Health Technology Assessment 2005; Vol. 9: No. 39

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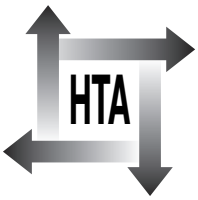
October 2005

Health Technology Assessment
NHS R&D HTA Programme



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Is hydrotherapy cost-effective? A randomised controlled trial of combined hydrotherapy programmes compared with physiotherapy land techniques in children with juvenile idiopathic arthritis

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Declared competing interests of authors: none

Published October 2005

This report should be referenced as follows:

Epps H, Ginnelly L, Utley M, Southwood T, Gallivan S, Sculpher M, *et al*. Is hydrotherapy cost-effective? A randomised controlled trial of combined hydrotherapy programmes compared with physiotherapy land techniques in children with juvenile idiopathic arthritis. *Health Technol Assess* 2005;**9**(39).

Health Technology Assessment is indexed and abstracted in *Index Medicus*/MEDLINE, *Excerpta Medica*/EMBASE and *Science Citation Index Expanded (SciSearch®)* and *Current Contents®*/Clinical Medicine.

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ISSN 1366-5278

Published by Gray Publishing, Tunbridge Wells, Kent, on behalf of NCCHTA.
Printed on acid-free paper in the UK by St Edmundsbury Press Ltd, Bury St Edmunds, Suffolk.

Abstract

Is hydrotherapy cost-effective? A randomised controlled trial of combined hydrotherapy programmes compared with physiotherapy land techniques in children with juvenile idiopathic arthritis

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Objectives: To compare the effects of combined hydrotherapy and land-based physiotherapy (combined) with land-based physiotherapy only (land) on cost, health-related quality of life (HRQoL) and outcome of disease in children with juvenile idiopathic arthritis (JIA). Also to determine the cost-effectiveness of combined hydrotherapy and land-based physiotherapy in JIA.
Design: A multicentre randomised controlled, partially blinded trial was designed with 100 patients in a control arm receiving land-based physiotherapy only (land group) and 100 patients in an intervention arm receiving a combination of hydrotherapy and land-based physiotherapy (combined group).
Setting: Three tertiary centres in the UK.
Participants: Patients aged 4–19 years diagnosed more than 3 months with idiopathic arthritides, onset before their 16th birthday, stable on medication with at least one active joint.
Interventions: Patients in the combined and land groups received 16 1-hour treatment sessions over 2 weeks followed by local physiotherapy attendances for 2 months.
Main outcome measures: Disease improvement defined as a decrease of ≥ 30% in any three of six core set variables without there being a 30% increase in more than one of the remaining three variables was used as the primary outcome measure and assessed at 2 months following completion of intervention. Health services resource use (in- and outpatient care, GP visits, drugs, interventions, and investigations) and productivity costs (parents' time away from paid work) were collected at 6 months follow-up. HRQoL was measured at baseline and 2 and 6 months following intervention using the EQ-5D, and quality-adjusted life-years (QALYs) were calculated. Secondary outcome measures at 2 and 6 months included cardiovascular fitness, pain, isometric muscle strength and patient satisfaction.
Results: Seventy-eight patients were recruited into the trial and received treatment. Two months after intervention 47% patients in the combined group and 61% patients in the land group had improved disease with 11 and 5% with worsened disease, respectively. The analysis showed no significant differences in mean costs and QALYs between the two groups. The combined group had slightly lower mean costs (–£6.91) and lower mean QALYs (–0.0478, 95% confidence interval –0.11294 to 0.0163 based on 1000 bootstrap replications). All secondary measures demonstrated a mean improvement in both groups, with the combined group showing greater improvements in physical aspects of HRQoL and cardiovascular fitness.
Conclusions: JIA is a disease in which a cure is not available. This research demonstrates a beneficial effect from both combined hydrotherapy and land-based physiotherapy treatment and land-based physiotherapy treatment alone in JIA without any exacerbation of disease, indicating that treatments are safe. The caveat to the results of the cost-effectiveness and clinical efficacy analysis is that the restricted sample size could have prevented a true difference being detected

between the groups. Nevertheless, there appears to be no evidence to justify the costs of building pools or initiating new services specifically for use in this disease. However, this conclusion may not apply to patients with unremitting active disease who could not be entered into the trial because of specified exclusion criteria. For this group, hydrotherapy or combined treatment may still be the only physiotherapy option. Further research is suggested into: the investigation and development of appropriate and sensitive outcome measures for use in future hydrotherapy and physiotherapy trials of JIA; preliminary studies of methodologies in complex interventions such as physiotherapy and hydrotherapy to improve recruitment and ensure protocol is acceptable to patients and carers; hydrotherapy in the most common paediatric user group, children with neurological dysfunction, ensuring appropriate outcome measures are available and methodologies previously tried; patient satisfaction and compliance in land-based physiotherapy and hydrotherapy and European studies of hydrotherapy in rare disorders such as JIA.

Contents

List of abbreviations

BCH	Birmingham Children's Hospitals
BNF	British National Formulary
BSA	body surface area
CHAQ	Childhood Health Assessment Questionnaire
CHQ	Child Health Questionnaire
CI	confidence interval
DMARD	disease-modifying antirheumatic drug
DMEC	Data Monitoring and Ethics Committee
ESR	erythrocyte sedimentation rate
GOSH	Great Ormond Street Children's Hospital
HRQoL	health-related quality of life
JIA	juvenile idiopathic arthritis
MAU	Middlesex Adolescent Unit
NSAID	non-steroidal anti-inflammatory drug
PSSRU	Personal Social Services Research Unit
QALY	quality-adjusted life-year
QoL	quality of life
RCT	randomised controlled trial
ROM	range of motion
SD	standardised difference
SE	standard error
SIG	special interest group
TNF	tumour necrosis factor
TMC	Trial Management Committee
TSC	Trial Steering Committee
UCL	University College London
UCLH	University College London Hospital
VAS	visual analogue scale

All abbreviations that have been used in this report are listed here unless the abbreviation is well known (e.g. NHS), or it has been used only once, or it is a non-standard abbreviation used only in figures/tables/appendices in which case the abbreviation is defined in the figure legend or at the end of the table.

Executive summary

Objectives

The objectives of this study were to compare the effects of combined hydrotherapy and land-based physiotherapy (**combined**) with land-based physiotherapy only (**land**) on cost, health-related quality of life (HRQoL) and outcome of disease in children with juvenile idiopathic arthritis (JIA). Also to determine the cost-effectiveness of combined hydrotherapy and **land**-based physiotherapy in JIA.

Design

A multicentre randomised controlled, partially blinded trial was designed with 100 patients in a control arm receiving land-based physiotherapy only (**land** group) and 100 patients in an intervention arm receiving a combination of hydrotherapy and land-based physiotherapy (**combined** group).

Participants

Patients aged 4–19 years diagnosed more than 3 months with idiopathic arthritides, onset before their 16th birthday, stable on medication with at least one active joint were recruited from three tertiary centres in the UK.

Intervention

Patients in the **combined** and **land** groups received 16 1-hour sessions of treatment at one of the three centres over 2 weeks followed by local physiotherapy attendances for 2 months.

