NCCHTA

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Project title: Cognitive behaviour therapy for Health Anxiety in Medical Patients (CHAMP) 07/01/26

Investigators:

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Planned investigation

Objectives:

1. To determine if health anxiety directed cognitive behaviour therapy is effective in reducing health anxious symptoms and improving the social function and quality of life of those with pathological health anxiety 1 and 2 years after therapy;
2. To determine whether health anxiety directed cognitive therapy is cost-effective; if the costs of the experimental intervention are offset by savings from reduced use of other health services in comparison to the control group (primary outcome) after two years, or, if the additional costs of the intervention can be justified in terms of improvements in outcomes.

Existing research

Health anxiety – and its older synonym, hypochondriasis – is a relatively common

problem in both primary and secondary medical care settings [1-3]. Health anxiety also places a substantial burden on health services[4], this is unsurprising as its central feature is sufficient fear of having a serious disease to lead to medical consultation. In genitourinary clinics we have found previously that nearly one in ten of consecutive attenders had significant health anxiety (using a standard scale, the Health Anxiety Inventory[5]), that these patients were less likely to have a sexually transmitted infection, and their fears tended to persist over time, leading to more medical consultations than those with low health anxiety[6]. Although there has been a tendency to regard health anxiety as difficult to treat there have been significant advances recently that may make the condition amenable to intervention in medical settings. CBT adapted for health anxiety has been found to be effective in patients recruited from primary care[7] and improvement was shown after only a few sessions of treatment, and a subsequent study in the US has confirmed these findings, but this was still only in primary care[8]. No randomized controlled trials had been carried out in the population attending secondary medical clinics where health anxiety is likely to be more common and has a greater impact on services, until we carried out our pilot trial described below.

In our previous work we have identified that in genitourinary medicine clinics that significant health anxiety (recorded using the Health Anxiety Inventory[5]) is present in 8-10% of all attenders[6] and, when severe, tends to persist over a period of 6 months. It was less common in patients with sexually transmitted infections than in those with other disorders. A subsequent pilot randomized controlled trial [9] to test the cost-effectiveness of cognitive behaviour therapy (CBT) focused on health anxiety was carried out in a genitourinary medicine clinic in Kings Mill Hospital, North Nottinghamshire, with the administration of treatment by a staff grade doctor in the clinic. This involved two groups; an active treatment group of up to 7 sessions of CBT and a control group of simple assessment and placement on a waiting list for treatment. The results showed the effectiveness of the treatment after a mean of just over 4 sessions per patient and that there were also cost savings, maximum in the period immediately after treatment had been completed.

Research methods

The study proposed is a randomized controlled trial with two parallel arms and equal randomization of eligible patients to an active treatment group of 5-10 sessions of cognitive behaviour therapy and to a control group. After baseline assessment and allocation, a single explanatory interview will be given to those allocated to the control group that explains the nature of health anxiety. This was found to be of some benefit in earlier pilot studies. Subsequently the control group will only receive whatever care might normally be available in the clinics (which is usually very limited).
Form of randomisation: Block randomisation in blocks of 8 at each centre (with no stratification as it is not known what factors influence successful treatment). Allocation will be from the London School of Hygiene and Tropical Medicine, a location independent of all other centres, by a telephone randomisation system.

Settings: Cardiology, endocrine, gastroenterology and respiratory medicine clinics in general hospitals in North Nottinghamshire, St Mary's and Charing Cross Hospitals, London. The following consultants to date have agreed to refer patients and to be collaborators in the study – Professor Martyn Partridge, Drs Kevin Fox, Susan Connolly, Karim Meeran, and Andrew Thillainayagam (Charing Cross Hospital, London W6), Drs Nick Wight, John Rowley, Devaka Fernando, G Cox, Simon Beshir, Nabeel Ali and Dr Robert Logan (Kings Mill Hospital, Sutton-in-Ashfield), Professor Huw Thomas, Drs Jamil Mayet, Stephen Robinson, Rupert Negus, and Sarah Elkin (St Mary's Hospital, London W2). Several others have indicated interest and meetings have taken place with staff. Most clinics are ready to start recruiting immediately.

