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The Impact of a Functional Circuit Training Program in People with Chronic Stroke: A Non-Randomized Feasibility Study

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Abstract

Individuals with chronic stroke may experience a sedentary lifestyle that puts them at risk for continued health concerns and lack of participation in community activities. This feasibility study was implemented to determine if a novel training program performed at moderate intensity would result in improvements across multiple domains of the International Classification of Functioning, Disability and Health (ICF). This novel program included cardiorespiratory conditioning, balance retraining, upper extremity and lower extremity strengthening with cognitive retraining (motor/motor and motor/cognitive). Additionally, this study was implemented to determine the feasibility of performing a battery of outcome measures to address deficits in multiple domains of the ICF. Thirty-six subjects expressed interest in beginning the program, with 6 subjects completing the twelve-week intervention. This study resulted in many individual changes on the domains of the ICF, but no one subject made improvements in all 3 areas. Of concern was the lack of tolerance by the individuals with stroke to perform the intervention three days a week (four subjects completed 24 sessions in 12 weeks). Multiple reasons were given for difficulty adhering to the three day per week program including fatigue, transportation issues, and weather. The lack of subject fitness resulted in mixed results and will be addressed in the full study. It was determined that it was feasible to implement this functional circuit training program with cognitive retraining and capture the changes using multiple outcome measures that spanned the domains of the ICF. The impact on people with stroke realized by completing this study is varied with some individuals experiencing minimal change and others experiencing changes in multiple domains. The impact to clinicians and researchers is an improved understanding of the difficulties of higher intensity and increased frequency of treatment in people with chronic stroke.

Keywords: Stroke, moderate intensity continuous exercise, circuit training, cognitive retraining

Introduction

Approximately 795,000 Americans experience a new or recurrent stroke each year [1]. Individuals can experience cognitive impairment, depression, strength, and balance deficits which can impact their functional mobility and ability to perform self-care activities [2]. One of the most devastating results is the lack of participation in household and community activities. These issues contribute to a sedentary lifestyle upon discharge from rehabilitation services which creates an increased risk of health concerns [3,4], increased risk of mortality [5], and a cycle of functional decline and continued inactivity.

Current rehabilitation interventions aim to maximize functional independence and allow people to lead an active lifestyle upon discharge. Cardiorespiratory and resistance training at appropriate intensity can result in positive functional outcomes [6,7]. However, determining the optimal exercise program to efficiently and effectively address deficits in the domains of the ICF in people with stroke has been challenging. Additionally, the impact of exercise on cognitive function is unclear and is poorly addressed in rehabilitation, although motor performance and executive functioning are closely linked [8,9]. After synthesizing information from the literature regarding best practice in stroke rehabilitation, a functional circuit training program (FCTP) was created using equipment typically found in rehabilitation centers. The training program included moderate intensity aerobic conditioning, resistance exercises for the upper and lower extremities, and balance retraining. The program also attempted to address cognitive deficits using dual task training in the form of motor-cognition or motor-motor tasks throughout each circuit.

The purposes of this pilot study were to: 1) determine the feasibility of individuals with stroke completing the evaluations and FCTP intervention; and 2) determine the feasibility of completing a battery of outcome measures to capture change in various domains of the International Classification of Functioning, Disability and Health (ICF) to guide future research.

Feasibility studies in physical activity research can be used to determine the number of participants needed for a larger study, optimum inclusion and exclusion criteria, assessment of intervention adherence and appropriate length of the study [8]. Evidence has shown that many exercise programs have failed to show benefits to this patient population which may, in part, be attributed to choosing outcome measures that failed to capture change [7,9]. To address this, our battery of outcome measures were selected to be those most likely to change as a result of our intervention.

Background for Methodology

BDNF is a neurotrophin that crosses the blood-brain barrier and is involved with neuroprotection, neurogenesis, and neuroplasticity. BDNF has been noted to be a key mediator of motor learning and recovery [10] and is especially important in individuals post stroke. BDNF levels are increased with participation in aerobic exercise of moderate intensity [10] and with resistance training in young adults [11,12] and individuals with stroke [13]. Lower levels of BDNF have been found in people with depression indicating a relationship between them [14]. Moreover, other authors have found an inverse relationship between depression and cognition in older adults [15] and individuals with stroke [16]. Because there is a paucity of research linking these four constructs: BDNF, cognition, and depression, and exercise, BDNF levels were examined.