Main outcome measures

Disease improvement defined as a decrease of ≥ 30% in any three of six core set variables without there being a 30% increase in more than one of the remaining three variables was used as the primary outcome measure and assessed at 2 months following completion of intervention. Health services resource use (in- and outpatient care, GP visits, drugs, interventions, and investigations) and productivity costs (parents' time away from paid work) were collected at 6 months follow-up. HRQoL was measured at baseline and 2 and 6 months following intervention using the EQ-5D, and quality-adjusted life-years (QALYS) were calculated. Secondary outcome measures at 2 and 6 months included cardiovascular fitness, pain, isometric muscle strength and patient satisfaction.

Results

Seventy-eight patients were recruited into the trial and received treatment. Two months after intervention 47% patients in the **combined** group and 61% patients in the **land** group had improved disease with 11 and 5% with worsened disease, respectively. The analysis showed no significant differences in mean costs and QALYs between the two groups. The **combined** group had slightly lower mean costs (–£6.91) and lower mean QALYs (–0.0478, 95% confidence interval –0.11294 to 0.0163 based on 1000 bootstrap replications). All secondary measures demonstrated a mean improvement in both groups, with the **combined** group showing greater improvements in physical aspects of HRQoL and cardiovascular fitness.

Conclusions

Implications for healthcare

JIA is a disease in which a cure is not available. This research demonstrates a beneficial effect from both **combined** hydrotherapy and land-based physiotherapy treatment and land-based physiotherapy treatment alone in JIA without any exacerbation of disease, indicating that treatments are safe.

The caveat to the results of the cost-effectiveness and clinical efficacy analysis is that the restricted sample size could have prevented a true difference being detected between the groups. Nevertheless, there appears to be no evidence to justify the costs of building pools or initiating new services specifically for use in this disease. However, this conclusion may not apply to patients with

unremitting active disease who could not be entered into the trial because of specified exclusion criteria. For this group, hydrotherapy or **combined** treatment may still be the only physiotherapy option.

Recommendations for research

- The following areas are suggested for further research: investigation and development of appropriate and sensitive outcome measures for use in future hydrotherapy and physiotherapy trials of JIA.
- Preliminary studies of methodologies in complex interventions such as physiotherapy and hydrotherapy to improve recruitment and ensure protocol is acceptable to patients and carers.
- Investigation of hydrotherapy in the most common paediatric user group, children with neurological dysfunction, ensuring appropriate outcome measures are available and methodologies previously tried.
- Comparison of patient satisfaction and compliance between land-based physiotherapy and hydrotherapy.
- European studies of hydrotherapy in rare disorders such as JIA.

Chapter 1
Background

Juvenile idiopathic arthritis (JIA) is defined as a disease of childhood onset characterised primarily by arthritis persisting for at least 6 weeks, and currently having no known cause. Approximately one in every 1000 children and adolescents in the UK suffer from JIA,[1] around 30% of patients have active disease after 10 years and many have disability continuing into adulthood.[2–6] No curative treatment is available, but the anatomical, physiological and emotional abnormalities that occur as a direct result of disease[7] can be reduced or prevented in many cases. One treatment which may reduce the pathophysiological consequences of JIA is hydrotherapy. The term hydrotherapy is derived from the Greek words 'hydro' meaning water and 'therapeia' meaning healing. Hydrotherapy is a form of exercising in warm water for therapeutic purposes and has been used since the Roman era for the treatment of patients.[8]

Consequences of pathophysiology of JIA

Anatomical, biomechanical and physiological changes can occur as a direct result of increases in intra-articular pressure and subsequent neural responses during the inflammatory stages of JIA. Intra-articular pressure is highest when joints are fully extended.[9] Therefore, children with active JIA tend to adopt flexed postures, which can lead to contractures and soft tissue shortening. In addition, pain from increased intra-articular pressure can cause muscle inhibition and weakness.[10,11] Once joint inflammation subsides, the main limitation to repair of synovial tissue is the early establishment of fibrous adhesions with resultant connective tissue shortening and soft tissue contractures, which further accentuate pain and muscle inhibition reducing joint mobility.[12–14]

These pathophysiological changes often lead to poor posture, body alignment and growth disturbance with reduced weight bearing, bone demineralisation and adapted gait patterns. In addition, individual factors such as growth and development, opportunity to exercise and behaviour may be affected. As the child develops and grows, they may be excluded from learning new skills, such as hopping, running, jumping, climbing and skipping or joint movements may be adapted so that function and independence are impaired.[3–5,7] Children with JIA may be less fit[15–17] and active[18] than healthy children, and functional limitations and pain may affect their ability to perform some physical or social activities as more energy and effort are required.[19,20]

Evidence to date

Hydrotherapy and land-based physiotherapy treatments are designed to increase range of motion, muscle strength, physical fitness, quality of life (QoL) and function, in addition to reducing pain.[21–27] Both modalities of treatment are advocated in the management of JIA as they may have a direct effect on the pathophysiological consequences of this incurable disease.

Hydrotherapy has been reported as the treatment of choice by physiotherapists, parents and children in preference to land-based physiotherapy alone (Epps, King's College London, 2002). Water is a useful unencumbered environment in which to mobilise joints. Movement may be facilitated by utilising water buoyancy and the elimination of gravity. The application of physical principles such as leverage, streamlining, force production with floats and positioning body parts from the water's surface can further facilitate movement. Multiple joint activity is possible, reducing treatment time, and a number of techniques employ the use of momentum, turbulence and 'drag' to increase passive movement without increasing pain in affected joints. Furthermore, exercise may be adapted to suit the individual to allow participation of and interaction with more able-bodied peers, which is of great psychological importance in young children. For those more severely disabled, buoyancy and gravity may be used to permit simulated functional movements. Importantly, children usually perceive activity in water as fun and enjoyable. Compliance with treatment is often improved and the treatment is not associated with other medical, painful or potentially frightening experiences that can occur in the hospital setting. Water may be the only medium whereby some patients feel on an equal

footing with their peers and exercise programmes can become a family activity.[8]

Although hydrotherapy is commonly used in JIA,[28] little scientific evidence exists to support the use of this modality of treatment. Verhagen and colleagues published a systematic review assessing the effects of hydrotherapy (balneotherapy) for rheumatoid arthritis and osteoarthritis.[29] Although heterogeneous outcome measures and methodologies make comparisons of studies and pooling of results difficult, most studies of hydrotherapy report positive findings including improved flexibility, muscle strength, function and QoL. Scott reviewed the evidence for hydrotherapy in JIA and concluded that there is little research to support its use.[27]

There are only three small studies evaluating the effects of hydrotherapy in JIA. In one study, a cross-over design was used with six subjects in each group receiving hydrotherapy and home-based exercise.[30] Although the aim of the study was to evaluate the effects of hydrotherapy on a number of variables, it is not possible to draw any conclusions from the results because of serious flaws in the methodology. Another study reported improvements in range of motion and fitness following hydrotherapy in JIA,[31] but the results may be misleading as the small sample size led to clinically unimportant changes reaching statistical significance. More recently, QoL improvements were described in an uncontrolled pilot study involving 10 children with JIA who undertook weekly hydrotherapy treatments for 15 weeks.[32] Again, the sample size is too small for the results to be conclusive, the improvements were not statistically significant and the study used repeated measures and multiple outcomes.

