**Dependent personality and its influence on the short and long-term outcomes of cognitive behaviour therapy for health anxiety: randomised controlled trial**

Peter Tyrer, Duolao Wang, Helen Tyrer, Mike Crawford, Sylvia Cooper, Janice Morgan, Rahil Sanatinia & Barbara Barrett

Rahil Sanatinia, MD, Centre for Mental Health, Hammersmith Campus, Imperial College, London; Duolao Wang, PhD, Department of Clinical Sciences, Liverpool School of Tropical Medicine, Liverpool; Peter Tyrer, FRCPsych, FMedSci, Centre for Mental Health, Hammersmith Campus, Imperial

College, London; Helen Tyrer, MB, PhD, Centre for Mental Health, Hammersmith Campus, Imperial College, London; Mike Crawford, MD, FRCPsych, Centre for Mental Health, Hammersmith Campus, Imperial College, London; Sylvia Cooper, BSc, Centre for Mental Health, Hammersmith Campus, Imperial College, London; Gemma Loebenberg, MSc, North West London Clinical Research Network, Hammersmith Hospital, London; Barbara Barrett, PhD, King’s Health Economics, Box P024, King’s College London, De Crespigny Park, London

Correspondence: Professor Peter Tyrer, Centre for Mental Health, Imperial College, Hammersmith Hospital, London W12 0NN, UK. Email: p.tyrer@imperial.ac.uk.

**Dimensions of dependence and their influence on the short and long-term outcomes of cognitive behaviour therapy for health anxiety: randomised controlled trial**

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**Background**: The personality trait of dependence is somewhat difference from many others in that it is often regarded as adaptive and, when maladaptive, is of less pathological significance than many other traits. There is also some evidence that it may be a positive trait in health seeking behaviour. We therefore examined its impact in a large randomised controlled trial of psychological treatment for health anxiety.

**Aims:** To test whether dependent personality traits were positive or negative in determining the outcome of an adapted form of cognitive behaviour therapy for health anxiety (CBT-HA) over their otv ce erh the hypotheses that personality dysfunction recorded using the new ICD-11 diagnostic system had a negative influence on the outcomes of treatment with cognitive behaviour therapy for health anxiety over 2 years and that personality dysfunction would be associated with increased cost.

**Method**: Personality dysfunction was assessed at baseline in a randomised controlled trial of 444 patients from medical clinics with pathological health anxiety treated with a modified form of cognitive behaviour therapy for health anxiety (CBT-HA) or standard treatment in the medical clinics, with assessment on four occasions over 2 years. Personality dysfunction was assessed at baseline using a procedure that led to five ICD-11 proposed groups (0 = no personality dysfunction, 1 = personality difficulty, 2 = mild personality disorder, 3 = moderate personality disorder, 4 = severe personality disorder). The statistical analysis used a mixed model with the primary outcome as change in health anxiety scores after one year. Total costs over follow-up were calculated from service use and hospital data and compared by personality group.

**Results**: In total, 381 patients (86%) had some personality dysfunction with 184 (41%) satisfying the ICD criteria for personality disorder. Those with no personality dysfunction showed no difference in health anxiety response to CBT compared with standard care (P=0.90) and showed worse social function (P<0.03) whereas those with any form of personality dysfunction derived significant benefit from CBT-HA maintained over two years (P<0.001) with lesser benefit in those with more severe personality disorders (P<0.05) There was slight evidence that costs were relatively higher in participants with moderate and severe personality disorder with CBT-HA and lower with less personality pathology.

**Conclusion**: The results suggest that anxiety disorders in the absence of personality dysfunction do not require specific psychological treatment and that personality abnormality is not a bar to success with CBT in this population.

**Declaration of Interest:** PT and MC are members of the World Health Organisation ICD-11 work group for the revision of the classification of personality disorder.

