Home-based Reach-to-Grasp training for people after stroke is feasible: a pilot randomised controlled trial

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Running title – Pilot trial of Reach-to-Grasp training after stroke'

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Abstract

Objective: To determine feasibility of a randomised controlled trial (RCT) of home-based Reach-to-Grasp training after stroke.

Design: single-blind parallel group RCT.

Participants: Residual arm deficit less than 12 months post-stroke.

Interventions: Reach-to-Grasp training in 14 one-hour therapist's visits over 6 weeks, plus one hour self-practice per day (total 56 hours). Control: Usual care.

Main Measures: Action Research Arm Test (ARAT), Wolf Motor Function Test (WMFT), pre-randomisation, 7, 12, 24 weeks post-randomisation.

Results: 47 participants (Reach-to-Grasp=24, usual care=23) were randomised over 17 months. Reach-to-Grasp participants received a median (IQR) 14 (13,14) visits, and performed 157 (96,211) repetitions per visit; plus 30 minutes (22,45) self-practice per day. Usual care participants received 10.5 (5,14) therapist visits, comprising 38.6 (30,45) minutes of arm therapy with 16 (6,24) repetitions of functional tasks per visit. Median ARAT scores in the reach-to-grasp group were 8.5 (3.0,24.0) at baseline and 14.5 (3.5,26.0) at 24 weeks compared to median of 4 at both time points (IQR: baseline (3.0,14.0), 24 weeks (3.0,30.0)) in the usual-care group. Median WMFT tasks completed at baseline and 24 weeks were 6 (3.0,11.5) and 8.5 (4.5,13.5) respectively in the reach-to-grasp group and 4 (3.0,10.0), 6 (3.0,14.0) in the usual care group. Incidence of arm pain was similar between groups. The study was stopped before 11 patients reached the 24 weeks assessment.

Conclusions: An RCT of home-based Reach-to-Grasp training after stroke is feasible and safe. With ARAT being our preferred measure it is estimated that 240 participants will be needed for a future two armed trial.

Introduction

Each year 15 million people world-wide have a stroke,[1] and three quarters of them experience upper limb weakness, making everyday tasks like using a knife and fork or doing up buttons difficult or impossible. [2] Current therapeutic practices leave the majority of patients with limited capacity to use their affected arm even by six months after stroke. [3]

A Cochrane overview of systematic reviews concluded that, no high quality GRADE evidence exists for any routine clinical interventions to improve arm function after stroke, but that intensive repetitive task practice with a dose of 20 extra hours or more is emerging as a promising contender. [4] National stroke guidelines advocate that stroke survivors should practise upper limb activities, [5,6,7] yet adoption into practice is constrained by limited, ambiguous evidence. [4] Sufficiently powered, high-quality RCTs are required to strengthen the evidence and provide leverage for implementation into clinical practice. [4]

Home based task-specific upper limb training specifically focusing on Reach-to-Grasp movements is particularly relevant, as reaching and grasping are essential for everyday functions. [8] To address the gap in clinical practice and research, a home based task-specific Reach-to-Grasp training intervention for people with stroke has been developed that is acceptable to participants. [9] This study was designed to establish the feasibility and safety of a future definitive RCT of home-based Reach-to-Grasp training after stroke and to provide pilot outcome data.

Objectives were to:

1. Estimate recruitment rates and retention of participants.

2. Measure outcomes for both groups to obtain information to determine the sample size for a definitive trial and to estimate the completeness of outcome data.
3. Determine the dose and content of upper limb treatment delivered to both intervention (Reach-to-Grasp) and control (usual care) groups.
4. Decide on the most appropriate primary outcome measure, the Action Research Arm Test (ARAT) or the Wolf Motor Function Test (WMFT), for use in a definitive trial.
5. Capture adverse events in both groups
6. Collect data on health and social care resource use to inform data-collection methods for an economic evaluation in the subsequent definitive trial of clinical and cost effectiveness.