However, benefits of hydrotherapy have been reported from both immersion and exercise in heated water. Immersion to the neck in heated water results in a number of physiological responses triggered by an increase in hydrostatic pressure. An increase in distal venous pressure leads to central hypovolaemia, with subsequent cardiovascular responses resulting in increases in cardiac output and stroke volume,[33,34] which lead to inhibition of the sympathetic nervous system, which in turn reduces vagal vasomotor tone, inducing muscle relaxation and central sensitisation to pain.[35,36] Furthermore, superficial heating of the skin and underlying structures leads to a reduction in striated muscle tone, cutaneous vasodilatation and a reduction in peripheral vascular resistance. This results in increased blood flow that carries away metabolites and toxins that stimulate pain by increasing aerobic metabolic activity leading to analgesia. It has been suggested that these processes lead to anti-inflammatory activity.[23] Passive stretches and active movements might therefore be performed more easily and comfortably in heated water, which is particularly beneficial if a child is anxious or in pain.

A number of benefits have been attributed to hydrotherapy treatments in adult populations, which may be of value to children with JIA. These include improved physical health, reduced pain and improved function and QoL. Reduction in pain following hydrotherapy has been demonstrated in adults with arthritis.[37,38] However, in one study there was no separation of hydrotherapist from hydrotherapy effect, and both studies had small sample sizes. Reduction in back pain has also been demonstrated retrospectively in adults,[39,40] but the results may have been biased as the researcher also administered the hydrotherapy treatment. Furthermore, the reliability and validity of outcome measures were not ascertained, and statistical analyses were inappropriate for study design. In contrast, two studies reported no significant reduction in pain following hydrotherapy in adults with arthritis.[41,42] Other studies suggest no additional reduction in pain with hydrotherapy than with immersion to the neck in heated water.[24,43] Nonetheless, these results have clinical relevance, and increased joint pain has been reported as the main reason for patients with rheumatoid arthritis stopping land-based exercises.[44] Hydrotherapy may be the only means of exercising without pain for some patients with arthritis, and can be of particular benefit to children with low thresholds to pain or during an acute exacerbation of symptoms.

High-impact aerobic activity may not be possible in JIA owing to the compressive forces that occur through articulating surfaces leading to pain and further joint damage, thus preventing maximum intensity exercise. It has been suggested that the reduced loading on lower limb joints during immersion in water may enable strenuous activity during hydrotherapy.[45–47] Hydrotherapy may therefore be one of the few modalities of treatment whereby high levels of energy can be expended. Furthermore, water may be a suitable medium for exercise in JIA as patients often have low initial working capacities owing to reduced physical activity and opportunities to exercise. Improved fitness and levels of physical activity in rheumatoid arthritis[42,48–50] and an enhanced cardiorespiratory response in healthy adults have been demonstrated following exercise in water.[51,52]

There is only one small study investigating the effects of hydrotherapy on muscle strength in JIA. Oberg and colleagues reported increases in quadriceps strength and improved electromyographic responses to fatigue following a 3-month hydrotherapy programme in 10 children with JIA.[53] The effects of buoyancy and Archimedes principle permit the activation of muscle in positions not possible on land owing to gravity, and reduce the mechanical stress through joints and soft tissue structures while undertaking muscle strengthening activities.

Improvements in QoL and psychological well-being have been recognised following hydrotherapy interventions,[24,54,55] but only two randomised controlled studies in arthritis show significant increases in function following hydrotherapy.[24,55]

None of the studies mentioned have conclusively determined the efficacy of hydrotherapy in either adult or paediatric arthritis. It would appear that little scientific evidence exists to support the use of this modality of treatment in conjunction with, or in preference to, other forms of physical rehabilitation. Only two randomised controlled trials (RCTs) have compared hydrotherapy with land-based physiotherapy treatment in rheumatoid arthritis; although additional benefits were demonstrated in the hydrotherapy group, neither study demonstrated significant differences in outcome at follow-up between the two groups.[24,50] In addition, the balance between the potential benefits of hydrotherapy and cost incurred in initiating and maintaining a hydrotherapy service has only been explored in one RCT in osteoarthritis. Hydrotherapy was not found to be cost-effective compared with 'usual' treatment when using population preference-weighted QoL measures to estimate the quality of life-years gained, although patient weighted and disease-specific QoL and functional outcomes showed statistically significant improvements.[55] The trial was of high methodological quality, however the outcome measures were taken immediately after the intervention finished which did not allow any analysis of longer term effects.

Rationale for undertaking a cost-effectiveness study in hydrotherapy in JIA

JIA is a potentially disabling disease in children, with no known cure. Hydrotherapy is a recognised form of treatment administered in conjunction with land-based physiotherapy. It is widely accepted by patients and advocated by medical and allied health professionals in the management of this condition. However, initial capital and running costs are high, and rapid developments in drug management may prevent or reduce the pathophysiological consequences of the disease, reducing the need for this expensive treatment. However, if hydrotherapy improves the QoL, function and level of independence of these children, then their lives will be less disrupted and school and future employment difficulties reduced. This investigation will determine whether hydrotherapy combined with land-based physiotherapy provides measurable improvements as a method of treatment, thereby facilitating objective decisions to be made by the NHS with regard to the provision of physiotherapy for patients with JIA. If combined physiotherapy is found to be cost-effective, then it increases the range of options for the treatment of a condition, where options are limited. Owing to the chronicity of the disease, any alternative to pharmaceutical interventions that may prevent or reduce deformity and disability with no recognised side-effects should be investigated. Although the costs of hydrotherapy are higher than those of land-based physiotherapy treatment, costs may be offset against efficiency gains if less staff time is required with individual patients and fewer drugs and resources are needed to support the development and functioning of the child. Furthermore, additional benefits to the family may include less distress to the parent and child, improved compliance with treatment and in the medium to long term improved physical health and QoL.

The hypothesis is that combined hydrotherapy and land-based physiotherapy will be more clinically and cost-effective than land-based physiotherapy alone in the treatment of JIA.

Chapter 2
Methods

This study is a clinical and economic evaluation of combined hydrotherapy and land-based physiotherapy treatment for children with JIA. It was designed as a multicentre randomised controlled, partially blinded trial with 100 patients in a control arm receiving land-based physiotherapy only and 100 patients in an intervention arm receiving combined land-based physiotherapy and hydrotherapy. The principal investigator, health economist and independent statisticians were blinded to the intervention group. However, the treating physiotherapist, physician, patient and parent could not be blinded, as they were involved in treatment.

Objectives

The trial had the following two objectives

1. To compare the effects of combined hydrotherapy and land-based physiotherapy (**combined**) with land-based physiotherapy only (**land**) on cost, health-related quality of life (HRQoL) and outcome of disease in children with JIA.
2. To determine the cost-effectiveness of combined hydrotherapy and land-based physiotherapy in JIA.