Target population and procedure: Patients suspected of having excessive concerns over their health will be identified by the consultants, clinical nurse specialists or the research nurse working at each centre and given the short form of the Health Anxiety Inventory (HAI)[5], a rating scale of 14 questions that takes 5-10 minutes to complete. Those that score at least 20 on the scale will be assessed using the questions for hypochondriasis in the Structured Clinical Interview for DSM-IV diagnosis (SCID-I)[11]. If the requirements for a DSM-IV diagnosis of hypochondriasis are met the patients will be given an information sheet about the study and invited to participate. If they agree, and each patient will be given a week to decide, they will give written consent and be assessed on the measures below at baseline by an independent research assistant. They will also receive a standard explanation of the nature and significance of health anxiety that puts their problem into context. The research assistant will then inform the project manager of the new patient recruited and once all data have been received and checked randomization will be made to either (i) active treatment group - 5-10 60 minute sessions of cognitive behaviour therapy from the research nurse at the clinic backed up by a short take home manual, or (ii) a control group who would not receive specific treatment but will already have received a short summary of the essentials of health anxiety.

Assessments: The following assessments will be carried out at base-line only; quick personality assessment using the quick version of the Personality Assessment Schedule[11] followed by the 5 questions from the hypochondriasis subsection of the full schedule (as this may handicap treatment success)[12] , the Short Obsessional Compulsive disorder Screener (SOCS)[13] (a set of 7 questions that identifies the likely presence of obsessive compulsive disorder, and the Dependent Personality Questionnaire[14] , as both dependence and obsessional symptoms another condition may handicap or complicate treatment). The remaining assessments will be carried out at baseline, 6m, 12m and 24m (or earlier and at intervening periods if drop-out or loss to follow-up likely); (i) the HAI, (ii) the Hospital Anxiety and Depression Scale, a self-rated scale including 7 anxiety questions (HADS-A (anxiety) and 7 depression ones (HADS-D (depression))[15], (iii) quality of life using the EQ-5D[16] , the Social Functioning Questionnaire (SFQ) , an 8 item self-rated scale of perceived functioning[17]and the Adult Service Use Schedule (AD-SUS), designed by one of the applicants and based on previous economic evaluations in adult mental health populations[18,19] The AD-SUS records information on the use of all hospital and community health and social services, as well as information on occupation, income,

productivity losses and accommodation. In addition the SCID-I hypochondriasis questions[10] will be administered again at 24 months to determine if each patient still satisfies the requirements for DSM-IV hypochondriasis. All these instruments are given at face to face interview but also have the advantage that they can be given over the telephone if necessary, and this can be useful in reducing loss to follow up. All assessments will be carried out by independent research assistants who will have no contact with the patient at other times and who will be carefully masked to avoid disclosure of allocation (including assessment at a neutral venue suitable for both groups).

Treatment in the two arms of the trial:

Active group: As the aim is to replicate the conditions of treatment that would be likely to prevail in the future if the trial found benefit from CBT, we want the therapy to be given within or close to the clinic so that it is perceived by patients to be part of the clinic's function combining help for mental and physical instead of being a (stigmatized) external psychiatric service. We therefore intend to recruit a full-time research nurse (G-grade or equivalent) by secondment at each centre and for these to be trained fully before and at the beginning of their treatment of the first patients in the study. For this we plan a fifteen month secondment in which the first three months will involve training and close supervision of initial treatment sessions with somewhat fewer patients than in the later phases of the study. Following this initial period, therapists would have fortnightly supervision until the last patients had been recruited and treated. Four of the applicants (PS, JG, DM and HS) would be involved in this training and also in the ratings of treatment fidelity using double-sided recorders in which one recording could be given to the patient for homework as needed. Fidelity would be tested using the Cognitive Therapy Rating Scale[19] with some additional questions adapted for health anxiety, which also assesses use of the manual. A random sample of tapes would be chosen from those recorded by the research nurses at 1 in 2 of their treatment sessions. This issue is important as better treatment fidelity is associated with greater treatment effects[20-21] It is also worth noting that the staff grade doctor in the pilot study, who started treatment with cognitive behaviour therapy after only three sessions of training, demonstrated a significantly larger active/control difference in health anxiety scores with the second group of patients than in the first, suggesting that more initial training might have improved performance further. As each nurse would be involved in the treatment of about 70 patients over the course of 15 months (which at an average of 7 sessions of treatment could take up to 15 treatment sessions per week in the middle of the year) we would also train additional staff to back up the research nurse at times of extra work.