Methods

The study was an assessor blinded, multicentre parallel group, individually randomised feasibility RCT comparing home based Reach-to-Grasp training with usual care upper limb therapy. Ethical approval was obtained from a South West Research Ethics Committee (REC) (ref number: 10/H0102/83). The trial was registered [ISRCTN56716589] and the trial protocol has been published. [10]

Participant selection and recruitment

Inclusion criteria were: diagnosis of stroke less than 12 months prior to joining the study; discharged home (which could be a care home); informed consent; and having a residual deficit in upper limb movement due to stroke. Residual arm deficit was defined as being unable to pick up a 6mm ball bearing from the table top,

between index finger and thumb, and place it on a shelf 370 mm above the table which is a 'pinch' task from the ARAT. [11] Patients were excluded if they: had pre-stroke pathology preventing reach and grasp actions, could not lift their hand off their lap (a gross motor task from the ARAT), had severe fixed contractures of elbow or wrist (i.e. grade 4 on the Modified Ashworth Scale). [12]

The target sample size was 60 participants recruited over 12 months from an area served by two large teaching hospitals and a smaller general hospital in the South West of England. Patients were identified and given an information sheet by therapists and research nurses in the three stroke services, and asked if they could be contacted after discharge from hospital. Referrals were also sought from community rehabilitation services in the locality. Caregivers indicated willingness to be contacted by the research team by returning a tear-off slip in a stamped addressed envelope. They were asked to provide written informed consent.

Randomisation and allocation concealment

After completion of the baseline assessment, participants were randomly allocated in a one to one ratio to the Reach-to-Grasp or to the usual care group. Randomisation used minimisation to balance time since stroke, severity of upper limb impairment; and distribution of group numbers within our small trial. Time since stroke was categorised as less than or equal to three calendar months post stroke, or more than three months post stroke. This three month cut off was chosen to balance participants between groups who might be recovering at a faster rate. Baseline severity of upper limb impairment was categorised using ARAT scores as defined in a previous trial. [13] Group 1: score 0-3; Group 2 score 4-28; Group 3 score 29-56. The research physiotherapist providing Reach-to-Grasp treatment accessed

the allocation by logging into a secure computer server. He informed participants of their group allocation and intervention commenced within a week of randomisation to group.

Data collection, assessor blinding and outcome measures

Demographic and stroke details were collected at baseline only. All other measures were assessed at baseline (i.e. before randomisation), at seven weeks post-randomisation (i.e. immediately following the six week intervention period) and at 12 and 24 weeks after randomisation.

The assessments were performed in the participant's home by a researcher who was trained in the assessment procedures and blinded to group allocation. The research therapist made the appointments for the assessment by telephone, and reminded participants not reveal details of any treatment they had received to the assessor. The assessors were asked to fill in a questionnaire at the end of their involvement in the study to identify whether they knew or had guessed each participant's group. These data were compared with the actual group allocation to determine the success of the blinding. [14]

Arm function was assessed using the ARAT, [11; 15,16] and the WMFT. [17,18] The ARAT consists of 19 items which are divided into four domains (grasp, grip, pinch and gross movement). The maximum score for the whole assessment is 57. Each domain is Guttman scaled so that it is not necessary for patients to attempt every test item. [15] The WMFT measures time to complete each of 15 tasks, eight of which require hand function. A maximum of 120 seconds is allowed for each task and quality of movement for each task is rated by the assessor on a 6-point ordinal scale (0-5). [17] Other outcomes measured were: the Motor Activity Log, a patient reported

rating of quality of movement and amount of use, [19] and the Stroke Impact Scale, version 3.0. [20]

Caregiver interviews comprised assessing carer burden using the Carer Strain Index. [21] Data on use of health and social care resources were collected by means of a bespoke questionnaire administered by telephone at 12 and 24 weeks post randomisation.

To help inform the choice of primary outcome measure for a future trial, participants were asked at their final assessment whether they preferred the ARAT or WMFT.

Interventions

The Reach-to-Grasp intervention has been described in detail elsewhere, [9] using the Template for Intervention Description and Replication. [22] Table 1 (online) provides a summary of the intervention content which enables even those with no active hand function to undertake goal-orientated activities with their affected arm. The therapist kept a log of activities performed and the number of repetitions of actions completed at each visit. Participants were asked to log the time spent and number of repetitions achieved in their independent practice. The Reach-to-Grasp training replaced any usual care provided for improving arm function. All other usual care therapy services available to them, e.g. to improve balance, mobility, speech and language, cognition and activities of daily living, were continued.

