Institution: University of Essex

Unit of Assessment: 2 – Public Health

Title of case study: Psychological treatments for persistent depression - informing international treatment guidelines

Period when the underpinning research was undertaken: 2000-2019

Details of staff conducting the underpinning research from the submitting unit:

Name(s):	Role(s) (e.g. job title):	Period(s) employed by submitting HEI:
Phil Richardson	Professor	1998-2007 (deceased)
Susan McPherson	Professor	2006-present

Period when the claimed impact occurred: 2013-2020

Is this case study continued from a case study submitted in 2014? N

1. Summary of the impact

The impact described derives from two sources: a Randomized Controlled Trial (RCT) of long-term psychodynamic psychotherapy (LTPP) for treatment resistant depression (TRD), which showed significant positive outcomes at 2 year follow-up; and research addressing the complexities of evaluating psychological therapies for long-term conditions.

Two domains of impacts are claimed. Firstly, the RCT findings were used to inform European and American guideline recommendations. Secondly, related psychological therapy outcome research led the UK's National Institute for Health and Care Excellence (NICE) to commit to a change in approach to analysis of long-term outcome data and quality-of-life/functioning outcomes for the depression guideline update (now due 2022). Essex research shows that analysis of these outcomes will lead to changes in the range of psychological therapies recommended for people with depression to choose from.

2. Underpinning research

Long-term psychodynamic psychotherapy for adults (used for a wide range of mental health diagnoses including depression) has been available within the NHS since its inception, yet lacked a formal evidence base in the form of RCTs. In 1998, the Tavistock Clinic (an NHS provider of LTPP) and the University of Essex appointed a joint Chair (Richardson) to lead a programme of outcome research in LTPP. Richardson, a leading outcomes researcher in Psychological Therapies (PTs), undertook and contributed to the development of methodologies for evaluating PTs [R1, R2].

Richardson and McPherson completed a systematic review of PTs for Treatment Resistant Depression (TRD) [R3] which identified key methodological limitations of existing TRD efficacy research including the limited availability of long-term follow-up and quality-of-life/functioning (QOL/F) data. These omissions are significant given a. the extremely chronic nature of TRD, defined as a minimum of 2 years, but in practice 2-29 years [R4]; b. QOL/F outcomes (as opposed to symptom outcomes) are more closely aligned with patient recovery [R5]. McPherson and Richardson re-reviewed RCTs of PTs reviewed in the NICE 2004 depression guideline by QOL/F outcomes. This demonstrated that a focus on QOL/F outcomes produces different review findings: effect sizes of certain PTs recommended by NICE reduce and the effects of certain other PTs not recommended by NICE become apparent [R5].

Supported by McPherson, Richardson designed and led an RCT based at the Tavistock Clinic which examined the efficacy of LTPP for TRD and which ran from 2002-2015 [R6]. On Richardson's death (2007), McPherson, who was the lead researcher co-ordinating the RCT until 2007, remained involved as a collaborating researcher until completion. The completed RCT [R7] was the first RCT of LTPP in the NHS and was unique among RCTs for persistent forms of depression in its duration of follow-up (2-years post-treatment). Inclusion criteria required participants (N=129) to have moderate or severe depression as well as complex personality and/or

psycho-social difficulties, meaning the sample was more clinically complex than is typical in RCTs of PTs for depression.

Key findings were:
Symptom outcomes: at end-of-treatment (once weekly for 18 months), there was no benefit over treatment-as-usual for LTPP on symptom outcomes (ES=0.2). However, positive treatment effects (on symptoms) were evident at 2 years after end-of-treatment: ES=0.63.

QOL/F outcomes: the mean score of the General Assessment of Functioning Scale (GAF) at baseline was 49 (serious impairment). The LTPP group mean GAF score at 2-year follow-up was 60 (borderline moderate-mild impairment). There were statistically significant differences between the LTPP and treatment-as-usual group at end-of-treatment and at 2-year follow-up on the GAF with the effect size increasing between end-of-treatment and 2-year follow-up. The same pattern occurred with the Quality of Life Enjoyment and Satisfaction Questionnaire.

Of 124 RCTs reviewed by NICE in the most recent draft update to the depression guideline, for either TRD or chronic depression, only 11 had post-treatment follow-up data of 6 months or more [R4]. Of these, the Tavistock RCT had the longest follow-up. Further examination of pre-post effect sizes (for symptoms) at follow-up for these 11 RCTs demonstrates that many (but not all) PTs become more effective at follow-up [R4]. LTPP is one such PT that becomes more effective at follow-up [R4].

Note that there is ongoing work to examine the cost-effectiveness of LTPP for TRD. A cost-effectiveness evaluation of a recent UK based RCT of Cognitive Behavioural Therapy for TRD (the "COBALT" trial) found an incremental cost-effectiveness ratio of GBP 14,911 (see Wiles et al 2014 – HTA report [S3a]). While the cost of treatment in the Tavistock LTPP RCT is likely to be 3-4 times that in the COBALT trial, this is counterbalanced by the LTPP sample being a more chronic, severe and costly group (including lost work and high levels of informal care) at baseline (see McCrone et al 2017 [S3b]). Taking these factors into account, the cost of treatment for patients with the more intransigent low functioning forms of depression as seen in the Tavistock RCT are likely to be within the NICE range of cost-effectiveness.