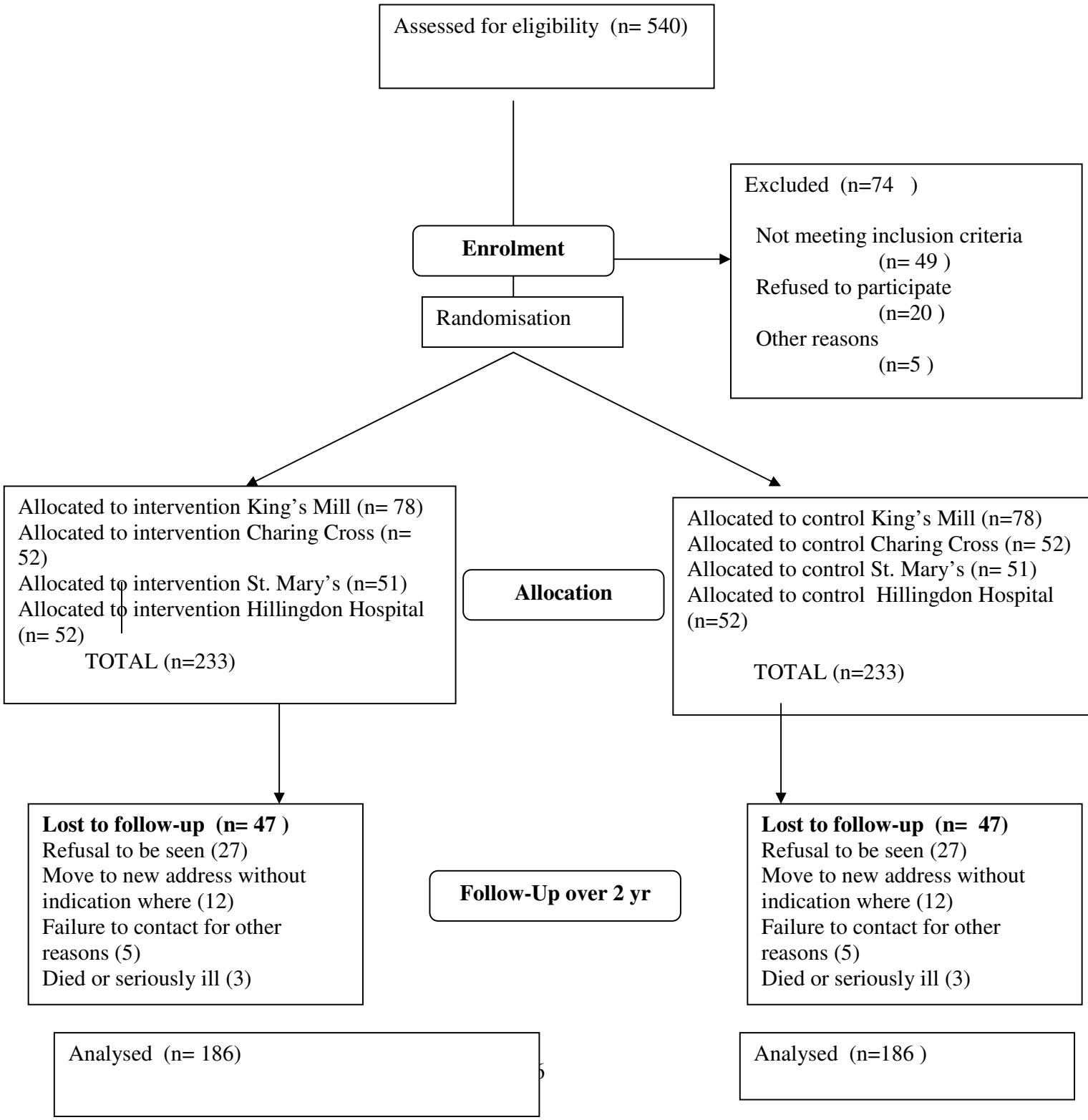
Control group: As the only planned intervention in the control group is a single explanatory interview of the nature of health anxiety it could be argued that not enough input is being given to this group. However, the interview that made all subjects aware of health anxiety in the pilot trial was very similar to the planned intervention here and was recognized as valuable by many participants. We therefore judge that this form of intervention is appropriate.