The control group received a package of usual care, delivered by National Health Service (NHS) occupational therapists and physiotherapists. The NHS therapists recorded the time spent on the arm and the content of therapy sessions. They also recorded the number of repetitions for each functional arm movement

practised. The log sheets were adapted from a checklist of physiotherapy treatments developed by Donaldson et al. [23]

Participants of both groups were provided with a booklet about recovery after stroke. The Reach-to-Grasp group additionally received information about the Reach-to-Grasp training.

Adverse event data collection

At each assessment visit participants reported any pain experienced in the shoulder, upper arm or hand, oedema in the hand, falls, or potential study-related adverse events. Incidents caused by equipment taken into the home for outcome assessment were monitored at each visit. NHS therapists, research therapists and assessors were asked to report any serious adverse events to the trial manager as soon as they were made aware of them.

Analysis

This pilot trial was not powered to detect a clinically important difference between the groups; therefore, no formal statistical comparisons were made. [24] Continuous measures were summarised using mean and standard deviation or median and interquartile range if the distribution was skewed. Category measures were summarised as number and percentage. Unit costs were applied to resource required for trial treatment and resource use.

Results

Results are presented in an order that responds to the list of the study objectives.

Recruitment and retention of participants

Recruitment of 48 participants took place from December 2011 to April 2013 (average rate 2.8/month). There were 2156 stroke admissions during this period, 102 (4.7%) of whom were identified as potential study participants. Of these 102 potential participants, 60 were provided with information about the study (2.8% of admissions) and 52 assented to referral to the research team. The main reasons for not providing study information were physical ability/disability (33/42) or because the patient was not discharged home (9/42) (see Figure 1 for full details).

[Figure 1 near here]

One participant withdrew before randomisation, 24 were allocated to the Reach-to-Grasp intervention group and 23 to the usual care group. The duration of funding for the project allowed us to follow-up all participants to 12 weeks post randomisation, but only 32/47 (68%), to 24 weeks (see Figure 1).

Participant characteristics

[Table 2 Participant characteristics near here]

Table 2 shows participants' characteristics. The sample had predominantly severe or moderately impaired arm function; 85% scoring less than 29/57 on the ARAT; 38% had no active hand function (scoring 3 or less on ARAT). Median time post-stroke on entry to the study was 124 days (approximately four months) (IQR: 88, 227 days). With flexibility to join the study at any time up to 12 months post stroke, most participants opted to take part once any involvement with Early Supported Discharge teams or early support from other rehabilitation services had finished; 73% of participants entered the trial when they were over three months post-stroke, i.e. after the period of most rapid recovery.

As anticipated with the randomisation by minimisation process similar numbers were allocated to each group, and the time post-stroke (≤3months versus >3months) and arm function severity (ARAT strata) were balanced across the groups (see Table 2). However, the median ARAT score at baseline was higher in the Reach-to-Grasp group (8.5 versus 4, Table 4) and median time post-stroke was shorter (111.5 days in the Reach-to-Grasp group versus 135 days in the usual care group, Table 2). Other baseline characteristics were similar.

Completeness of data collection

At assessment visits the ARAT was completed for all available participants at each time point. A breakdown of data missing from outcome measures is given in Figure 1 (and table 3 online). Adverse events information was collected at 130/162 (80%) visits. The health and social care use questionnaire, completed predominantly by telephone, had a high response rate of 92% (43/47) at 12 weeks. The 32 participants assessed at 24 weeks all completed the questionnaire at the final follow up phone call. Data collection from caregivers was sparse. Overall, 37/47 (79%) participants lived with others and yet only 26 (55%) participants gave consent for their family member to be approached, and only 12 carers consented to participate. Nine carers completed the Carer Strain Index at 12 weeks and six at 24 weeks.

Dose and content of upper limb treatment delivered to Reach-to-Grasp and usual care groups

Twenty-three of the 24 participants allocated to the Reach-to-Grasp group completed the intervention, with 94% of the intended treatment visits completed (median 13.5/14 visits). Visits lasted a median 60.7 minutes (IQR: 59.8, 62.1), of

which, 38.5 minutes (median; IQR: 35.4, 48.8) were engaged in active Reach-to-Grasp training. The median total number of repetitions per therapist-delivered session was 157 (IQR: 96, 211). The amount of self-practice outside of the therapist's visits was poorly documented with no records available for three participants and only partial records for the remaining 21; (i.e. logs not completed on all 42 days). Median amount of practice recorded was 30 minutes (IQR: 22, 45) per day (see supplementary file Table i. for more details).