**Background**

There is increasing evidence that the relatively new diagnosis of health anxiety, linked to hypochondriasis but sowing important differencs, is an important condition that is recognised as common in epidemiological studies1-2 but not often in clinical practice, mainly because the patients with the highest prevalence are seen in non-psychiatric settings3. Patients attending outpatient clinics with health anxiety also have a high prevalence of personality disorder, mainly with anxious, avoidant, obsessional and dependent features4. There is also good evidence that the presence of personality disorder impairs outcome in depression5-6 and, possibly, to a slightly lesser extent in anxiety disorders7. Because of these considerations the assessment of personality status, including dependence, was included in a randomised study of the cost-effectiveness of a modified form of cognitive behaviour therapy for health anxiety (CBT-HA) 8. Two hypotheses related to personality were given in the published protocol. First, that CBT-HA would be less effective in patients who have additional personality disorder and would be associated with increased costs. However, a previous study had shown that those with a lesser degree of dependent disorder, personality difficulty, had a worse outcome in the pilot study that led to the CHAMP trial9 and although this seemed to be counter-intuitive, it was an additional reason for assessing dependent personality in the trial.

**Method**

***Study design***

The assessment of dependent personality was part of the Cognitive behaviour therapy for Health Anxiety in Medical Patients (CHAMP) trial. This is a pragmatic large randomised controlled trial; full details of the trial are given elsewhere8. Patients attending medical out-patient clinics were randomised to either 5-10 sessions of CBT-HA (from initially naïve but subsequently trained therapists) or to standard care in primary and secondary care clinics. Cardiology, endocrine, gastroenterology, neurology and respiratory medicine clinics were included from six hospitals in London, Middlesex and North Nottinghamshire. Patients who were attending these clinics completed the short form of the Health Anxiety Inventory (HAI) 10, a self-rated scale of 14 questions with a score range of 0-42. Patients who scored 20 or more on the scale and who qualified for other inclusion criteria, were invited to take part in the trial and an information sheet about the study was given. In addition, the initial assessment involved asking key questions from the Structured Clinical Interview for DSM-IV11 covering the formal diagnosis of hypochondriasis. The inclusion criteria were patients aged between 16 years and 75 years, a formal diagnosis of hypochondriasis, living in the area covered by the hospital, with sufficient understanding of English to read and complete study questionnaires and interviews, and who had given written consent for interviews, audio-taping of 50% of treatment sessions, and for access to their medical records13. All those eligible were then offered randomisation to the trial, and, if they agreed, full baseline assessments were completed and written informed consent obtained.

The study was approved by the North Nottingham Ethics Committee (08/H0403/56) before the start of data collection.

***Assessments***

The primary outcome measure was the Health Anxiety Inventory (HAI) 10. Other measures included generalised anxiety and depression using the Hospital Anxiety and Depression Scale (HADS-A and HADS-D) 17, health-related quality of life using the short Euroqol measure (EQ-5D) 18, and social function using the Social Functioning Questionnaire (SFQ) 19. All measures were recorded at baseline, 6m, 12m and 24 months (with the exception of the HAI which was also recorded at 3 months). Assessments were made completely independently by research assistants. Service use data for the economic evaluation were collected at baseline, 6 months, 12 months, and 24 month follow-up using the Adult Service Use Schedule (AD-SUS), a self-report instrument assessed in interview and designed on the basis of previous economic evaluations in adult mental health populations20.

[Table 1 near here]

Personality assessment was carried out using the quick version of the Personality Assessment Schedule (PAS-Q) 21, which records both the severity and the type of personality disorder using a four point scale (see Data Supplement). This contains a series of screening questions for each area of personality dysfunction, and those that score positive are asked further questions. The PAS-Q was administered by a trained research assistant, and the assessment forms include both numerical ratings and written comments on each of the sections. During the course of the study the Working Group for the Reclassification of Personality Disorder in ICD-11 completed its initial work on a new system of classification based on severity criteria (April, 2010)22. The ICD-11 classification at that stage is summarised (Table 1). Subsequently, RS, PT, and GL reclassified the personality status of the patients in the study to convert them to ICD-11 severity equivalents by examining the PAS-Q data and written comments23 as well as interviewing assessors if the data were not clear. For 30 of the assessments RS and PT completed independent assessments and achieved a good level of agreement (kappa = 0.84, 95% CI, 0.60-1.0).