As noted, two primary concerns following stroke, include cognitive impairment and depression, both of which can persist even as people recover functionally [17,18]. Up to half of the individuals with stroke will experience cognitive impairment [19,20]. The specific difficulties seen following stroke will depend on the areas of the brain that have been damaged and the vascular damage that has occurred. Cognitive impairment following stroke can lead to a diagnosis of vascular cognitive impairment (VCI). Reduced processing speed and executive dysfunction are common impairments with VCI [21,22]. Executive dysfunction can more specifically be described as reduced initiative, difficulty in multi-tasking, difficulty in planning, sequencing and finalizing actions. Some behavioral changes can also result, including loss of interest in usual activities, irritability or distractibility [23]. Addressing executive function deficits through rehabilitation is important as they are associated with poor motor recovery and difficulty learning complex movement patterns that may be necessary for optimal functional mobility [23,24]. Additionally, motor performance and executive functions are closely linked so investigating the changes in movement and executive function through participating in an exercise program would be worthwhile.

Along with the changes with executive functions and functional mobility, this study will investigate depression in people with stroke. This is important as between 30% and 50% of people post stroke experience depression [16,25,26], and individuals with stroke with cognitive deficits and depression may have more limited social interactions as well as decreased life satisfaction [17].

Methods

Subjects

Subjects who were 18 years of age or older and who sustained one or more strokes at least 6 months previously were recruited to participate in this non-randomized pilot study. Other inclusion criteria included a signed medical clearance, ambulatory without physical assistance of another person (orthotic devices, canes or walkers allowed), ability to follow instructions, and communicate with the investigators as assessed by specific NIH Stroke Scale Questions 1b and 1c. Exclusion criteria included the presence of bone or joint problems that limited the ability to walk, resting heart rate outside of the range of 40-100 beats per minute, resting blood pressure outside of the range of 90/60 to 170/90 mmHg, chest pain, or shortness of breath without exertion. Subjects were recruited from local physical therapy clinics and stroke support groups.

The study was approved by the University of the Sciences Institution Review Board and all subjects provided written informed consent.

Testing

At the initial assessment, gait speed via six meter walk test was calculated to classify individuals into household, limited community, and unlimited community ambulators [27]. A battery of testing was completed that addressed different domains of the ICF. For the domain of Body Functions and Structures, subjects completed the Fugl-Meyer Motor Assessment of Recovery after Stroke for both the upper and lower extremities, provided blood samples to measure brain derived neurotrophic factor (BDNF) levels, and completed depression and cognitive testing.

For the assessment of BDNF, a 10ml of blood sample was

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collected by trained phlebotomist from each patient and immediately processed. Genomic DNA was extracted from total blood using Qiagen Blood & Tissue Kit (Qiagen, Redwood City, CA) following manufacturers protocol and underwent genotyping of BDNF v66m SNP by differential PCR as described by Sheikh and colleagues [28]. Serum sample was collected by centrifugation at 1500 rpm for 10 min, aliquoted and stored in -20C. Serum sample was collected by centrifugation at 1500 rpm for 10 min, aliquoted and stored in -20C. BDNF protein concentration in plasma was measured by ELISA using the BDNF Emax ImmunoAssay System (Promega, Madison WI, USA). Additionally, BDNF gene expression was measured using RT-qPCR. RNA sample was prepared from total blood sample using RNEasy kit (Qiagen, Redwood City, CA). 1 microgram of total RNA was then reverse transcribed using a poly dT primer. Resulting cDNA was diluted 1:100 and used for quantitative PCR using SYBR green (Bio-Rad, Hercules, CA) for the detection of BDNF. BDNF gene expression results were normalized to glyceraldehyde-3-phosphate dehydrogenase (GAPDH).

Targeted assessment of executive functions included tests of problem solving (Stockings of Cambridge), inhibition and cognitive flexibility (Attention Switching), and sustained attention (Rapid Visual Information Processing) using the Cambridge Neuropsychological Automated Test Battery ((CANTAB), Cambridge, UK) which contains well documented measures of executive function. The Verbal Fluency Test (VFT) and the Cognitive Assessment scale for Stroke Patients (CASP) were also completed. Each subject completed Becks Depression Inventory II (BDI®-***II***) to document his/her level of depression.