3. References to the research [can be supplied by HEI on request]

[R1] Richardson PH (2000). Clinical Effectiveness and Psychological Treatments: Introduction to Special Section. *Journal of Mental Health,* 9(3), 235-236. DOI: 10.1037/bar0000148

[R2] Richardson, PH (2001). Evidence based practice and the psychodynamic psychotherapies. Chapter 11 In C Mace, S Moorey and B Roberts (Eds): Evidence in the Psychological Therapies. London: Routledge, pp154-169) ISBN: 0415212480

[R3] McPherson S, Cairns P, Carlyle J, Shapiro D, Richardson P, Taylor D (2005). The effectiveness of psychological treatments for refractory depression: A systematic review. *Acta Psychiatrica Scandinavica*, 111, 331-340. DOI: 10.1111/j.1600-0447.2004.00498.x

[R4] McPherson S, Hengartner M. (2019). Long-term outcomes of trials in the National Institute for Health and Care Excellence depression guideline. *BJPsych Open*, *5*(5). doi:10.1192/bjo.2019.65

[R5] McPherson, S., Evans, C. & Richardson. P (2009). The NICE Depression Guidelines and the recovery model: Is there an evidence base for IAPT?, *Journal of Mental Health*, 18:5, 405-414, DOI: 10.3109/09638230902968258

[R6] Taylor D, Carlyle J, McPherson S, Rost F, Thomas R, Fonagy P (2012). The Tavistock Adult Depression Study (TADS): A randomised controlled trial of psychoanalytic psychotherapy for treatment-resistant/treatment-refractory forms of depression, *BMC Psychiatry*, 12:60. https://bmcpsychiatry.biomedcentral.com/articles/10.1186/1471-244X-12-60

[R7] Fonagy P, Rost F, Carlyle J, McPherson S, Thomas R, Fearon P, Goldberg D, Taylor D (2015). Pragmatic randomized controlled trial of long-term psychoanalytic psychotherapy for treatment-resistant depression: the Tavistock Adult Depression Study (TADS). *World Psychiatry*, 14(3), 312–321. https://onlinelibrary.wiley.com/doi/full/10.1002/wps.20267 (Citations: 92)

4. Details of the impact

1) The RCT results were used to inform European and American depression guideline recommendations

The long-term outcomes reported in the Tavistock RCT [R7] are the basis of recommendations for LTPP for TRD in the following guidelines:

- European Psychiatric Association (EPA) guideline on PTs for persistent forms of depression [S1a]
- American Psychological Association (APA) guideline for depression [S1b]
- European Community based Mental Health Service Providers (EUCOMS) Network [S1c]

The EPA guideline used the Tavistock RCT [R7] to conclude that "*both observer-based and self-reported depression scores showed steeper declines in the LTPP group, alongside greater improvements on measures of social adjustment. These data suggest that LTPP can be useful in improving the long-term outcome of treatment-resistant depression*" [S1a]. The guideline recommends LTPP as a third-line treatment. The recommendation could not be first- or second-line because the Tavistock RCT was "*published after closure of literature search and not included into database for evidence grading and the Delphi process*". The EPA has 44 National Psychiatric Association members representing over 80,000 psychiatrists across Europe. The EPA collaborates with WHO Europe and the EU Compass project to promote evidence-based practice in member states informed by its portfolio of peer-reviewed published guidelines.

EUCOMS, comprising 61 organisations from 21 countries, used the Tavistock RCT [R7] as a basis for recommending psychodynamic psychotherapy as an evidence-based treatment for community mental health care [S1b].

The APA 2019 guideline [S1c] was developed based on systematic reviews only (rather than reviewing primary research). Of the systematic reviews included, one was on the effectiveness of psychodynamic psychotherapies [S1d] and was the source for several statements about LTPP in the guideline. The conclusions in this review concerning LTPP for depression were based solely on the Tavistock RCT [R7]. The APA guideline recommends psychodynamic psychotherapies as an option among first and second-line treatments; it notes that "*psychotherapies seem to have longer term effects*" and that "*LTPP relative to treatment-as-usual (which could include antidepressant medication) may have similar effects as well*" (p55-6). It also notes "*some evidence suggests that effects of some psychotherapies persist longer than the effects of medication*" (p88). The APA is the registration and accrediting body for clinical psychologists in the US and has 121,000 members.

2) Essex research led NICE to commit to a change in approach to analysis of long-term outcome data and quality-of-life/functioning outcomes for the depression guideline update (due 2022).

In February 2017 McPherson was invited to speak at the Association for Psychoanalytic Psychotherapy in the NHS 'Annual Phil Richardson Memorial Lecture' [S2a]. In this talk McPherson anticipated some of the methodological issues that might arise in the forthcoming draft of the NICE depression guideline and encouraged mental health professional bodies concerned with these methodological issues to work together to identify and raise key concerns with NICE jointly and constructively [S2a].