NHS therapists' records showed that 18 of the 23 participants in the usual care group (78%) received visits and upper limb treatment over the course of the six week intervention period. Those visited received a median 10.5 (IQR: 6.0, 17.0) visits, with upper limb treatment lasting median 38.6 minutes (IQR: 15.5, 44.2) per visit. Predominant aims of treatment (top 5 of 12 aims) for the upper limb in usual care were to improve: i) muscle activity in the paretic upper limb (21.0%); ii) range of motion (16.6%); iii) manipulative ability (10.7%); iv) alignment (10.1%); and v) incorporation of arm into balance and mobility activity (9.3%). A wide variety of treatment methods were recorded with passive, active assisted and active movements being most frequently used. Functional task practice was reported on 110 occasions. However the number of repetitions of functional tasks recorded per session was low: median 16.3 repetitions (IQR: 6.3, 24.3).

Upper limb performance outcomes between groups

[Tables 4 ARAT & Table 5 WMFT near here]

Any interpretation of outcome results must be treated with caution since the groups were small and this feasibility study was not powered to test the efficacy of the intervention.

The median ARAT scores post-intervention were unchanged in the usual care group, i.e. at 24 weeks the median scores were 4, (n=16 at 24 weeks). The median scores in the Reach-to-Grasp group increased from a median of 8.5 at baseline to 14.5 at 24 weeks, (n=16 at 24 weeks) (see Table 4 and Figure 2A online); a difference of 6 points from baseline.

At baseline, 20 participants in the Reach-to-Grasp group and 19 in usual care group were unable to do the eight tasks requiring hand function in the WMFT. Given the large proportion of tasks truncated at 120 seconds, (see supplementary file, results Table ii), we also summarised the number of tasks completed within 120 seconds. This method for representing performance has been used previously. [25] Though this metric departs from the conventional scoring methods, which have been tested for validity and reliability, normative data collected has demonstrated that healthy subjects can achieve all the tasks well within the 120 second cut off and so it provided a reasonable means for summarising the data in our sample. [26] The number of tasks completed within 120 seconds increased in the Reach-to-Grasp group from median (IQR) 6 (3.0, 11.5) at baseline to 8.5 (4.5, 13.5) at 24 weeks (n=16 at 24 weeks) and in the usual care group median (IQR) from 4 (3.0, 10.0) at baseline to 6 (3.0, 14.0) at 24 weeks, (n=16 at 24 weeks) (see Table 5 and Figure 2B online).

The sensitivity to change in participants with differing severity of upper limb impairment is pertinent to the selection of primary outcome measure. Figures 3A and 3B (online) show changes over time in subgroups of participants based on their ARAT score at baseline: Subgroup 1: score 0-3; subgroup 2 score 4-28; subgroup 3 score 29-56. The figures illustrate how the WMFT task completions were better for

measuring change in the most severely impaired subgroup; while the ARAT was better for measuring change in those in the higher scoring subgroup at baseline.

Participants completing the 24 week assessment were consulted about their preference for the primary outcome (i.e. ARAT vs WMFT). 23/32 (72%) gave a preference. Of these, the 18 participants with some active hand function (scoring > 3 on ARAT) were evenly split with nine preferring ARAT and nine preferring WMFT. The remaining five participants who scored 3 on ARAT preferred the WMFT, because they could do more of the test items on the WMFT.

Secondary outcomes

Motor Activity Log: A rating of 3 or more is needed to report that the affected limb is effective for completing the task. [27] The number of scores ≥3 increased marginally for both groups over the assessment times (see Table 6).

[Table 6 MAL near here]

Stroke Impact Scale: Scores generally increased over time in all eight domains in both groups (see supplementary file results table iii). The median perceived amount of overall recovery on the visual analogue scale was 50% in the usual care group at all the measurement time points, whereas the in the Reach-to-Grasp group the median increased from 40% at baseline to 55% at 24 weeks.