Patients

Inclusion criteria

Inclusion criteria for trial patients were:

- Diagnosed with idiopathic arthritides of childhood with onset before their 16th birthday for more than 3 months.
- Aged 4–19 years inclusive.
- Stable on medication (Appendix 1).
- At least one active joint, core set criteria 1.[56]
- At least two out of any five of the remaining core set criteria below.[57]
- The physician global assessment of disease activity >10 mm on a 100-mm visual analogue scale (VAS).
- The parent global assessment of well-being >10 mm on a 100-mm VAS.
- Childhood Health Assessment Questionnaire scores >0.
- More than one joint with limited range of motion (joint motion reduced by at least 5° from normative range for age[58]).
- An elevated erythrocyte sedimentation rate (ESR) (>5 mmHg in children and >10 mmHg in adolescents).

Exclusion criteria

Patients were excluded from the trial if they:

- Suffered from severe systemic disease or any other condition that is unstable.
- Suffered from quotidian fevers (daily recurrent fever for at least 2 weeks to >39°C between spikes).
- Were unable to give informed consent or complete questionnaires owing to language barriers.
- Had musculoskeletal surgery within the previous 6 months.
- Had a neuromuscular condition which increases muscle tone.
- Had received intensive physiotherapy defined as more than 1 week of daily treatment within the previous 6 months.
- Had no access to outpatient physiotherapy or hydrotherapy.
- Met general hydrotherapy exclusion criteria, such as chlorine allergy.[59]

Sample size calculation

As there was no firm evidence as to the proportion of patients with JIA likely to improve in the control arm of the study, it was not possible to carry out a sample size calculation relating to the exact context of this trial. Instead, sample size was calculated using data from an observational study of adult rheumatoid arthritis.[60] Steinbrocker functional grades II and above were taken as a surrogate measure of poor outcome or non-improvement, and a reduction of 25% in the proportion of subjects in these functional grades was taken to be clinically significant.

Let p_1 be estimated proportion that will not improve in the **land** (control) group; this was estimated as 0.6 using adult data[60]. Let p_2 be estimated proportion that will not improve in the **combined** (intervention) group if there is to be a clinically significant difference between the two groups; this was estimated as 0.45. Then,

$$\text{standardised difference (SD)} = \frac{p_1 - p_2}{\sqrt{\bar{p}(1-\bar{p})}}$$

where $\bar{p} = (p_1 + p_2)/2$ and

$$\text{SD} = \frac{0.6 - 0.45}{\sqrt{0.525(0.475)}} = \frac{0.15}{0.5} = 0.3$$

This gave an estimated power of 0.57 for a trial of the proposed size.[61]

Procedure

Recruitment into the trial

Physiotherapists known to have treated children with JIA were identified from physiotherapy and medical notes at the three largest paediatric centres for JIA in the UK, Middlesex Adolescent Unit (MAU), Great Ormond Street Children's Hospital (GOSH) and Birmingham Children's Hospitals (BCH). A questionnaire was sent to physiotherapists to determine hydrotherapy availability and requesting support for the trial. The British Paediatric Rheumatology group, Chartered Society of Physiotherapy, Frontline, and Hydrotherapy and Paediatric Physiotherapy SIGs (special interest groups) published letters requesting support from physiotherapists treating JIA, including provision of outpatient treatment and informing patients of the trial. Physiotherapists and heads of department were contacted by telephone and given trial details. Information sheets were sent to physiotherapists to distribute to patients, and letters were sent to the Chronic Children's Arthritis Association and Young Arthritis Care asking parents and children interested in the trial to contact one of the centres. Posters and information sheets were posted in clinics at the three centres, and teaching sessions were held for multidisciplinary teams to explain the trial.

Patients were recruited from outpatient clinics at the three centres. The principal investigator examined case notes of all patients attending JIA clinics and entered eligibility forms in notes where patients could be eligible (unless local physiotherapists had not agreed to participate in the trial or hydrotherapy was not available). The examining physician determined if a patient met eligibility criteria and would be suitable for recruitment. Patients admitted on to an eight-bedded unit at GOSH were identified as potential recruits by the treating physician and local rheumatology consultants were contacted to further help with recruitment. Trial involvement was discussed with any eligible patients and their family and a patient information sheet was provided. Local physiotherapists were contacted to ensure that outpatient treatment was still accessible to the patient (as staffing levels changed over the recruitment period). Verbal consent was gained from the family or guardian prior to intervention and written consent or assent obtained when the patient attended for assessment.

Randomisation

An independent statistician conducted three separate block randomisations allocating patients to the **land** or **combined** group, hence ensuring a balance between groups at each treatment centre. The block sizes were chosen to match envisaged recruitment (50, 76 and 76 for BCH, MAU and GOSH, respectively). This reduced the effects that general differences between centres might have on treatment outcome and reduced the predictability of allocations.

Each patient was allocated a unique identification number at recruitment by the principal investigator, starting at 1 for BCH, 201 for GOSH and 401 for MAU. The treatment group allocated to each of these numbers was stored in sealed envelopes by an independent research assistant based at the Rheumatology Research Centre for University College London. Prior to intervention, treating physiotherapists contacted this research assistant to obtain the treatment allocated to their patient (based on identification numbers assigned by the principal investigator). To ensure accuracy of treatment allocation, the treating physiotherapist faxed identification numbers and treatment allocations to the independent statistician every 3 months.

Protocol

The chairperson of the Hydrotherapy Association of Chartered Physiotherapists and six senior chartered physiotherapists, all with extensive experience and expertise in JIA, developed protocols for both groups. All active and passive joint movements and the main muscle groups affected by disease were identified. The

physiotherapists demonstrated how they would perform hydrotherapy or land-based techniques at each joint. The various techniques, including starting positions, physiotherapist hand positions and stabilisation of the patient, were discussed and tried by each physiotherapist. A consensus opinion was gained by considering safety, ease of movement, ability for the patient to undertake the technique independently and comfort of both therapist and patient.

Once the protocol had been agreed, it was incorporated into the pretrial physiotherapy treatment of patients not entering the trial at the three centres. The protocol was then adapted until physiotherapists agreed that it achieved treatment aims, could be used as part of group treatment and was suitable for outpatient physiotherapists with limited experience in JIA.

Intervention

Trial patients were admitted on to a ward, stayed in hotel accommodation or travelled daily from home for 2 weeks of intensive physiotherapy treatment.

Patients in the **land** group undertook 16 hourly sessions of land physiotherapy (Appendix 2) at one of the trial centres over 2 weeks. Following this block of intensive treatment, they received land physiotherapy once per week or fortnight for 2 months on an outpatient basis. Community physiotherapists then used their clinical judgement to decide whether a patient's treatment should continue or stop (*Figure 1*), but were asked to exclude hydrotherapy until a 6-month follow-up assessment had been completed. Swimming was not excluded from patient's usual activities at any time during the trial.