The 2017/8 consultation drafts of the guideline had analysed end-of-treatment symptom outcomes only. The recommendations concerning PTs for depression were therefore based on end-of treatment symptom outcomes, which concerned several professional bodies because this significantly narrowed the choice of therapies that will be made available for patients to choose among (which is important because patient choice and preference is known to impact on outcomes). McPherson engaged with various professional bodies and patient organisations, supporting them to engage jointly with NICE around key methodological issues, thus influencing and shaping the debate around guideline methodologies concerning PTs for depression. This resulted in:

a) Key stakeholders (Royal College of Psychiatrists [RCPsych], British Psychoanalytic Association and Society for Psychotherapy Research UK) cited Essex research [including R3, R4 and R7] in their stakeholder responses to NICE's 2017 consultation draft. Citing this Essex research, RCPsych specifically requested that functional outcomes be given more priority [S2b p259-60] and that "*Proper weight should be given to outcomes reported at long-term follow-ups/observation periods, where these are available, rather than exclusively treatment endpoint*." [S2b p416]

b) McPherson was invited to co-author (with the President of the Society for Psychotherapy Research UK) a joint stakeholder response to a second stakeholder consultation [S2c]. This was signed by 14 organisations (including the RCPsych, MIND, UK Council for Psychotherapy, British Association for Counselling and Psychotherapy and National Survivor User Network) plus 6 individuals (including Prof Sir Simon Wessely and Prof Clare Gerada MBE), submitted June 2018. This was resubmitted to NICE in May 2019, having been signed by 40 organisations (now including the British Psychological Society and Association for Clinical Psychologists) plus 53 individuals. The response highlighted 6 methodological issues, including the importance of examining long-term outcomes and QOL/F outcomes because of the importance of these outcomes to patients and because prioritising these outcomes in developing recommendations would lead to greater patient choice of PTs [R4, R5] [S2c p7,17].

c) McPherson attended and took a key role in stakeholder discussions with NICE executives (including Sir Andrew Dillon and Paul Chrisp), to explore methodological issues (April 2018 and May 2019) [S2d]. Subsequently, in December 2019, NICE confirmed their response to these discussions [S2e]. NICE committed to a substantial new programme of work to address stakeholder methodological concerns. Concerning long-term outcomes NICE stated: *"NICE will now include long-term follow-up data in all its treatment reviews. The committee has previously considered that long-term follow up data were not available across all comparisons of interests in the guideline and consequently long-term effectiveness would be subject to large potential biases. However, we accept that long-term effectiveness is an important outcome and we will now look for it in all treatment reviews*." Stating similar reasons, NICE also committed to *"include quality of life and functional status as outcomes in the treatment reviews"*. [S2e] The third consultation draft including this additional work is now due in May 2022. Essex research shows that analysis of QOL/F outcomes [R5] and long-term outcomes [R4] will change the range of PTs recommended and therefore made available to people presenting with depression.

5. Sources to corroborate the impact

1) <u>The RCT results were used to inform European and American depression guideline recommendations</u>

[S1a] EPA guideline on psychotherapy in chronic depression (2016)
http://www.europsy.net/app/uploads/2016/05/Psychotherapy-in-chronic-depression-across-Europe.pdf
[S1b] EUCOMS consensus paper (2019): principles and key elements of community-based mental health care
https://doi.org/10.1186/s12888-019-2162-z (see page 6; reference 60)

[S1c]: American Psychological Association Guideline Development Panel for the Treatment of Depressive Disorders. (2019). *Clinical practice guideline for the treatment of depression across three age cohorts*.
https://www.apa.org/depression-guideline/guideline.pdf
[S1d] Fonagy P (2015) The effectiveness of psychodynamic psychotherapies – an update. World Psychiatry, 14(2), 137-150.

2) Essex research led NICE to commit to a change in approach to analysis of long-term outcome data and quality-of-life/functioning outcomes for the depression guideline

[S2a] APP Annual lecture 2017: McPherson as discussant + slides
[S2b] NICE Depression Guideline Documents – "Comments and responses" (NICE published full stakeholder comments along with NICE responses from the 1st consultation May 2018).
[S2c] Joint stakeholder statement June 2018 (updated May 2019)
[S2d] Minutes of methodology discussions with NICE (April 2018 and May 2019)
[S2e] NICE decision December 2019

[S3a] Wiles et al. (2014) Clinical and cost-effectiveness of cognitive behavioural therapy as an adjunct to pharmacotherapy for treatment resistant depression in primary care: the CoBalT randomised controlled trial. *Health Technology Assessment*. 18 (31), https://doi.org/10.3310/hta18310
[S3b] McCrone et. al. (2018) The economic cost of treatment-resistant depression in patients referred to a specialist service. *Journal of Mental Health.* 27 (6), 567-573. https://doi.org/10.1080/09638237.2017.1417562