Inclusion criteria: Patients who satisfy the criteria for excessive health anxiety above and are (i) aged between 16 and 70 (ii) permanent resident in the area, (iii) have sufficient understanding of English to read and complete the questionnaires, (iv) give written consent for the interviews, audio-taping of 50% of treatment sessions, and for access to their medical records .
Exclusion criteria: Patients who are (i) felt by their consultants to be too ill in medical terms to be considered for the study, or (ii) in the process of being investigated for significant pathology and for whom cognitive behaviour therapy might confuse or cause distress.

Numbers of patients: 465 patients need to be recruited at the foru centres. Because the Kings Mill centre in North Nottinghamshire has the most experience of treating this group of patients a larger proportion of patients is planned to be recruited as it is expected that in the first phase of recruitment they will able to recruit at full capacity. The planned numbers are 156 (Kings Mill), Charing Cross (104), Hillingdon Hospital (104), St Mary's Hospital (102), which anticipates a 20% drop-out by 2 years to a total of 372 completed. These are to be distributed in the proportion; 27% for each of the cardiology, respiratory medicine and gastroenterology clinics and 19% for the endocrinology (as the latter in our prevalence study revealed fewer patients attending even though they had high health anxiety levels. Although a drop-out rate of only 12% was noted in our pilot study[9] it is considered more realistic to set this at 20%

Rate of recruitment: All patients will be recruited over a 15 month period beginning on 1st October 2008. In the first three months the research nurses are being trained and will take on fewer patients for treatment (approximately 8 per month from each centre), whereas over the next year 11 patients per month will be recruited from each centre. Recruitment will end on December 31st 2009. The proposed CONSORT diagram is attached.

The Consort E-Flowchart for CHAMP



Action to be taken if recruitment falls short of target: It is important to anticipate recruitment shortfall. We have three strategies; (i) varying the proportion of patients by clinic type. Although it is of some interest what differences in health anxiety are found between clinics the exact numbers given above do not need to be adhered to, and so if one discipline has many more eligible patients than another we are likely to take more from that clinic and less from others, (ii) increasing the level of distribution of HAI forms to attendees at the clinic, as many of those with high health anxiety are not suspected of having the condition, (iii) using the Clinical Studies Officers (CSO's) of the East Midland and North London Hubs of the Mental Health Research Network (UK) to help in recruitment by increasing their visits to the poorly recruiting clinics, backing up the research nurses in their work and generally facilitating the staff at the clinics in their work. Full approval for this support has been given by the relevant Hubs and two CSO's have been trained at each centre to take part. In addition members of the service users support group CHASSIS, are also very willing to visit the clinics and talk to staff, including consultants, about their experiences and to aid in the recruitment of prospective patients.

Ethical aspects

Risks and anticipated benefits: We do not think there are any major risks for patients in the trial. Both active and control groups will receive an initial explanation of health anxiety and its significance and this is more than most patients receive at present. A very small proportion , around one in 30 of those with health anxiety, would be referred to a psychologist in the current NHS services, and as these would not be referred because of the trial there is a small cost-offset to be gained. Under these circumstances, and the evidence from our pilot study that simple explanation has some benefit, justifies the control group on ethical grounds. The risks of cognitive behaviour therapy in health anxiety are low and no problems or difficulties were encountered in our pilot study. There is a theoretical risk that a patient could misinterpret a symptom indicating serious pathology as a health anxious one but we have not encountered this in our work. The potential of confusion arising in those being investigated for serious pathology and simultaneously being treated with cognitive behaviour therapy will be avoided by not including these patients in the study.

Data will be retained for 15 years after completion of the study at Imperial College in a secure setting. We agree with the principles of data sharing and would be willing to collaborate with any initiatives that the HTA introduce in this growing area. The sponsor of the study is Imperial College.

Measurement of costs, justification of sample size and selection of primary and secondary outcomes:

The perspective of the economic evaluation will be societal including (i) the costs of clinic attendance including the CBT intervention (ii) other health care costs and (iii) other community health and social services, including social, private and voluntary sectors, and (iv) productivity losses. As the likely success of extending the technology of CBT for

health anxiety in these clinics is more likely to depend on cost savings in the clinic than on clinical relief of symptoms (even though on straight clinical ground the latter is more important) we have decided to choose total costs at the 2 year end-point as our primary outcome. Our pilot study demonstrated reductions in service use over follow-up, however over 1 year this was not sufficient to off-set the cost of the CBT intervention. We hypothesise that it is likely that over a 2 year follow-up, including medical specialties where the cost of investigations are higher than in genito-urinary medicine, the cost of the CBT will be off-set, i.e. we will see cost-equivalence at follow-up. For example, in a gastroenterology clinic, it will only be necessary to prevent the patient from having an endoscopy to save the cost of the CBT intervention.