Patients in the **combined** group undertook eight hourly sessions of hydrotherapy (Appendix 3) and eight hourly sessions of land physiotherapy at one of the trial centres over 2 weeks. Following this block of intensive treatment, they received hydrotherapy only, once per week or fortnight for 2 months on an outpatient basis. Community physiotherapists then used their clinical judgement to decide whether a patient's treatment should continue or stop (*Figure 1*).

Land-based exercises were designed to increase range of motion (ROM), muscle strength, function, independence and fitness. They included passive stretches and hold–relax techniques, which were performed in each restricted anatomical direction of movement at any of the child's joints affected by the disease process. A muscle-strengthening programme incorporated the use of repetitive movement, and ankle weights were used if the child's joints were considered to be inactive by the treating physiotherapist (Appendix 2).

Hydrotherapy exercises were designed to have the same effects as land exercises. They incorporated the use of hydrodynamic and hydrostatic principles, hold–relax techniques, passive stretches, simulated function and aerobic activity. The position of the patient when performing the exercises was varied so that buoyancy could be used to assist or resist movements. The muscle force needed to generate movement was also varied by the use of flexing or extending the limb (leverage), altering the speed of movement performed (creating water turbulence), altering the streamlining of a limb (using flippers or bats) and using partially and fully inflated floats (Appendix 3).

The frequency and duration of specific land-based and hydrotherapy exercises were dependent on the child's ability and speed of progress. Functional activity was dependent on the joints affected by disease and the child's level of independence. Aerobic and functional activities were performed in both groups and function was facilitated in hydrotherapy by using the combined effects of buoyancy and gravity. The protocol was designed to enable children to perform a large proportion of the exercises independently under supervision and most of the exercises could be performed as part of a group session. This enabled a patient to be treated with other children, preventing isolation and reducing the time commitment needed by staff.

Home exercise programme

A home exercise programme was adapted to suit each individual patient dependent on the stage of intervention reached when they finished the intensive block of treatment. Each patient had his or her own programme. They were asked to carry out this programme every day except when attending for outpatient physiotherapy.

Standardisation of intervention

During the trial, an independent clinical expert observed physiotherapists treating patients at the three centres, ensuring that intervention followed protocol. The principal investigator provided training sessions at local physiotherapy centres where groups of children with JIA were being treated. However, in some centres the staff changed regularly and staffing constraints

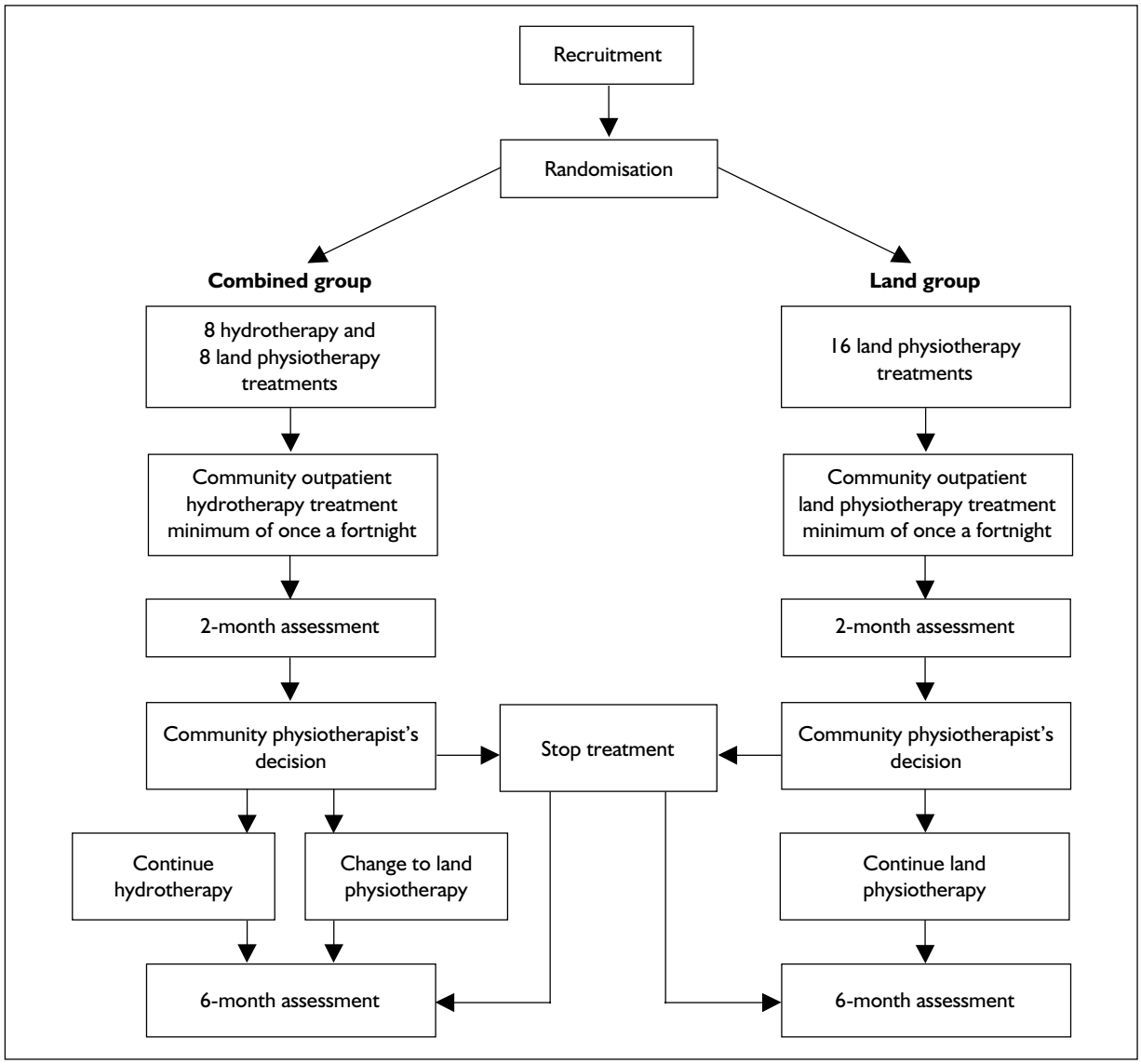

FIGURE 1 *Trial procedure*

prevented a large number of physiotherapists from attending these sessions. All outpatient physiotherapists were therefore sent the trial protocol with guidelines, contacted by the trial physiotherapist to discuss patients' main complaints and treatment priorities and offered an observational day at one of the trial centres.

Termination of intervention

Patient interventions were terminated or modified if any of the following occurred during the intervention period:

- An increase in physiotherapy above the level determined by study protocol.
- Onset of medical complications as determined by the treating physician.
- Surgery during the intervention period.
- Disease flare.[62]
- Unstable disease (current medication increased by >10% of dosage within 1 month, yet symptoms remain).

Withdrawal criteria

Patients were only withdrawn from the study if the child, their parents or guardian withdrew consent.

Blinding

The principal investigator, health economist and independent statisticians were blinded to the intervention group. However, the treating physiotherapist, physician, patient and parent could not be blinded, as they were involved in treatment.