Blinding of assessor

Assessor blinding was maintained in 33/45 (73%) of assessments at 7 weeks; 35/44 (79.5%) at 12 weeks and 21/32 (65%) at 24 weeks. The increase in blinding success between weeks 7 and 12 may be explained by a change in personnel. Thirty nine instances of unblinding were described in the case report forms, resulting from

participants' conversations with the outcome assessor or viewing evidence of the Reach-to-Grasp intervention in the home. However in 20% of events the assessor drew the wrong conclusion regarding group allocation.

Frequency of adverse events

Total incidence of upper limb adverse events (i.e. all instances of shoulder pain, hand pain or hand oedema) was similar between groups (baseline assessment: Reach-to-Grasp 22; usual care 19; all post intervention assessments Reach-to-Grasp 27; usual care 25). These results include repeat reports from the same 18 (38%) participants. Nine falls were reported at post intervention assessments (Reach-to-Grasp 3; usual care 6). There were no injuries caused by equipment brought into the home for the study. A total of 12 serious adverse events (death, hospitalisation) were reported, six in the Reach-to-Grasp group and six in the usual care group; all deemed 'unlikely to be' or 'not related' to the intervention.

Health and Social Care resource use

There was a high completion rate for the questionnaire at 12 and 24 weeks respectively (43/44; 32/32), suggesting its content and format were appropriate for this study population. However, some amendments will be made for a future RCT, such as increasing the number of resource use items listed to reflect a more diverse range of rehabilitation services that were used by participants. Mean cost of the Reach-to-Grasp intervention was calculated to be £677 per participant.

Discussion

This feasibility study has provided realistic estimates of recruitment, retention and data completeness. It has established the characteristics of the participants recruited to the study, the dose and content of usual care upper limb therapy and Reach-to-Grasp training received, and the safety of the intervention. The study has also provided data to inform the primary outcome measure and sample size for the future RCT. It adds to the findings of our previous publication, which described the intervention and indicated that participants found the intervention acceptable, sufficiently challenging and enabled them to achieve activities that were meaningful to them. [9]

The size of the population from which the sample is recruited in stroke rehabilitation trials is rarely reported therefore gauging the success of recruitment is difficult. Recruitment as a percentage of stroke population, at 2.8% is very low. The reasons why patients admitted were not considered as potential participants by staff identifying patients was not recorded. These would include deaths, people missed from the screening procedures, not fitting eligibility criteria and people who may not have been discharged in time to participate in the study. However it is also likely that therapists may have chosen not to approach some patients for other reasons that have been reported for another UK stroke rehabilitation trial. [28] Our average recruitment rate of 2.8 participants per month, although less than our target, is comparable to the best recruitment rate (2.5 per month) seen in a previous hospital-based stroke rehabilitation trial recruiting from inpatient stroke rehabilitation services in 12 hospitals in the UK. [29]

Recruitment of caregivers was low, partly because only about two thirds of participants living with family gave permission for their relative to be approached. With caregivers not always being present in the home when the researcher visited

the participant, recruitment was often reliant on caregivers expressing willingness to be recruited by post. Effective strategies to boost engagement of family members will be needed if caregiver burden is to be measured in future trials. These strategies could include having clearer explanation about expectations of caregivers.

There was low attrition (7%) up to 12 weeks post-randomisation and although we were unable to fully determine retention at 24 weeks, 89% of those who reached 24 weeks before the end of the study were assessed. This fact suggests that attrition is unlikely to be a serious problem to the successful completion of a future large trial. Other stroke rehabilitation trials have reported retention of 80% at 6 months, [30] and 69% at 9 months. [31]

Completion of outcome measures was high at each time point, but there were notably more missing data within the WMFT and the Motor Activity Log, suggesting that these were less easy to complete. Carrying out both ARAT and WMFT along with the secondary measures was a lengthy process; taking up to two hours. Rigour in recording adverse events, at 80%, was lower than for completion of the outcome measures and complicated by repeat reporting of pain from the same individuals. An efficient method identifying repeat events will be needed for future studies.

Blinding is an acknowledged problem in rehabilitation trials. [14] The use of performance rated outcome measures necessitates face to face contact of the assessor and participants and it seems that, despite reminders not to reveal details of any treatment, participants sometimes revealed their group allocation. This is a potential source of bias and reminders could be strengthened in future studies.

