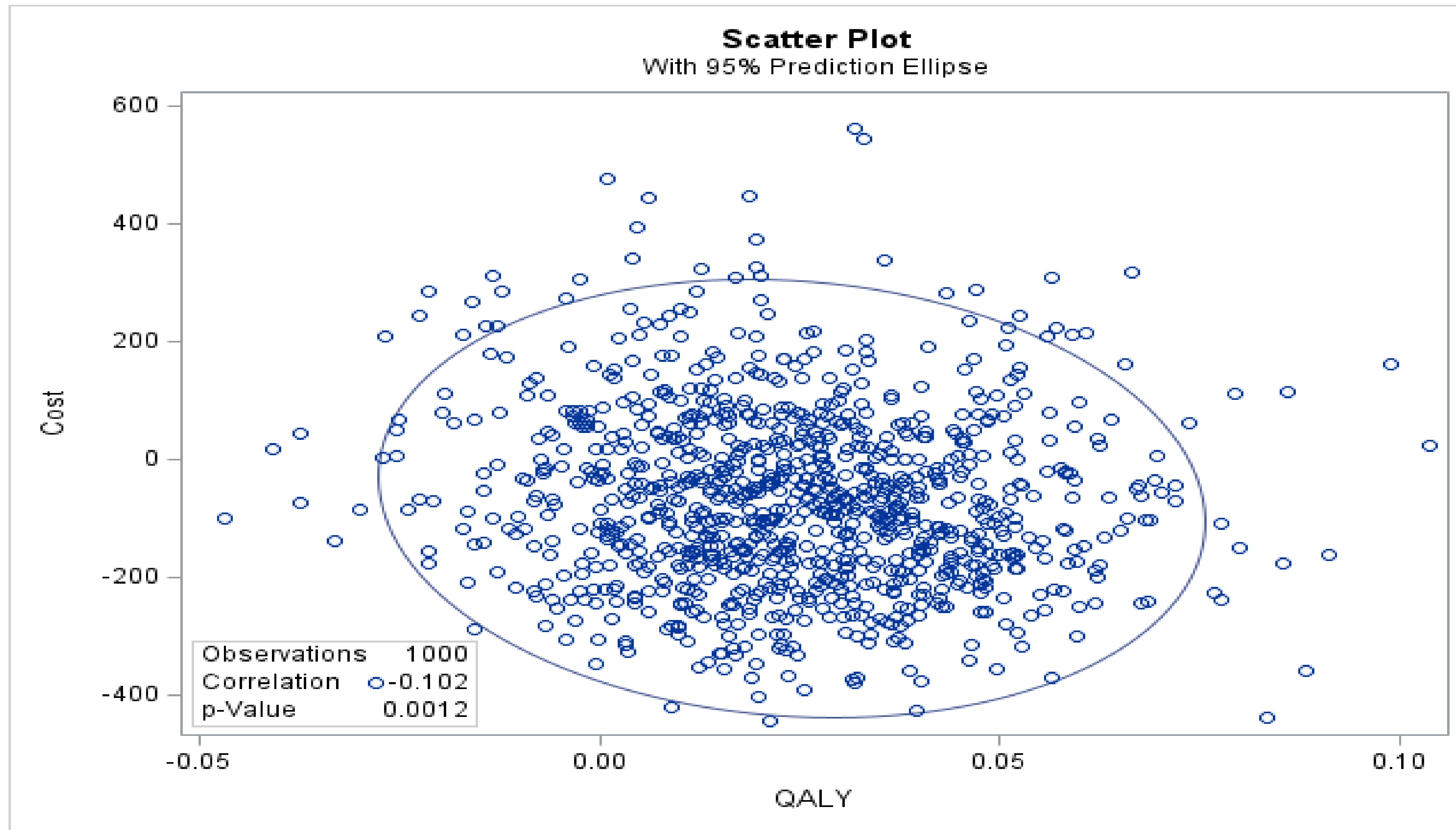
Costs, QALYs and Incremental cost-effectiveness ratios (ICERS) based on EQ5D

Group	Cost (£) mean (95%CI)	Incremental Cost (£) mean (95%CI)	QALYs mean (95%CI)	Incremental QALY mean (95%CI)	ICER (£/QALY) mean (95%CI)
Control	666 (662, 808)		0.805 (0.806, 0.832)		
Intervention	597 (582, 828)	-69 (-77, 207)	0.829 (0.83, 0.851)	0.024 (0.023, 0.059)	-2839 (-30024, 22227)