***Randomisation and masking***

Randomisation to the two treatment groups was carried out by an independently operated computerised system (Open-CDMS), with a computer-generated random sequence using block randomisation with varying block sizes of four and six. The allocation sequence was not available to any member of the research team until databases had been completed and locked.

***Statistical analysis***

The calculation of the sample size for the main study has been described previously13; it was powered to assess the superiority of CBT-HA over standard care. The current study was a secondary analysis of the outcomes for different levels of severity of personality disturbance and so no formal sample size calculation was performed.

The primary endpoint (HAI) was analysed using a mixed model with time, treatment group, and time x treatment interaction as fixed effects, baseline measurement as covariate, and patient as random effect by personality severity group in order to test for the first hypothesis, that the CBT-HA would be less effective in participants with a personality disorder. The treatment differences between the four ICD-11 personality groups were calculated at each time point (3m (HAI only)), 6m, 1 year and 2 years). Other secondary endpoints were analysed in the same way. All analyses were based on the intention-to-treat principle.

***Economic analysis***

The economic evaluation is described in detail elsewhere13. Total costs were calculated by combining the service use data collected from the AD-SUS together with hospital use from electronic records with nationally applicable unit costs24-26. Costs were calculated and analysed in UK pound sterling for the financial year 2008-09 and were discounted in the second year at a rate of 3.5% as recommended by the National Institute for Health and Clinical Excellence27. Complete case analysis was used for the economic evaluation13. The second hypothesis, that participants with personality disorder would have increased costs was explored through the examination of differences in costs over the 24 month follow-up period between ICD-11 groups. Analysis was performed using ordinary least squares regression as is appropriate for cost data, with the robustness of the tests confirmed using bias-corrected, non-parametric bootstrapping28-29. Differences in all analyses were adjusted for baseline costs and randomised group.

**Results**

[All figures and Tables 2 onwards near here]

445 patients were randomised in the study but one patient was referred and randomised twice – both times to the standard care group – and the first date was taken for inclusion. All 444 patients had their personality status assessed at baseline (Table 1). Nine patients died during the study, 6 in the standard care group, 3 in the CBT-HA group. Of the patients who died 1 had no personality dysfunction, four had personality difficulty, 1 had mild personality disorder, and 3 had moderate personality disorder.

Using the ICD-11 classification only 63 (14.2%) had no personality dysfunction but 197 (44.3%) had personality difficulty (a sub-threshold condition not qualifying for disorder). Only 3 people assessed had severe personality disorder and so they were included with the moderate group. No differences in patient characteristics at baseline were identified and there was an even spread of male/female and a similar age profile between the ICD-11 personality groups (Table 2). However, there were significant differences in symptoms of health anxiety and generalised anxiety, depression and social functioning at baseline; participants with moderate to severe personality disorder had significantly higher scores than those with no personality disturbance (Table 2). There were no differences in total cost at baseline.

The outcome data over follow-up by ICD-11 classification are detailed in table 3 and in Figure 1. Contrary to our hypotheses the results show that those with no personality dysfunction showed no benefit from CBT-HA at any time point in the study; overall standard care was superior (P<0.05). For all other groups the picture was different. For participants with personality difficulty and mild personality disorder, there was evidence of strong gains from CBT-HA at all time-points compared with standard care (P<0.001). For participants with moderate and severe personality disorder the initial benefit was not retained at two years resulting in a less strong relationship over follow-up (P<0.05). Improvement in social function was similar in all groups except in those with no personality dysfunction (P<0.02 in favour of standard care). Clinical symptomatology increased and social dysfunction was greater with each increment of personality pathology and although the results were most marked in those with health anxiety they were also found with generalised anxiety and depressive symptoms (Table 3).

Total costs over 24 months follow-up by randomised group and personality score are detailed in table 4. Costs were broadly similar across groups, though highest in those with personality dysfunction and lowest in those with moderate to severe personality disorder. Regression analysis suggested that the differences in cost between groups fell well short of significance.

