# Cost-utility analysis of Adapted Problem Adaptation Therapy for depression in mild to moderate dementia caused by Alzheimer's disease: PATHFINDER randomized controlled trial

Panca M[1], Howard R[2], Cort E[2], Rawlinson C[2], Gould RL[2], Wiegand M[3], Downey AM[4], Banerjee S[5], Fox C[6], Harwood R[5], Livingston G[2], Moniz-Cook E[7], Russell G[8], Thomas A[9], Wilkinson P[10], Freemantle N[1], Hunter RM[4]

1.Comprehensive Clinical Trials Unit, UCL, UK 2.Division of Psychiatry, UCL, UK 3.Department of Statistical Science, UCL, UK, 4.Priment Clinical Trials Unit, UCL, UK, 5.University of Nottingham, UK, 6.University of Exeter, Norfolk, UK, 7.University of Hull, UK, 8.Bradford District Care NHS Foundation Trust, UK, 9.University of Newcastle, UK, 10.Department of Psychiatry, University of Oxford, UK

## INTRODUCTION

- The numbers of people with dementia are rising with an ageing population. In England, it is estimated that the cost of long-term care for older people with dementia will increase from £5.4 billion in 2002 to £16.7 billion in 2031 [1].
- Depression is common in dementia, with meta-analysis suggesting that 14.8% people with Alzheimer's disease (AD) have a major depressive disorder [2]. Depression in dementia reduces quality of life and functional abilities [3,4] and increases caregiver burden [5].
- PATHFINDER (Problem Adaptation Therapy for Individuals with Mild to Moderate Dementia and Depression) was a multicenter, single-blind, parallel, two-arm, randomised clinical trial (RCT) to assess the clinical and cost-effectiveness of an adapted intervention for depression in mild to moderate dementia caused by AD.

## INTERVENTION

- **Problem Adaptation Therapy (PATH)** aimed to improve emotion regulation through situation selection and modification, attentional deployment, cognitive change, and response modulation, using a problem-solving approach and caregiver participation.
- The adapted PATH intervention [6] (N=168) consisted of up to eight manualized 1-hour sessions involving a trained and supervised therapist, the patient participant and the caregiver, over 12 weeks: two assessment sessions, five sessions focusing on problem solving using PATH tools, and one review session. One-hour booster sessions at 6 and 9 months reviewed key problem-solving and emotional regulation strategies used in PATH.
- Caregivers were involved as co-therapists to help to identify problems that were maintaining depression.

## METHODS

- Cost of PATH intervention: micro-costing approach of the cost of training the therapists and the cost of delivering the intervention.
- Resource use: a specifically designed questionnaire based on the Client Service Receipt Inventory (CSRI) [7]. Costs were estimated at 2021/2022 UK pounds (£) from the National Health Service/personal social services (NHS/PSS) and societal perspectives.
- Quality adjusted life years (QALYs): calculated as the area under the curve adjusting for baseline differences using responses to EQ-5D-5L and the crosswalk mapping algorithm [8]. Supporting analyses included QALYs calculated from responses to DEMQOL/DEMQOL-Proxy, a dementia-specific preference-based measure of quality-of-life instrument [9].
- Time horizon: 12 months with assessments of costs and outcomes at the following points: baseline and 3-months, 6-months (all asking for previous 3 months) and 12-months follow-up (asking for previous 6 months).
- Statistical analyses: mixed effects logistic regressions, adjusting for baseline values, treatment allocation and baseline use of antidepressant medication (stratification factor) as fixed effects, with sites as random effects. A bias-corrected and accelerated bootstrap method was used to calculate 95% confidence intervals (Cis).
- Missing data: 46 data sets were imputed, with site, sex, age, use of antidepressant, and baseline depression level included in the imputation model as baseline predictors of missingness.
- Incremental cost-effectiveness ratio (ICER): mean incremental cost per QALY gained of PATH intervention was calculated by dividing the group randomisation covariate obtained in the cost bootstrap analysis by the randomisation covariate obtained in the QALY bootstrap analysis.
- Cost-effectiveness acceptability curve (CEAC): report probability that PATH intervention is cost-effective compared with treatment as usual (TAU) for a range of values of willingness-to-pay (WTP) for a QALY gained (£20,000-£30,000).