In the domain of activity, outcome measures provided objective information on quality of life, balance confidence, upper extremity function, walking ability, walking endurance, and dynamic balance. Subjects completed the Stroke Specific Quality of Life Scale (SS-QOL), Activities Specific Balance Confidence Scale (ABC), Wolf Motor Function Test, Walk-12, Timed Up and Go (TUG), $TUG_{cognitive}$, TUG_{manual}, Functional Gait Assessment, Six Minute Walk Test, and Four Square and Modified Four Square Step Test, respectively.

Walking activity at home and in the community was monitored using the StepWatch Activity monitor (SAM; Modus Health, LLC, Washington, DC). The output was analyzed using a Matlab program (Mathworks, Natick, MA) to provide information on steps taken daily, the length of the walking bouts and the total time individuals spend walking. Subjects were asked to wear the monitor during waking hours for 1 week. The objective information provided by the pedometers will be the sole measure in the Participation domain, although inferences can be made from other outcome measures used in the Activity domain including ABC and SS-QOL.

At the conclusion of 12 weeks, all subjects who completed at least 2 sessions/week or 24 sessions underwent post-testing. Outcome measures were completed again three months after termination of the training sessions. In that 3-month period of time, subjects were instructed to perform their regular exercise activities, but not attend formalized physical or occupational therapy. Feasibility studies are not powered to detect significant changes in outcome measures. Therefore, change scores are presented for each of the categories of the ICF to allow for interpretation (See **Appendix 1-4**).

Intervention

Following baseline testing, subjects were assigned to a team consisting of a physical therapist and two physical therapy students who monitored the time each subject spent in moderate intensity throughout each session. Each subject's target heartrate range was calculated using Karvonen's Formula:

Target Heart Rate (THR) = ((maximum HR – resting HR) × %Intensity) + resting HR

Subjects strived to maintain moderate intensity exercise (50-70%) throughout each session of the FCTP. Subjects were encouraged to complete the circuit training intervention for 3 sessions per week for 12 weeks.

Each circuit training session began with 15 minutes of treadmill walking (TM), but individuals who had difficulty walking on the intervention day were able to perform the recumbent stepper (RS) (NuStep LLC, Ann Arbor, MI). For cardiorespiratory conditioning, subjects completed a 2 minute to warm-up at comfortable TM speed and then walked at an intensity and incline that elevated heart rate into their individually prescribed moderate intensity level. All subjects used the handrail during TM walking although encouraged to walk without it whenever possible. Subjects who used RS had resistance level and steps per minute increased until heart rate was in the moderate intensity range.

The remaining activities in the circuit included 3 stations each of standing exercises to strength the upper extremities (UE), lower extremities (LE) and dynamic balance. Throughout each station (TM, UE, LE, Balance), individuals underwent cognitive retraining. Each physical and cognitive task was chosen by the physical therapist to meet the individual's need and to maintain a moderate intensity of exercise. If the subject stopped performing the physical task to successfully complete the cognitive task, then the cognitive challenge was decreased to maximize physical performance. Conversely, if subjects were exercising at their maximal effort, but heart rate and/or Rate of Perceived Exertion was below their prescribed moderate intensity range, the exercise was advanced in difficulty and more difficult cognitive tasks were given. See **Table 1** for listing of the typical tasks performed during the training intervention.

Results

Subjects were enrolled in this study during a 2-year period. Thirty-six subjects expressed interest in the study however only 13 completed baseline testing (36%; See **Figure 1**). Of those thirteen, six completed the outcome measures post-training

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Table 1. Examples of Activities Included in the Functional Circuit Training Program (FCTP).