**Discussion**

The results of this study illustrate two important principles; the value of recording severity of personality disturbance in general in research studies, and the advantages of  randomised controlled trials in examining specific personality trait outcomes.  criticism has been made of the ICD-11 classification because a simple dimensional classification of severity  does not properly encompass the range ofvpersonality dysfunction, but this study shows that there is no reason why a personality dimension cannot be examined in the context of a severity continuum. In a previous trial a better outcome with CBT-HA was found in patients with dependent personality disorder  compared with personality difficulty. with There is also a great deal of data from categorical studies of personality that appear to be nullified by the replacement with dimensions.

(Friborg get al, 2013 - dependent personality

Bornstein et al 2014 j pers dis interpersonal functioning main pd sympto

Bornstein 2012. Book chapter. From dysfunction to adaptation .. Dependency may be adaptive in certain contexts such as complying with medical and psychological treatment regimes.

Bornstein 2011 single dimension of personality dysfunction best (cf ICD-11)Bornstein 1992 psychol bull dependence desire for 'nurturant supportive relationships'

O'Neill !& Bernstein 2001 more medical consultations in CPD.

The challenging finding of this study was that both the hypotheses concerning personality status were soundly contradicted. These results should be seen in the context of the main primary aim of the trial; in the analysis of outcomes independently of personality status CBT-HA was markedly superior to standard care with respect to clinical symptoms of anxiety (and to some extent depression) but no marked changes were found in social function30. People with no personality dysfunction did not benefit from health anxiety adapted cognitive behaviour therapy (CBT-HA) and as their social functioning deteriorated with CBT this treatment cannot be regarded as effective in this population. By contrast those with any form of personality abnormality (personality difficulty, mild or moderate personality disorder) did benefit from CBT-HA and their improvement was maintained over two years except in those with moderate or severe personality disorder. Such a finding has not been reported before and as it contradicted our main hypothesis (with the possible exception of worse outcome in more severe personality disorder) other explanations need to be considered before it can be accepted as valid. In addition there was no evidence that costs were higher in participants with personality disorder. In the original paper30 the costs were equivalent in both treatment groups and no clear saving was made with CBT-HA. A large part of the costs was taken up with the care of patients with severe medical illness and this may have disguised any savings made by CBT-HA.  Nonetheless, the costs were less, but not significantly so, in all groups receiving CBT-HA compared with standard care, with the exception of those with moderate and severe personality disorder who cost more in the CBT-HA group (mean £1166)(Table 4).  This suggests the possibility that for those who have moderate or severe personality disorder there is a greater cost with CBT-HA, for reasons that are not completely clear but seem to be independent of medical status, and, as suggested in a previous paper31, may be related to poorer social function.

It is worth emphasising that this is the first study to report on the effect of personality status using the new ICD-11 coding and so there are no other studies by which this one can be compared. The small number of patients with no personality dysfunction (n=63) may appear surprising but there are other data suggesting that when personality difficulty is taken into account this sub-syndromal group accounts for a large proportion of the total32-35. Patients with health anxiety commonly have symptoms for many years before they present for treatment35 and people with chronic anxiety conditions have a high prevalence of personality disorder36 and so the overall prevalence of personality disorder of 42% in this sample is in keeping with other figures.

It also could be argued that a proportion of the population may have been misdiagnosed with health anxiety and this could be explained by the cut-off of 20 points on the Health Anxiety Inventory (HAI) as being too low. This score equates to around 62 on the long version of the HAI, and a score of 67 on the long HAI has been found to be a good cut-off point for discriminating between severe and less severe health anxiety37. Thirdly, it could be argued that the patients with no personality dysfunction had appropriate health anxiety because of incipient and concurrent medical illness but this view is not supported by the figures as the costs were lower in those with no personality dysfunction compared to those with personality difficulty and personality disorder, although these differences were not statistically significant.

It is also fair to add that the ICD-11 classification of personality disorder is not yet approved by the World Health Organisation and more is currently being done to confirm the cut-off points for the levels of personality disturbance38. The version of the ICD-11 classification used in the study22 shows some slight differences to the current version, but not to any substantive degree. There are also other suggestions that personality status may improve during the course of psychological treatment for health anxiety, and whilst one needs to be aware of the well-established evidence that standard personality measures tend to improve as mood39 improves there are some reasons to think that the change is more substantial40.