## RESULTS

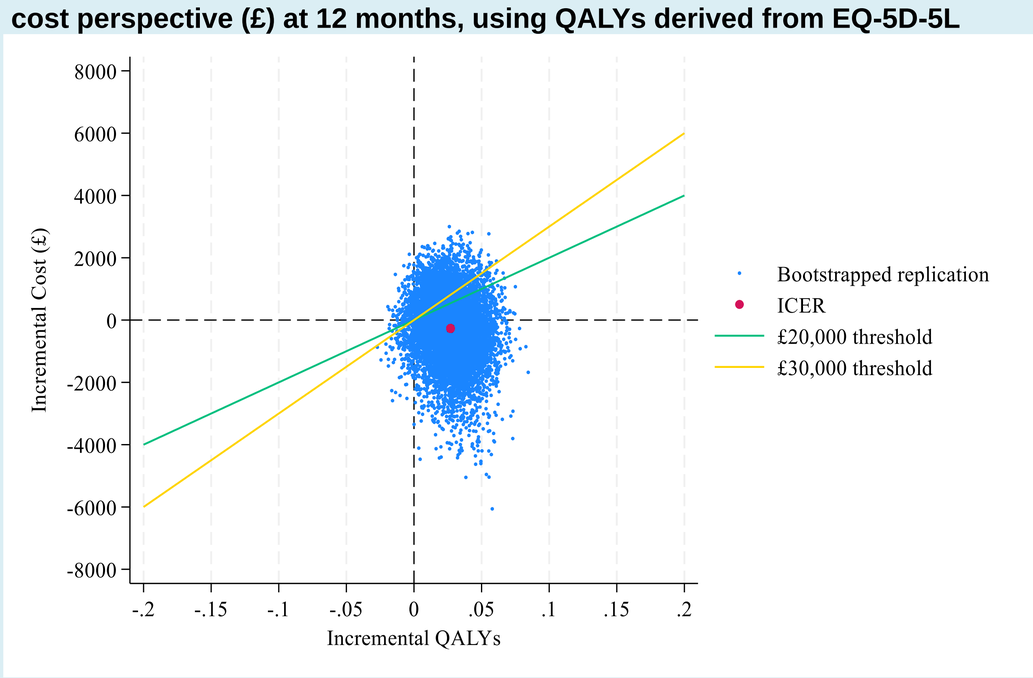
**Breakdown of the cost of implementing the PATH intervention**

| Items | Costs |
|---|---|
| **Training of therapists** | |
| 82 therapists; 21 training/ booster sessions | £79,795 |
| **Delivery of intervention** | |
| 8 manualised 1-hour sessions over 12 weeks | £36,149 |
| Supervision fortnightly; 2-3 therapist per session | £93,539 |
| **Materials used in training and delivery of intervention** | £2,785 |
| **Cost per participant in adapted PATH arm** | **£1,141** |

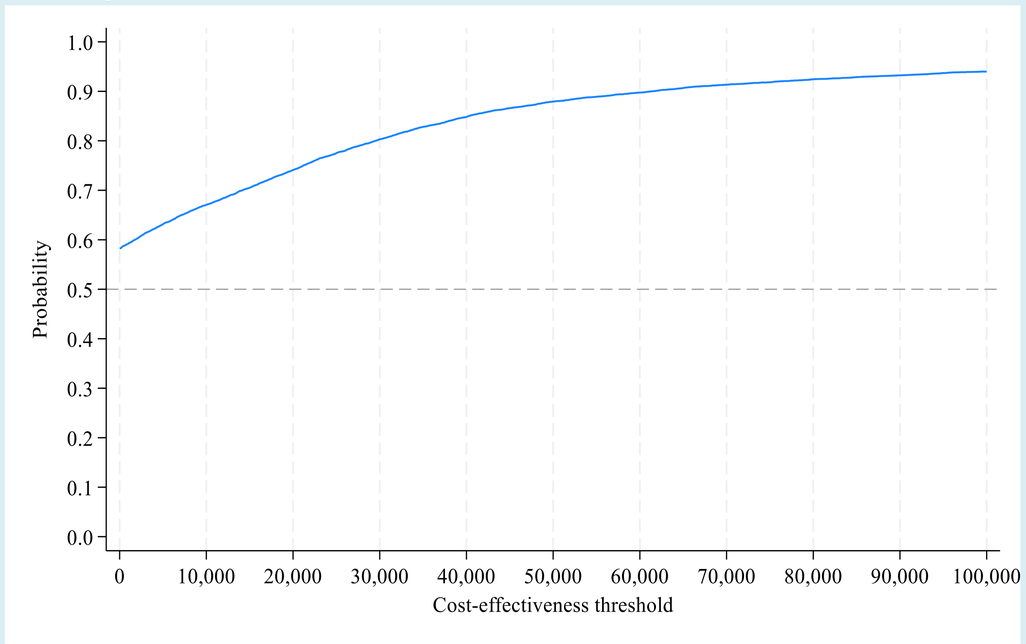
**Mean incremental costs, QALYs, and probabilities of the adapted PATH being cost-effective at £20,000 and £30,000 per QALY gained value thresholds (multiple imputation)**

| | Incremental Cost (95%CI) | Incremental Benefit (95%CI) | Probability CE £20,000 | Probability CE £30,000 |
|---|---|---|---|---|
| **NHS/PSS perspective** | | | | |
| QALYs from EQ-5D-5L | -£74 (-£1,942 to £1,793) | 0.027 (-0.004 to 0.059) | 74% | 80% |
| QALYs from DEMQOL | -£74 (-£1,942 to £1,793) | 0.009 (-0.009 to 0.292) | 64% | 66% |
| QALYs from DEMQOL-Proxy | -£74 (-£1,942 to £1,793) | 0.011 (-0.006 to 0.027) | 66% | 68% |
| **Societal perspective** | | | | |
| QALYs from EQ-5D-5L | -£671 (-£9,144 to £7,801) | 0.027 (-0.004 to 0.059) | 68% | 70% |
| QALYs from DEMQOL | -£671 (-£9,144 to £7,801) | 0.009 (-0.009 to 0.292) | 65% | 65% |
| QALYs from DEMQOL-Proxy | -£671 (-£9,144 to £7,801) | 0.011 (-0.006 to 0.027) | 65% | 66% |