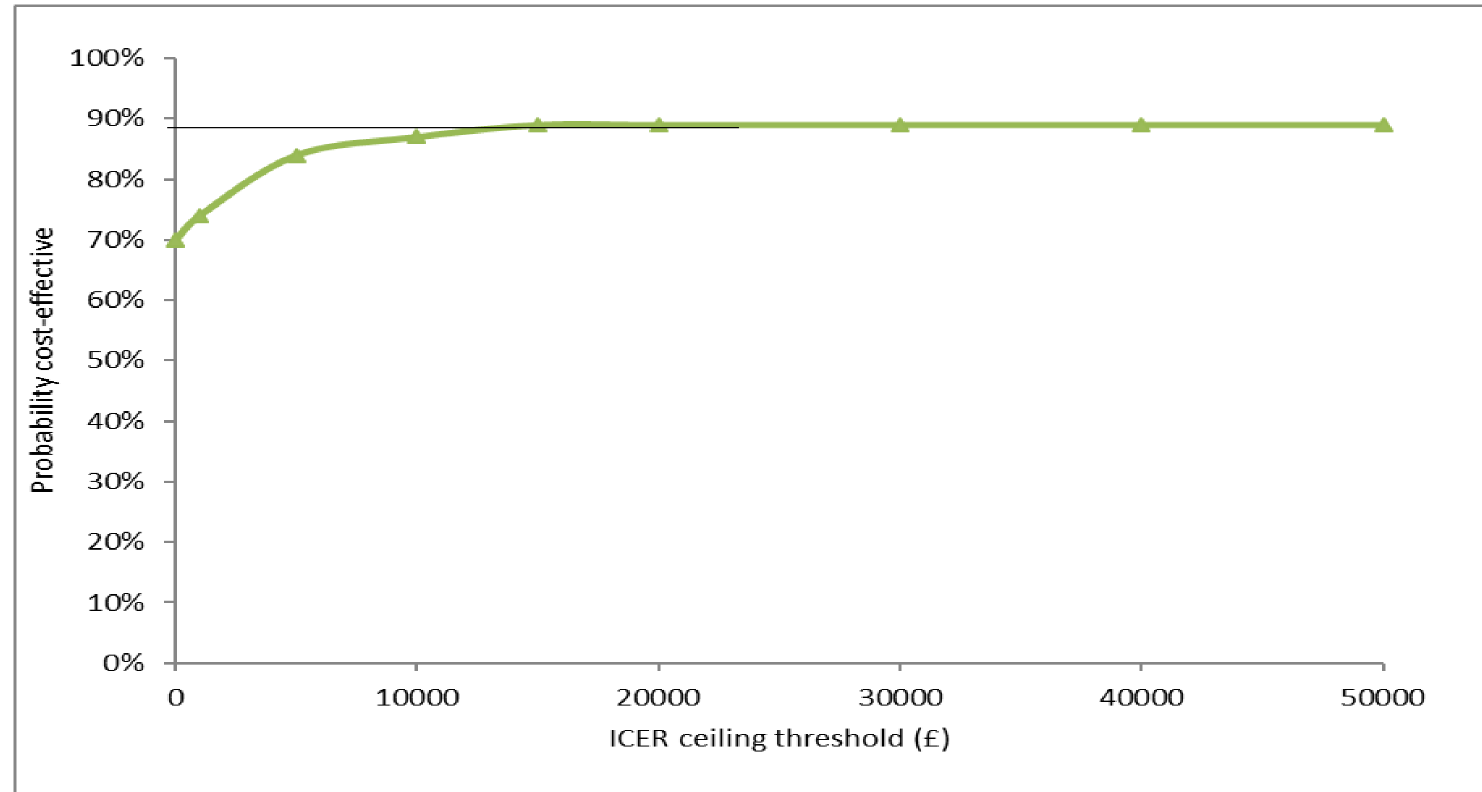
Costs, QALYs and Incremental cost-effectiveness ratios (ICERS) based on SF12

Group	Cost (£) mean (95% CI)	Incremental Cost (£) Mean (95% CI)	QALYs mean (95% CI)	Incremental QALY mean (95% CI)	ICER (£/QALY) mean (95% CI)
Control	666 (662, 808)		0.717 (0.698, 0.736)		
Intervention	597 (582, 828)	-69 (-77, 207)	0.733 (0.716, 0.751)	0.016 (0.016, 0.042)	-3312 (-42043, 38998)

Incremental cost and QALYs (EQ5D5L) scatter plot with 95% confidence ellipse



Cost effectiveness acceptability curve of the intervention based on QALYs from EQ-5D-5L values over one year



Key Findings on REDUCE Trial

- Clinical finding: More than 40% of patients taking long-term antidepressants, who are well and willing to discontinue them, can succeed with primary care practitioner review and tapering alone. Internet and telephone support may protect patients against depressive and withdrawal symptoms and conserve mental wellbeing, but the benefits are modest and replication is warranted.
- The intervention appeared highly likely to be cost-effective compared to usual care at the NICE thresholds for acceptability in terms of societal willingness to pay. This is an important prerequisite for successful dissemination of the findings and implementation of the intervention throughout the NHS in due course. However, the findings are based on the single year of the trial's duration.

Limitation of Economic Evaluation on Trial

- Limited follow up
- Intermediate outcome
- Partial measurement
- Unrepresentative practice
- Partial comparison

Thank you!
Any question?