With a sample size of 186 per group, a one-sided t-test will have 80% power to reject the null hypothesis that the cost of the CBT and control are not equivalent (where the difference in mean costs is +/- £150) in favour of the alternative hypothesis that the means of the two groups are equivalent, assuming the expected difference in means is 0 and the common standard deviation is 580 (from pilot data). Assuming a 20% drop-out we will need to recruit a total sample of 466, split between the three sites, see CONSORT diagram.

All the clinical outcomes, (i) health anxiety (using the HAI), (ii) quality of life using the EQ-5D, anxiety and depression scores (measured using the Hospital Anxiety and Depression Scales (HADS)), and social function (measured by the Social Functioning Questionnaire (SFQ), will be secondary outcomes.

Statistical analysis

Statistical analysis will be carried out primarily by analysis of variance at each time point, with adjustment for baseline differences for each variable, with further regression analysis for longitudinal data using random effects models. These models produce a matrix-weighted average of the between subjects and within subjects results.

Differences in total costs will be explored between the two groups using the student t-test. Although costs are often found to be skewed, the use of parametric tests enables inferences to be made about the arithmetic mean[22]. The validity of the parametric results will be confirmed using bootstrapping[23]. Cost-effectiveness analysis will explore the difference in costs between the two groups compared to differences in two outcomes: HAI score and quality adjusted life years calculated using the EQ-5D. Relative cost-effectiveness will be explored through the calculation of incremental cost-effectiveness ratios and cost-effectiveness acceptability curves[24-25]. Throughout all aspects of the analysis greater weight will be given to the differences between baseline and assessment at 2 years, as the maintenance of improvement over the longer time period is crucial in determining the longer term cost-effectiveness of the intervention. Previous studies, including a recent HTA study[26-27] , have suggested that the effects of cognitive behaviour therapy are often attenuated after treatment but in our pilot study[9] and the recent American trial in primary care[8] the gains were still maintained at one year.

Trial support groups

A group, called the Confederation of Health Anxiety Sufferers Supporting Increased Services (CHASSIS), has been established by successfully treated patients in our services. Its aim is to promote the development of treatments for health anxiety, and it is keen to support the trial and advise us on how to promote recruitment and retain patients in care. This will be affiliated with a proposed Trial Steering Committee and a Trial Steering Group, each of which will meet before the first patients are recruited and subsequently at agreed intervals (likely to be every 3 months in the first year and 6-12 monthly afterwards). Professor Roger Mulder, of the Department of Psychological Medicine in Christchuch, University of Otago, New Zealand, has agreed to be an external member of the Trial Steering Committee.

Role of investigators in study

Professor Peter Tyrer will act as the overall coordinator of the project, and specific coordinator at the Charing Cross site. He has been involved extensively in the organization of randomized controlled trials for many years and also organized the pilot study leading to this application. Professor Paul Salkovskis is a national trainer for cognitive behaviour therapy and one of the originators of the treatment adapted for health anxiety; he will play a key role in training therapists. Dr Helen Seivewright was the key person involved in the pilot trial and will train and supervise staff at Kings Mill Hospital as well as coordinating the recruitment at the Kings Mill site and providing additional assistance at the London sites as required. Drs John Green and David Murphy are senior clinical psychologists who will train therapists at St Mary's and Charing Cross Hospitals. Dr Mike Crawford is experienced in the organisation of trials of complex psychological interventions in mental health and will help both in the execution of the trial and in solving problems. Dr Steven Reid is a liaison psychiatrist who has carried out research into medically unexplained symptoms, including health anxiety; he will coordinate recruitment at St Mary's Hospital. Drs Tony Johnson and Ula Nur have special expertise in the analysis and design of randomized controlled trials and will carry out the statistical analysis. Sarah Byford and Barbara Barrett are leading authorities in the economic evaluation of mental health interventions and will carry out the economic component of the study in conjunction with the cost researcher, and Dr AT Beck, the originator of cognitive behaviour therapy, will advise on fidelity and the training of nurses in the practice of this treatment.

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