Primary outcome measures

The primary outcome was improvement in disease status at 2 months after the main intervention was completed. This was defined according to international guidelines,[57] and calculated from six core outcome measures: Childhood Health Assessment Questionnaire (CHAQ), physicians' global assessment of disease activity, parents' global assessment of overall well-being, number of joints with limited ROM, number of active joints and erythrocyte sedimentation rate.

Disease improvement was defined as a decrease of ≥ 30% in any three of these six measures without there being a 30% increase in more than one of the remaining three measures, and is termed the preliminary definition of improvement in JIA.[57] This definition and the six core outcome variables have been extensively psychometrically tested in JIA.[58,63–67]

The Childhood Health Assessment Questionnaire

The CHAQ[68] assesses function in eight areas: dressing and grooming, arising, eating, walking, hygiene, reach, grip and activities, and has been validated in the UK.[68,69] Two to five items are evaluated in each area with a total of 30 questions. Three components are evaluated for each area: difficulty in performing daily functions, use of special aids and assistance from another person. Patients or parents are directed to note only those difficulties that are caused by their child's arthritis. The responses relate to the previous week.

Secondary outcome measures

Child Health Questionnaire

The Child Health Questionnaire, parent-completed 50-item (CHQ-PF50) measure of QoL,[69–71] is a generic questionnaire specifically for use in children.[72] It is designed to measure 14 health concepts: physical functioning, bodily pain, role/social limitations – physical, general health perceptions, change in health, role/social limitations – emotional and behavioural, mental health, general behavioural, self-esteem, emotional impact on the parent, impact on the parent's personal time, limitations in family activities and family cohesion.

Profiles for each of the 14 health concepts can be aggregated to derive summary component scores for physical and psychological health. Responses are related to the 4 weeks prior to the assessment.

Muscle testing

Peak isometric muscle strength of the knee extensors, hip and shoulder abductors was tested using a Penny and Giles (Dorset, UK) hand-held dynamometer.[73] Standardised antigravity limb positions and placement of the myometer head were used to test each muscle group.[73–75] Three maximal contractions were performed for each muscle group and the highest strength measurement was recorded for analysis

Physical fitness

The procedure for the assessment of physical fitness was adapted from the bicycle ergometer protocol developed by Giannini and Protas.[15] This protocol determines the starting workload by the child's body surface area (BSA) and pedalling rate is to be maintained at 60 per minute. However, the patients in this trial had at least one joint with disease activity and loss of ROM, which affected their ability to cycle. In addition, only those children with very mild disease activity were able to maintain a pedalling rate of 60 per minute. The protocol was therefore adapted and the patient started pedalling on a Kettler (Germany) ergometer at a rate and resistance (25 or 50 W) that felt comfortable. Each patient established a pedalling rate before starting the exercise test and the seat of the bicycle was adjusted so that their knee was flexed to ~15° when the pedal was in the down position. The workload was increased by 25-W increments every 2 minutes until the child reached exhaustion or could no longer pedal against resistance (up to a maximum of 10 minutes). They then pedalled slowly at the lower resistance of 25 W for 2 minutes. The time and maximal and submaximal heart rates were recorded manually using the radial pulse. Peak heart rate was determined for the final minute of exercise at the highest work load. Submaximal heart rate was determined during the second minute of the period of gentle cycling. If the patient experienced any pain during the test it was terminated and documented.

Pain

Pain was determined by the use of a 100-mm VAS. Responses were related to the week prior to assessment.

Patient satisfaction

Fifty-five patients and parents were asked by a physiotherapy assistant not involved in study treatment, 'If you could choose either gym exercises or exercises in the pool, which would you like better and why?' To prevent questionnaire fatigue, this question was asked after their 6-month follow-up appointment. Answers were transcribed verbatim.

Outcomes for economic analysis

Costs per quality-adjusted life-year (QALY) gained at 6 months following the main intervention were calculated using a societal framework to reflect costs to society. This included calculating the hours of paid or unpaid work lost as a consequence of the patient's illness. For example, a carer or their partner may have to stay at home to look after a child who has a disease flare, or take them to hospital or physiotherapy appointments. QALYs were derived from heath states measured using an HRQoL questionnaire, the EQ-5D.[76,77] The measurement and calculation of costs and QALYs are described below.

Resource utilisation data

Resource utilisation data to calculate costs were collected by the principal investigator using questionnaires, telephone and face-to face interviews, with GPs, physiotherapists, community nurses, hospital staff, patients and carers. These data related to carer time lost from paid and unpaid work, medication (drug name, dose and duration), investigations (e.g. blood tests), interventions (e.g. joint injections), inpatient days and outpatient and GP visits. In addition, data were collected on study intervention, time spent in hydrotherapy or land-based sessions, physiotherapy staff grade, patient-to-staff ratio and number of individual or group treatments.

Costs

Unit costs were taken from a variety of sources. The cost of each land-based physiotherapy or hydrotherapy treatment was made up of two elements. First, the variable cost of the physiotherapists' time was based on staff present and the average length of a treatment session, using average wage rates for the relevant physiotherapy grade.[78] Second, overhead costs (i.e. heating, lighting and administration) were calculated using a top-down method based on mean costs and throughput from the Staffordshire Hospital for land-based physiotherapy (no hospitals within the trial could provide this information) and fixed costs (maintenance, running costs, heating, lighting) from GOSH, Royal Liverpool Children's Hospital and University College London Hospital for hydrotherapy. *Table 1* shows the unit costs used in the economic analysis and their sources. Where possible, specific paediatric costs were used and this is noted as such in *Table 1*.

Medications were assigned an acquisition cost from the BNF.[79] Costs for other resource use, interventions, inpatient days in hospital and outpatient and GP visits, were taken from estimates from a sample of NHS hospitals and other published sources,[80,81] and carers' lost time from paid work (owing to their child's illness) was taken from average daily wage rates from Government statistics[82] (*Table 2*).

EQ-5D

The EQ-5D is a generic measure of HRQoL which consists of two parts, a VAS ($EQ\text{-}5D_{vas}$) and a descriptive profile ($EQ\text{-}5D_{utility}$) using five dimensions to define health. The $EQ\text{-}5D_{utility}$ was used to calculate HRQoL for the economic analysis.

In the trial, parents were asked to consider their child's health state today and indicate whether their child had no problems, some problems or was unable to perform in three dimensions of health, mobility, usual activities and self-care. They were then asked the degree of anxiety/depression

TABLE 1 *Key unit costs used to value physiotherapy resource use during the trial (1999–2000 prices, UK £)*

Physiotherapy staff grade	Unit	Unit cost (£)	Source
Senior I	Per minute	0.47	PSSRU, 2000 + (73)
Senior II	Per minute	0.43	PSSRU, 2000 + (73)
Superintendent	Per minute	0.54	PSSRU, 2000 + (73)
Junior	Per minute	0.40	PSSRU, 2000 + (73)
Physio assistant	Per minute	0.31	PSSRU, 2000 + (73)
Teacher	Per minute	0.52	PSSRU, 2000 + (73)
Assistant teacher	Per minute	0.31	PSSRU, 2000 + (73)
Fixed costs			
Hydrotherapy	Per session	17.19	RLCH, GOSH and UCLH
Land-based physiotherapy	Per session	0.29	Staffordshire Hospital

GOSH, Great Ormond Street Children's Hospital; RLCH, Royal Liverpool Children's Hospital; UCLH, University College London Hospital.