Taken together, but subject to further replication studies, it is reasonable to suggest both that in the absence of personality dysfunction CBT is inappropriate for the treatment of health anxiety, and that an assessment of personality status is necessary in the evaluation of people with suspected pathological health anxiety, as those without any personality disturbance may be much more appropriately treated, as at present, with reassurance and support rather than formal psychological intervention. The findings also give some clinical credence to the notion of a sub-syndromal form of personality dysfunction in the form of personality difficulty.

In contrast with studies in depression and anxiety9, we found no evidence that personality disorder impacted on service use and cost. The results in terms of costs present a mixed picture, one which reflects those of the main study. Clear conclusions regarding differences in cost are difficult to make in this group because, irrespective of health anxiety and personality status, study participants often had substantial physical health problems that result in substantial levels of service use and therefore high costs. The relative influence of personality on service use behaviour may therefore be limited but overall the results are still consistent with previously reported evidence of greater service use at all levels of services in patients with personality disorder32.

**Acknowledgments**

This research was funded by the National Coordinating Centre for Health Technology Assessment (NCCHTA) programme (project number 07/01/26) and the National Institute for Health Research: Imperial Biomedical Research Centre. The views expressed in this publication are those of the authors and do not necessarily reflect those of the HTA programme, NIHR, NHS, or the Department of Health. We particularly thank Simon Dupont, Paul Salkovkis, Steven Reid, David Murphy, Georgina Smith and John Green for facilitating this research, the North London and East Midlands hubs of the Mental Health Research Network, for adopting, promoting, and aiding recruitment in the trial. We thank Aaron T Beck for acting as adviser to the project, and Gene Paykel (chair), Deborah Rutter, Paul Bassett, and John Brazier of the Data Monitoring and Ethical Committee and Richard Mayou (chair), Amrit Sachar,Rosemary Davidson, Devaka Fernando, Roger Mulder of the Trial Steering Committee, Sharandeep Bhogal, Faye Cooper, Rachel Evered, Mary Keeling, Stephanie Kings, Kofi Kramo, Antoinette McNulty, Amy Murphy, Jessica Nagar, Lorraine O’Connell, Richard Seivewright, Carol Sherwood, Julie Sinclair, David Trevor, Gemma Walker, and Charlotte Watson in their roles as research assistants and supervisors in the study, and special thanks to Sandra O’Sullivan for her help in coordinating the local recruitment strategies.

**References:**

1. Sunderland M, Newby JM, Andrews G. Health anxiety in Australia: prevalence, comorbidity, disability and service use. *Br J Psychiatry* 2013; **202:** 56–61.

2 Escobar JI, Gara M, Waitzkin H, Silver RC, Holman A, Compton W. DSM–IV hypochondriasis in primary care. *Gen Hosp Psychiatry* 1998, **20:** 155–59.

3 Tyrer H, Ali L, Cooper F, Seivewright P, Bassett P, Tyrer P. The Schedule for Evaluating Persistent Symptoms (SEPS): a new method of recording medically unexplained symptoms.

*Int J Soc Psychiatr* 2013; **59:** 281–87.

4. Tyrer P, Crawford M, Sanatinia R, Tyrer H, Cooper S, Muller-Pollard C, Christodoulou P, Zauter-Tutt M, Miloseska-Reid K, Loebenberg G, Guo B, Yang M, Wang D, & Weich S. (2014). Preliminary studies of the ICD 11 classification of personality disorder in practice**.** *Personality and Mental Health,* **8,** 254–263.

5. Newton-Howes, G., Tyrer, P. & Johnson, T. (2006). Personality disorder and the outcome of depression: a meta-analysis of published studies. *Br J Psychiatry,* **188**, 13-20.

6. Newton-Howes G, Tyrer P, Johnson T, Mulder R, Kool S, Dekker J, Schoevers R. (2014). Influence of personality on the outcome of treatment in depression: systematic review and meta-analysis. *pJ pers Disord* 2014;;**28::** 577-93.

7. Skodol

8. Tyrer P, Cooper S, Tyrer H, **Salkovskis P, Crawford M, Green J** et al. CHAMP: cognitive behaviour therapy for health anxiety in medical patients: a randomised controlled trial. *BMC Psychiatry* 2011; **11:** 99.