With activities:
1. Subjects were asked to perform slowly and then quickly. For some exercises, subjects were asked to hold the position
2. Subjects were given cognitive challenges that allowed movements to continue
3. Performed in standing position with no additional weight (some exceptions made for upper extremity movements, depending on participant ability)

Lower Extremity	**Upper Extremity**
Forward & sideways step-ups	Bottle, cup, mug (various weights) lifts to platforms
Forward & sideways step up & overs	Horizontal pulleys
Forward & sideways lunges	Reaching to cabinets
Squats	Block lifting
30 second Sit to Stand	Card matching
Hamstring curls	Zippering, buttoning, key turning activities
Heel raises	Figure tracing with laser light
Recumbent trainer	
Balance	**Cognitive**
Standing on trampoline/foam pad with & without upper extremity activity (ball/bean bag toss)	Counting
Backward walking	Subtraction
Forward & Backward Figure 8 walking	Verbal Fluency tests
Forward & Backward tandem walking	Naming words starting with letters of the alphabet
Four Square Step Test/modified FSST	Naming (based on individual interests)
Obstacle Course	Dual Task (motor/motor; motor/cognitive)
	Distinguishing objects of different colors (in areas of many objects)
	Memory games

and at the three-month follow-up (See **Table 2** Subject Demographics). Completion rate was 6/13 or 46.2%. One subject had an adverse event, sustaining an ankle sprain, however resumed training after resting for one week.

Subjects remained in the study if they were able to complete 24 sessions as compared to the thirty-six sessions planned. See **Table 3** for the time each subject was able to complete the sixty minute FCTP while maintaining moderate intensity.

Body Function and Structure

Significant changes were evident for 4 of the 6 subjects (CT1, CT4, CT28 and CT31) post training, with subjects CT1, CT4 and CT28 either maintaining or continuing to improve at follow up. Of note, five of six subjects improved over the minimal detectable change (MDC) in upper extremity function while none of the subjects increased over minimally clinically important difference for the lower extremity as measured by the Fugl-Myer Motor Assessment [29]. None of the six subjects had the allele for polymorphism that is associated with reduced capacity for neuroplasticity and motor recovery. There was a varied response to cognitive tests and measures with subjects showing improvements in some outcome measures while no improvements were seen in others (See **Appendix 1**).

Activity

Positive changes in activity outcome measures were found for

Table 2. Subject Demographics.

SUBJECT #	SUBJECT AGE (years)	TIME POST STROKE (years)	Side of Hemiparesis	Hand Dominance Involved	Use of Orthotic/Assistive Device	Initial Gait Speed (m/s)
1	50, female	5.3	Left	No	SPC	0.55
4	28, male	5.6	Left	No	Non-articulating AFO	1.5
10	63, male	5.3	Left	No	Articulating AFO	0.72
28	67, male	5.6	Right	Yes	NBQC	0.19
31	78, female	8.6	Left	No	NBQC	0.08
32	63, female	3.4	Left	Yes		0.99

Key:
m/s: Meters per second
NBQC: Narrow based quad cane
SPC: Single point cane
AFO: Ankle foot orthosis