TABLE 2 *Key unit costs (intervention and 6-month follow-up) used to value resource use measured during the trial (1999–2000 prices, UK £)*

Item of resource	Unit	Unit cost (£)	Source
Inpatient/outpatient visits			
Inpatient stay (paediatric)	Per day	310	PSSRU, 2000
GP	Per visit	25	PSSRU, 2000
Haematological	OP visit	91	CIPFA, 2000
Radiological	OP visit	101	CIPFA, 2000
Podiatrist	OP visit	9	PSSRU, 2000
Ophthalmologist	OP visit	51	CIPFA, 2000
Rheumatology (paediatric)	OP visit	193	CIPFA, 2000
Psychologist (paediatric)	OP visit	194	CIPFA, 2000
Orthodontist	OP visit	63	CIPFA, 2000
Nephrology	OP visit	81	CIPFA, 2000
Orthopaedic surgeon	OP visit	64	CIPFA, 2000
Occupational therapist	OP visit	40	PSSRU, 2000
Social worker	Per visit	23	PSSRU, 2000
District nurse	Per visit	19	PSSRU, 2000
Ear, nose and throat	OP visit	60	CIPFA, 2000
Diagnostic tests			
Full blood count	Per test	3	*Health Technol Assess* 1998;**2**(4)
Liver function test	Per test	9	*Health Technol Assess* 1998;**2**(4)
X-ray	Per test	17	*Health Technol Assess* 1998;**2**(4)
MRI	Per test	250	*Health Technol Assess* 1998;**2**(4)
Ultrasound	Per test	30	Specific NHS hospitals
ECG	Per test	15	Specific NHS hospitals
Gastroscopy	Per test	146	Specific NHS hospitals
Barium meal	Per test	65	Specific NHS hospitals
Time away from work			
Male away from work	0.5 day	45	Ref. 77
Female away from work	0.5 day	34	Ref. 77

CIPFA, Chartered Institute of Public Finance and Accountancy; ECG, echo-cardiogram; MRI, magnetic resonance imaging; OP, outpatient.

and pain/discomfort, from none to very severe. The responses place each patient into one of 245 mutually exclusive health states. These health states are then scored using a set of preferences estimated from interviews with 3395 adult members of the UK public.[83,84]

Standardisation of outcome measures

The same physician performed the baseline and 2-month follow-up global assessment of disease activity. If at all possible, the same physician also performed the 6-month follow-up assessment for secondary analysis, but difficulties arose when clinics were reduced or priority bookings were made. All physicians were experienced in the assessment of JIA and of at least consultant status. The principal investigator performed all other aspects of the assessment at baseline and 2- and 6-month follow-up. The majority of assessments were performed in the morning (after 9.30 a.m. owing to morning stiffness). The same apparatus was used throughout the trial and calibrated according to the manufacturer's instructions. An independent clinical expert, a professor of paediatric rheumatology and several physiotherapists, observed the assessments performed by the principal investigator to ensure that standards were maintained throughout the trial.

Data quality

Patient data were collected on paper forms during assessments and copied on to an ACCESS database by the principal investigator. An independent statistician checked the ACCESS databases against the original paper forms on completion of all assessments and data collection. A physiotherapy assistant checked patients' medical notes against the original paper forms to ensure that resource utilisation data had been recorded accurately. These checks showed data entry to be accurate with

the exception of two typing errors and an incorrect entry of medication dosage; these were corrected prior to data analysis. Data were then exported to an SPSS data file for analysis. The SPSS file was checked against the ACCESS database for accuracy. It was concluded that the transport of data could be performed with neither loss nor corruption. Data were unblinded and the statistician retained a 'read only' copy of the SPSS file.

Data analysis

The main focus of the analysis was how the **land** and **combined** groups compared at 2 months follow-up, using the primary and secondary outcome measures of disease improvement, QALYs gained and costs per QALY at 6 months. A large number of secondary outcomes were also measured and descriptive analyses were performed to meet the broader aim of the trial to inform future studies of hydrotherapy and physiotherapy in JIA.

Intention-to-treat analysis

Over the 2-week course of hospital-based treatment, the trial physiotherapists recorded treatment allocations and protocol violations, which were kept in sealed envelopes for study integrity checks prior to data unblinding. All patients were assessed as 'intention-to-treat' even if their intervention was terminated or modified. Every attempt was made to follow up all patients who had a baseline assessment, unless they were deemed ineligible for study entry during this assessment.

Primary analysis

The primary analysis consisted of a comparison of the proportion of patients in each group that showed improvement at their 2-month follow-up compared with baseline assessment.

$p_1 = A/(A + B)$

where A is the proportion improved and B the proportion not improved in the **land** group;

$p_2 = C/(C + D)$

where C is the proportion improved and D the proportion not improved in the **combined** group.

The results presented are the difference between the proportions in the **land** and **combined** groups with 95% confidence intervals (CIs):

difference $= p_1 - p_2$

The 95% CIs are calculated using the standard error on the difference, SE_{diff}, given by

$$SE_{\text{diff}} = \sqrt{\frac{p_1(1-p_1)}{n_1} + \frac{p_2(1-p_2)}{n_2}}$$

where $n_1 = A + B$ and $n_2 = C + D$.

The 95% CI is given as

$p_1 - p_2 - (1.96\ SE_{\text{diff}})$ to $p_1 - p_2 + (1.96\ SE_{\text{diff}})$

This calculation is performed using the continuity correction described by Armitage and Berry.[85] Reported along with this result is the proportion of patients in each arm of the trial falling into the five mutually exclusive groups: consent withdrawn, lost to follow-up, drug treatment changed beyond the protocol, intervention altered beyond the protocol and none of the above protocol violations.

In addition, as the '2-month assessments' did not occur exactly 2 months after completion of intensive treatment in all cases, the median and inter-quartile range of the time between completion of inpatient intervention and 2-month assessment are reported.

Cost-effectiveness analysis

The cost-effectiveness analysis used patients' EQ-5D scores to calculate mean health state values (plus a measure of variance) of patients in the **combined** and **land** groups at 2 and 6 months follow-up. These scores were converted to QALYs gained over the 6-month period using area under the curve analysis.[84] Intervention treatment sessions were recorded so that only the treatment patients' actually received was costed, irrespective of allocation or intended number of treatments. Owing to differential follow-up (resulting from gradual recruitment and a fixed final point of follow-up and difficulties in booking patients into a clinic for their 6-month assessments), 32% of patients did not receive a 6-month assessment, having received a 2-month assessment. Estimates of mean costs and QALYs gained, over 6 months of follow-up, were, therefore, calculated using Lin and colleagues' method to adjust for censored data.[86] Given that the time horizon of the analysis was <1 year, total costs and QALYs remain undiscounted, and QALYs were undiscounted. Statistical analysis was undertaken using STATA 7.0.[87]

Approximately 5% of patient resource-use questionnaires had some missing data, either on medication, GP visits, utilities or hospital data. As the extent of missing data was relatively minor, mean imputation was used to account for those missing data points. It is recognised that this method may result in underestimates of variance, but sensitivity analysis was used to explore whether the use of this method affected the conclusions of the analysis.