9. Tyrer H, Tyrer P , Barrett B. Influence of dependent personality on the outcome and service costs of health anxiety. *International Journal of Social Psychiatry* 2013*,* **59,** 274-280.

10. Salkovskis PM, Rimes KA, Warwick HMC, Clark DM. The Health Anxiety Inventory: development and validation of scales for the measurement of health anxiety and hypochondriasis. *Psychol Med* 2002, **32:** 843–53.

11. . First MB, Spitzer RL, Gibbon M, Williams JB. *Structured Clinical Interview for the DSM-IV Axis I Disorders.* Washington DC: American Psychiatric Press, 1996

5 Barsky AJ, Orav EJ, Bates DW. Somatization increases medicalTyrer P, Ferguson B, Fowler-Dixon R , Kelemen A. A plea for the diagnosis of hypochondriacal personality disorder. *J Psychosom Res* 1990; **34**: 637-42.

2. Tyrer P, Cooper S, Crawford M, Dupont S, Green J, Murphy D, et al (2011). Prevalence of health anxiety problems in medical clinics. *J Psychosom Res*2011;**71:** 392-4.

3.

5. Tyrer P, Seivewright H, &, Johnson T. The Nottingham Study of Neurotic Disorder: predictors of 12 year outcome of dysthymic, panic and generalised anxiety disorder. *Psychol Med* 2004; **34**: 1385-94.

6. Telch MJ, Kamphuis JH, Schmidt NB. The effects of comorbid personality disorders on cognitive behavioral treatment for panic disorder. *J Psychiatr Res* 2011; **45**: 469-74.

7. van Noorden MS, van Fenema EM, van der Wee NJ, van Rood YR, Carlier IV, Zitman FG, et al. Predicting outcomes of mood, anxiety and somatoform disorders: the Leiden routine outcome monitoring study. *J Affect Disord* 2012; **142**: 122-31.

8. Thiel N, Hertenstein E, Nissen C, Herbst N, Külz AK, Voderholzer U. The effect of personality disorders on treatment outcomes in patients with obsessive-compulsive disorders. *J Pers Disord* 2013; **27**: 697-715.

9. Knerer G, Byford S, Johnson T, Seivewright H, Tyrer P. The Nottingham study of neurotic disorder: predictors of 12 year costs. Acta Psychiatr Scand. 2005 Sep;112(3):224-32.

10.Tyrer P, Seivewright N, Ferguson B, Murphy S, and Johnson AL (1993). The Nottingham study of neurotic disorder: impact of personality status on response to drug treatment, cognitive therapy and self-help over two years. *Br J Psychiatry*, 162, 219-226.

11.Fournier JC, DeRubeis RJ, Shelton RC, Gallop R, Amsterdam JD, Hollon SD. Antidepressant medications v. cognitive therapy in people with depression with or without personality disorder. *Br J Psychiatry* 2008;**192:** 124-9.

12.Tyrer P, Seivewright N & Seivewright H. Long term outcome of hypochondriacal personality disorder. 1999;*J Psychosom Res* 1999; **46:**  177-885.

13.

14. 15. Seivewright H*. Prevalence and treatment of health anxiety in genitourinary medicine.* PhD Thesis; London: Imperial College, 2009.

16.

17. Zigmond AS, Snaith RP. The Hospital Anxiety and Depression Scale. *Acta Psychiatr Scand* 1983, **57:** 361–70.

18. EuroQol Group. EuroQol—a new facility for the measurement of health-related quality of life. *Health Policy* 1990; **16:** 199–208.

19. Tyrer P, Nur U, Crawford M, et al. The Social Functioning Questionnaire: a rapid and robust measure of perceived functioning. *Int J Soc Psychiatr* 2005; **51:** 265–75.

20. Barrett B, Byford S, Crawford M, et al. Cost-effectiveness of referral to an alcohol health worker in patients attending an accident and emergency department: a decision-making approach. *Drug Alcohol Depend* 2006, **81:** 47–54.