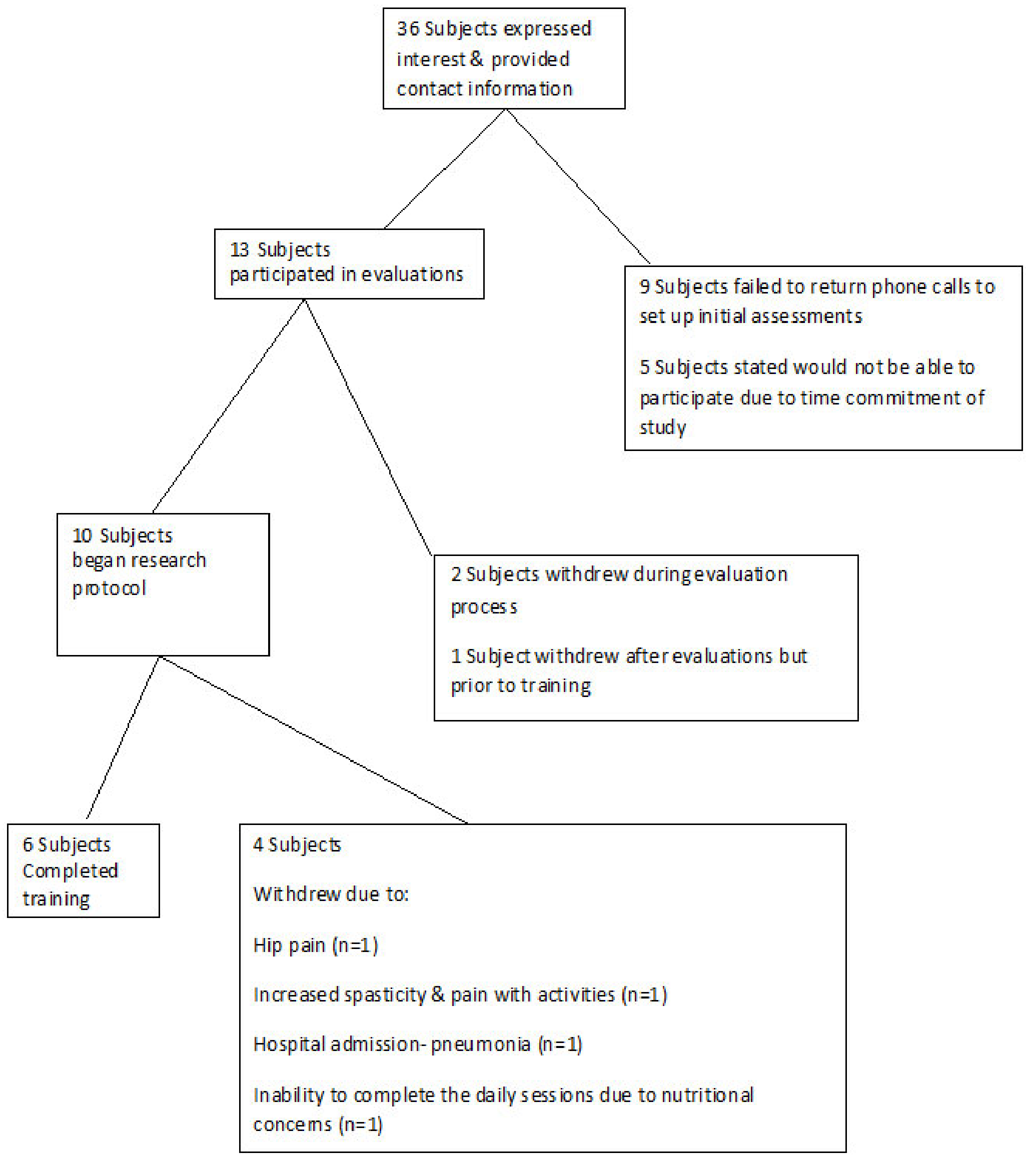

Figure 1. Subject Recruitment and Participation.

Table 3. Average Minutes in Moderate Intensity.

SUBJECT #	# of Sessions Attended	Sessions 1-11	Sessions 12-24	Sessions >25
		HR	HR	HR
1	24	39:49	44:17	--
4	24	16:54	31:31	--
10	24	1:06	0:10	--
28	30	39:41	41:15	42:37
31	24	30.56	32.43	--
32	26	48:37	48:14	54:38

Each session of the Functional Circuit Training Program was 60 minutes in length. Moderate intensity target heart rate was 50-70% using Karvonen Formula.

four of the six subjects, with two of the subjects maintaining those gains at follow up (CT1, CT4) and one subject continuing to make activity gains at follow up (CT28). One subject that demonstrated activity gains at the conclusion of training returned to pre-training baseline levels at follow up (CT10). Two of the six subjects exceeded MDC for walking endurance as measured by 6MWT [30]. Five of six subjects were a fall risk at study initiation and remained so at the conclusion of the intervention as measured by the FSST [31]. One subject was able to exceed the MDC for Functional Gait Assessment, but the remaining subjects did not show improvement either at post-training or follow-up in this outcome measure.

Participation and Patient Reported Outcomes

No changes were found for measures of participation or patient reported outcomes. At follow up, subject CT32 made a significant improvement on the SSQOL. All subjects walked considerably less at baseline than recommended by the Centers for Disease Control and Prevention as noted by the steps per day and the total time walking. This did not change at post-training or follow-up. Five of the subjects did not make any considerable change to their steps per day at post-training and follow-up. However, at follow-up, 2 of the subjectswith recorded data (CT1, CT28), took fewer number of walking-bouts indicating that they were taking more steps per bout.