The high number of repetitions achieved in Reach-to-Grasp training within the therapist's visits demonstrates that intensive practice is achievable with moderate to severely impaired stroke patients in a domiciliary setting; without additional upper

limb pain, oedema or falls. A larger trial in the UK will require that NHS therapists deliver the interventions. The trial will need to determine whether service therapists trained in the intervention can achieve such high repetition rates as in this feasibility study.

The difficulty in obtaining data from participants about their Reach-to-Grasp practice between therapist's visits reinforces the need for better methods for recording self-practice. [32] Providing tally counters to participants or more automated methods may improve reporting, but this requires further study. [33]

The usual care therapy data collected from community rehabilitation services indicated that 80% of participants were still seeing a community therapist, but that their intervention was less frequent than the Reach-to-Grasp training. Although more variable, on average, the usual care therapy sessions were of similar duration to the training time in the Reach-to-Grasp therapy visits. However the content was different; with more impairment oriented treatment and less intensity of task practice. Repetitions of functional tasks carried out in usual care therapy amounted to around 10% of that achieved in the Reach-to-Grasp group, which is probably insufficient to enable the neuroplastic changes necessary for motor learning to occur in the neural networks that mediate task specific motor functions [34-36].

Most participants in this study preferred the WMFT, notably those with the most severe upper limb impairment, because they could complete more items. However there are other factors that are important in choosing the primary outcome for a large trial. Both observer-rated assessments of upper limb performance (ARAT and WMFT) have strengths and limitations. They can be lengthy to complete and require cumbersome kits to be taken into the home; both factors being greater for WMFT than ARAT. Our results indicated differing suitability for measuring change

according to severity of upper limb impairment. The ease of test administration and scoring, facilitated by the Guttman scaling, favoured the ARAT over WMFT, resulting in a smaller number of missing data in the ARAT compared to the WMFT; an important consideration for a definitive RCT. Given these pragmatic reasons we have decided the ARAT will be our preferred primary outcome measure for the RCT. With a minimally clinical important difference of 5.7, [37] and based on the data from this feasibility trial (with a pooled standard deviation for the ARAT scores of 18, and with a correlation between baseline and follow-up scores of 0.72), 240 participants (120 per group) should provide the study with 90% power at the 5% significance level and allowing for attrition of 15% in a larger multicentre trial.

In our earlier article on this intervention, we reported that 85% of Reach-to-Grasp participants felt their arm had improved in activity domains including meal preparation and self-care, a considerable proportion of which requires bimanual coordination. [9] The ARAT, however, does not comprise any bimanual tasks. Patient reported outcomes should therefore be included in future trials to ensure that changes in bimanual activities are adequately captured.

A definitive RCT should contain a full economic evaluation to estimate the cost-effectiveness of the intervention versus usual care. Telephone administration of the Health and Social Care resource use questionnaire is suggested as the completion rate was very good. A health-related quality of life measure such as the EQ-5D or the SF-6D should be used in a full trial in order to estimate quality-adjusted life years.

In conclusion, the findings from this feasibility study indicate that a home-based, intensive task-specific upper limb rehabilitation programme to improve reach to grasp function after stroke is safe and a larger trial is feasible.

Clinical Messages

- Undertaking a relatively high number of repetitions; 10 times as many as in usual care, without additional adverse effects is feasible.
- Conducting a randomised controlled trial to compare home-based task-specific Reach-to-Grasp training with usual care practice after stroke is feasible and safe.

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Figure Legends

Figure 1. Flow of participants

Notes:

[1] Some patients may be ineligible for more than one reason
[2] due to recent bereavement and discharge to nursing home
[3] Number of patients with <u>any</u> outcome data available
[4] study was stopped before 11 patients reached 6 month follow-up

Figure 2. ARAT and WMFT scores over time points

Figure 3. ARAT and WMFT scores at each time point by ARAT baseline score

ARAT score at baseline: Subgroup 1: score 0-3; subgroup 2 score 4-28; subgroup 3 score 29-56

The marked reduction in median score at 6 months in subgroup 3 is explained by an individual who developed severe shoulder pain.

Supplementary results tables i-iii are accessible from the University of the West of England's research repository https://eprints.uwe.ac.uk/

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