**Cost-effectiveness plane of adapted PATH compared to TAU from NHS/PSS cost perspective (£) at 12 months, using QALYs derived from EQ-5D-5L**




**Cost-effectiveness acceptability curve of adapted PATH compared to TAU from NHS/PSS cost perspective (£) at 12 months, using QALYs derived from EQ-5D-5L**




## CONCLUSIONS

- The addition of the adapted PATH intervention to TAU for people with dementia and depression did generate cost savings alongside a positive mean point estimate in health-related quality of life (HRQoL) compared to TAU; however, the improvements in costs and HRQoL (QALYs) were not statistically significant.
- Strengths of the study include the sample size, representativeness of participants from many NHS community services for people with dementia, and the good levels of demonstrated adherence to and competence in delivery of the manualized intervention achieved by therapists recruited from participants' usual clinical teams.
- Study limitations include our choice of available multidisciplinary staff (nurses, clinical psychologists, assistant psychologists, occupational therapists), as therapists rather than dedicated trained therapists, for adapted PATH delivery.
- Although there is an ongoing debate about the appropriateness of using the EQ-5D instrument in people with dementia this is the preferred approach for generating utilities by across interventions and conditions by the National Institute for Health and Care Excellence (NICE) [10].
- We also used the dementia specific preference-based measure DEMQOL to generate utilities. Responses to DEMQOL/DEMQOL-Proxy also produced positive baseline-adjusted differences in QALYs at 12 months, however they were not statistically significant.
- Evidence about the cost-effectiveness of adapted PATH can help decision-makers make more efficient use of scarce resources.
- There is potential in the adapted PATH intervention as our results showed improvement in quality of life despite no reduction in depression [11].
- Such interventions could be relatively cheap if they were to be implemented within the NHS as therapy providers could be trained locally and could be cost saving in the long-term if the short-term improvements last.

**REFERENCES:**

**1.**Comas-Herrera A, Wittenberg R, Pickard L, et al. Cognitive impairment in older people: future demand for long-term care services and the associated costs. Int J Geriatr Psychiatr 2007; 22:1037-45. **2.**Asmer MS, Kirkham J, Newton H, et al. Meta-analysis of the prevalence of major depressive disorder among adults with dementia. J Clin Psychiatry. 2018;79:17r1177 **3.**Peters ME, Schwartz S, Han D, et al. Neuropsychiatric symptoms as predictors of progression to severe Alzheimer's dementia and death: the cache county dementia progression study. Am J Psychiatry. 2015;172:460-65. **4**.Kraup BA, Loreck D, Gruber-Baldini AL, et al. Depression and its relationship to function and medical status by dementia status in nursing home admissions. Am J Geriatr Psychiatry. 2007;15:438-442. **5**.Baharudin AD, Din NC, Subramaniam P, et al. The associations between behavioural-psychological symptoms of dementia and coping strategy; burden of care and personality style among low-income caregivers of patients with dementia. BMC Public Health. 2019;19:447 **6**.McCombie C, Cort E, Gould RL, et al. Adapting and optimizing problem adaptation therapy (PATH) for people with mild-moderate dementia and depression. Am J Geriatr Psychiatry. 2021;29:192-203. **7**.Beecham JK, Knapp MRJ. Costing psychiatric interventions. In: Thornicroft G, Brewin C, Wing JK (eds) Measuring Mental Health Needs. Gaskell. London. 1992: 200-224. **8**.Hernández-Alava M, Pudney S. Eq5Dmap: A Command for Mapping between EQ-5D-3L and EQ-5D-5L. The Stata Journal. 2018; 18: 395-415. **9**.Mulhern B, Rowen D, Brazier J, et al. Development of DEMQOL-U and DEMQOL-PROXY-U: generation of preference-based indices from DEMQOL and DEMQOL-PROXY for use in economic evaluation. Health Technol Assess. 2013; 17: v-xv, 1-140 **10**.NICE health technology evaluations: the manual. Process and methods. 2022. Available at: https://www.nice.org.uk/process/pmg36/resources/nice-health-technology-evaluations-the-manual-pdf-72286779244741. **11**. Howard R, Cort E, Rawlinson C, et al. Adapted problem adaptation therapy for depression in mild to moderate Alzheimer's disease dementia: A randomized controlled trial. Alzheimers Dement. 2024 Apr;20(4):2990-2999.