Discussion

One of the purposes of this study was to determine the feasibility of individuals with stroke to complete the three evaluations and the novel functional circuit program to enhance various domains of the ICF. Subjects were able to complete the outcome testing inclusive of blood draws without difficulty. The training program included evidenced based interventions aimed to address a myriad of issues often under addressed in rehabilitation such as cognition, depression, and participation. Moreover, the training program was designed to be pragmatically implemented using equipment and space commonly found in rehabilitation settings to enhance potential uptake in stroke rehabilitation settings. The study was designed to determine feasibility and was not powered for significance testing in the outcome measures. The feasibility of performing this novel circuit training program of balance retraining, upper and lower extremity strengthening with cognitive retraining at moderate intensity was confirmed. We determined that it is feasible to add dual tasks (motor/cognitive and motor/motor) to rehabilitation programs.

The second aim was to determine the feasibility of completing a battery of outcome measures to capture change in various domains of the ICF to guide future research. This aim was also met. While time consuming, the provision of the outcome testing by the researchers was felt to be valuable, as the large battery of tests enabled detection of changes across the domains of the ICF.

There were aspects of the study that may need to be amended such as the frequency of circuit training. Subjects had difficulty adhering to the exercise regimen of 3 times per week which is recommended for optimal neuroplasticity and motor learning [10,32]. Some subjects commented on the intensity of the dose of exercise (frequency and duration of sessions).This was not surprising as Ploughman and Kelly note that the cardiorespiratory fitness of individuals with stroke is below what is required for daily activities [33]. Other issues contributed to difficulty attending 3 sessions including transportation problems, weather concerns, and fatigue. Decreasing the frequency to 2 days per week allowed subjects to complete the research but may have contributed to a lack of notable change in many of the outcome measures. Recruitment may also need to be amended, as some subjects initially expressed interest in participating in the study but did not attempt evaluations stating they were unable to meet the time commitment. Again, decreasing the frequency to two days per week may enhance recruitment in a larger study.

Despite not being powered to detect significant changes, each subject demonstrated improvement in at least one domain of the ICF. None of the subjects improved in all areas: Body Functions and Structures, Activity or Participation. This result may be due to the person being at maximum capability at baseline. Particularly surprising is the lack of improvement in BDNF levels, cognitive status, level of depression, and walking activity at home and in the community. As cognitive function has a relationship with depression, it is imperative that we have outcome measures that can assess the change in subjects as well as interventions that can target these key deficits. With focused investigation, future research may determine key attributes of responders which will allow for efficiency with evaluations and treatments. In this patient population, future research needs to identify optimal time periods to collect BDNF levels, determine cognitive reserve of subjects prior to study participation, document depression that does not rely on patient report, and investigate methods that lead to carryover of clinical improvements to real-world walking activity.

Future research plans with individuals with chronic stroke will also include similarities to this research. Namely investigating changes across domains of the ICF by using a battery of outcome measures. The research intervention will change to a conditioning program for 4 weeks followed by the functional circuit training program being performed at high intensity for brief periods followed by low intensity activity for a recovery period. We anticipate that this regimen will result in better tolerance by individuals with stroke and more changes over baseline.

Limitations

Low sample size due to subject drop-out is the main limiting factor. Additionally, people included in the study had their stroke at least 3 years prior to beginning the study. Individuals with chronic stroke with less time since stroke may show the greatest gains across all domains of the ICF.

Conclusions

Having individuals with stroke participate in a functional circuit training program that includes cardiorespiratory fitness, balance retraining, upper extremity and lower extremity strengthening with cognitive retraining is feasible. Capturing change in all domains of the ICF by using a battery of outcome measures is also feasible in this patient group. Of concern is the decrease tolerance of individuals with stroke to easily perform the FCTP three times per week to potentially experience the most functional gains.

Data Availability

The baseline, post-testing and follow-up data used to support the findings of this study are included within the supplementary information files: **Appendix 1** through 4.

Additional files

Appendix 1
Appendix 2
Appendix 3
Appendix 4

Competing interests

The authors declare that they have no competing interests.

Authors' contributions

Authors' contributions	MAR	GTT	LP	STM	SK	ZAK
Research concept and design	√	√	--	--	--	--
Collection and/or assembly of data	√	√	√	√	√	√
Data analysis and interpretation	√	√	--	√	√	√
Writing the article	√	√	√	√	√	√
Critical revision of the article	√	√	--	--	--	--
Final approval of article	√	√	√	√	√	√
Statistical analysis	√	√	--	--	--	--

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