21. Tyrer P. Quick Personality Assessment Schedule: PAS-Q. In *Personality Disorders: Diagnosis, Management and Course, 2nd edition*. Edited by: Tyrer P. London: Arnold; 2000:181-90.

22. Tyrer P, Crawford M, Mulder R, Blashfield R, Farnam A, Fossati A, et al. The rationale for the reclassification of personality disorder in the 11th Revision of the International Classification of Diseases. *Personality and Mental Health* 2011;5**:** 246-59.

23. Tyrer P, Coombs N, Ibrahimi F, Mathilakath A, Bajaj P, Ranger M et al. Critical developments in the assessment of personality disorder. *Br J Psychiatry* 2007; **190,suppl 49,** s51-s59

24. Curtis L. *Unit costs of health and social care, 2010*. Canterbury: PSSRU, University of Kent, 2011.

25. British Medical Association & Royal Pharmaceutical Society of Great Britain. *BNF 59.* London: BMJ Books/Pharmaceutical Press, 2010.

26. Department of Health. NHS Reference Costs. London: Department of Health, 2011.

NIH.

27. National Institute for Health and Clinical Excellence 2008. Guide to the methods of technology appraisal, London: NICE, 2008.

28. Barber JA, Thompson SG. Analysis and interpretation of cost data in randomised controlled trials: review of published studies. *BMJ* 1998; **317:** 1195–200.

29. Efron B, Tibshirani R. An introduction to the bootstrap. New York: Chapman and Hall, 1993.

30. Tyrer P, Cooper S, Salkovskis P, Tyrer H, Crawford M, Byford S, et al. Clinical and cost-effectiveness of cognitive behaviour therapy for health anxiety in medical patients: a multicentre randomised controlled trial.. *Lancet* 2014;383: 219-25.

# 31. Barrett B, Tyrer P, Tyrer H, Cooper S, Crawford MJ, Byford S.trtAn examination of the factors that influence costs in medical patients with health anxiety*. J Psychosom Res* 2012 ; 73: 59-62.

32. Yang M, Coid J, Tyrer P (2010). A national survey of personality pathology recorded by severity. *Br J Psychiatry* 2010; **197:** 193-9.

 33. Kim YR, Blashfield R, Tyrer P, Hwang ST, & Lee HS. (2014). Field trial of a putative research algorithm for diagnosing ICD-11 personality disorders in psychiatric patients: 1. Severity of personality disturbance. *Personality and Mental Health*, **8**, 67-78.

34. Tyrer P, Crawford M, Sanatinia R, Tyrer H, Cooper S, Muller-Pollard C, et al (2014). Preliminary studies of the ICD 11 classification of personality disorder in practice**.** *Personality and Mental Health* 2014;**8:** 254–263.

35. Hedman E, Andersson G, Andersson E, Ljótsson B, Rück C, Asmundson GJ, Lindefors N. Internet-based cognitive-behavioural therapy for severe health anxiety: randomised controlled trial. *Br J Psychiatry* 2011 ; **198**: 230-6.

36. Latas M, Milovanovic S. Personality disorders and anxiety disorders: what is the relationship? *Curr Opin Psychiatry* 2014; **27**: 57-61.

37. Hedman E, Lekander M, Ljótsson B, Lindefors N, Rück C, Andersson G et al. Optimal cut-off points on the Health Anxiety Inventory, Illness Attitude Scales and Whiteley index to identify severe health anxiety. *PLoS One* 2015; **10**: e0123412.

38. Tyrer P, Reed GM, Crawford M (2015). Classification, assessment, prevalence, and effect of personality disorder. *Lancet* 2015;**385:** 717-726.

39. Coppen AL, Metcalfe H (1965). The effect of a depressive illness on MMPI scores. *Br J Psychiatry* 1965; **111:** 236-39.

40. Hedman E, Andersson G, Lindefors N, Gustavsson P, Lekander M, Rück C, et al. Personality change following internet-based cognitive behavior therapy for severe health anxiety. *PLoS One* 2014 ; **9**: e113871

41. Tyrer P, Alexander J. Classification of personality disorder. *Br J Psychiatry* 1979; **135**: 163-7.