Given the skewed nature of the data, standard errors for costs and QALYs gained were simulated using the non-parametric, bias-corrected bootstrap method.[88] The 95% CIs were calculated from the 2½ and 97½ centiles of mean costs and QALY distributions.

Incremental cost-effectiveness ratios were calculated to relate differential mean cost to differential mean QALYs gained associated with each group. To account for uncertainty due to sampling variation, a cost-effectiveness acceptability curve was plotted[89,90] to illustrate the probability of combined hydrotherapy and land-based physiotherapy being more cost-effective than land-based physiotherapy only given a range of values that society could attach to an additional QALY. Threshold willingness to pay values ranging from £0 to £200,000 per additional QALY were used (a Bayesian approach to the presentation of cost-effectiveness data[91]).

Secondary analysis

Sensitivity analysis

Sensitivity analysis was performed to investigate whether treating patients who were lost to follow-up, withdrew or had their protocol violated as 'improved' or 'not improved' changed the conclusions drawn from the results of this trial. During sensitivity analysis, primary analyses were repeated treating losses to follow-up, withdrawal and protocol violations as treatment failures or successes. The cost-effectiveness analysis was repeated excluding the data for patients without 6-month assessments. Additional analytical repetition used a fixed cost of £0.84 per minute [Personal Social Services Research Unit (PSSRU)] for land-based physiotherapy, as original estimates were taken from one hospital not included in the trial.

Analysis of secondary outcomes

The mean difference and standard deviation of that difference between core outcome variables, CHQ and EQ-5D (HRQoL), pain, muscle strength and fitness scores at baseline and 2 and 6 months were calculated for each patient in the two arms of the trial.

In addition, the proportion of patients who showed clinical improvement between baseline and 6-month assessments was calculated for each arm of the trial.

Study conduct

A Trial Steering Committee (TSC) was set up to monitor and supervise the progress of the trial towards its interim and overall objectives. It reviewed relevant information from the funding body and any meetings relating to the management and organisation of the trial. It considered recommendations from the Data Monitoring and Ethics Committee not to extend the trial beyond the original timescale despite a lower than expected recruitment rate. The TSC met prior to commencement of the trial and at 6-monthly intervals throughout the trial. The Chairperson of the TSC (employed by the Medical Research Council) and one other member [manager of therapies, University College London Hospital (UCLH)] were independent of the trial.

A Data Monitoring and Ethics Committee (DMEC) was set up to determine if analysis was needed in addition to the interim reports. They considered control data unblinded, to recalculate the power of the sample when it was clear that 200 patients could no longer be recruited within the timescale of the trial. There were no safety issues of concern during the trial. The TSC reported to the DMEC after each meeting.

A Trial Management Committee (TMC) was set up to monitor the day-to-day running of the trial. It consisted of therapists involved in administering treatment at each centre and an independent clinical expert in the field. It met during the initial phases of planning and then at 6-monthly intervals.

Patient/parent informed assent and consent

The purpose of the study was explained to each patient in the presence of a physician or physiotherapist. Each patient (or parent) enrolled received an approved information sheet containing information about the study, and an

approved informed consent form with a statement that he or she would permit study case record forms to be examined by a third party. Each enrolled adolescent was also provided with an information sheet and signed an informed assent form. Consent and assent forms were stored with patient data and an additional copy was kept with the patients' medical records.

Ethical approval

Ethical approval was obtained from

- South Birmingham Local Research Ethics Committee on 22 June 1999
- joint University College London (UCL)/UCLH Committees on the Ethics of Human Research on 1 April 1999
- Great Ormond Street Children's Hospital NHS Trust/Institute of Child Health Research Ethics Committee on 18 June 1999.

Patient confidentiality

All information pertaining to each patient was held on a confidential basis and this confidentiality was maintained throughout the data integrity checking process. The results of the trial are reported in a manner that does not identify individual patients.

Chapter 3
Results

Recruitment and flow of patients through the trial

The recruitment and flow of patients through the trial is shown in *Figure 2*.

A total of 152 patients were eligible for entry into the study during the recruitment period. Informed consent was not given in 51 cases; 25 patients were unable to commit to attending for treatment (owing to young children at home or family problems preventing them from being in London for 2 weeks), 12 did not want to be in the **land** group (because they would not receive hydrotherapy), 11 did not want to miss school, one worked full time and two gave no reason.

Furthermore, 87/217 physiotherapy services had no access to hydrotherapy facilities or were unable to commit to providing outpatient treatment for patients in the trial. Patients who relied on these services for physiotherapy or hydrotherapy treatment were therefore not considered for eligibility into the trial.

Therefore, of the 152 potentially eligible patients, only 101 were recruited into the trial. However, 23 of these patients lost eligibility or withdrew consent before intervention (13 **combined** group and 10 **land** group allocations), two developed mental health problems, three improved, seven became too unwell and needed other treatments, seven were no longer able to participate owing to family commitments, two changed schools and two underwent baseline assessment but were deemed ineligible owing to lack of disease activity and a medical complaint that could affect exercise tolerance. Nine of these patients were randomised (six **combined** group and three **land** group allocations) but lost eligibility before starting treatment. These patients were therefore included in sensitivity analysis.

In total, 78 patients undertook the intervention, 39 were allocated combined treatment and 39 land treatment, 15 at BCH (8 **combined** group, 7 **land** group), 47 at GOSH (23 **combined** group, 24 **land** group) and 16 at MAU (eight **combined** group, eight **land** group).

Protocol violations

In total, 13 and 11 patients had their trial protocol violated (including not receiving allocated treatment) in the **combined** and **land** groups (Appendix 4). One patient crossed over from land to combined treatment (because a consultant considered hydrotherapy necessary for that particular patient), the same patient then withdrew consent; four crossed over from combined to land treatment (because the hydrotherapy pool closed under health and safety and infection control policies); one had drug management changed; three had drug management and intervention changed; and 13 had intervention changed beyond trial protocol.

Four patients did not complete a 2-month assessment, two withdrew and two were lost to follow-up. Erythrocyte sedimentation rate was not available for a number of patients owing to insufficient blood samples or non-attendance at clinic. Two patients could not be entered into the primary analysis because the Preliminary Definition of Disease Improvement was inconclusive without this measurement. Therefore, of 78 potential data sets, 72 were available for primary analysis.

Two-month assessments did not occur exactly 2 months after completion of the intensive intervention period. The median time from 2 months to actual date of assessment was 5 and 0 days in the **land** and **combined** arms of the trial. However, although both groups were assessed 7 days before exact assessment date at the lower interquartile range, there was large variation between the groups at the higher interquartile range, with **land** group assessments performed 20 days after assessment date compared with **combined** group assessments performed 8 days after assessment date.

Patient characteristics

There were no differences between the groups in anthropometry, disease type or duration; however there was a higher proportion of females in the **land** than the **combined** group (*Table 3*).

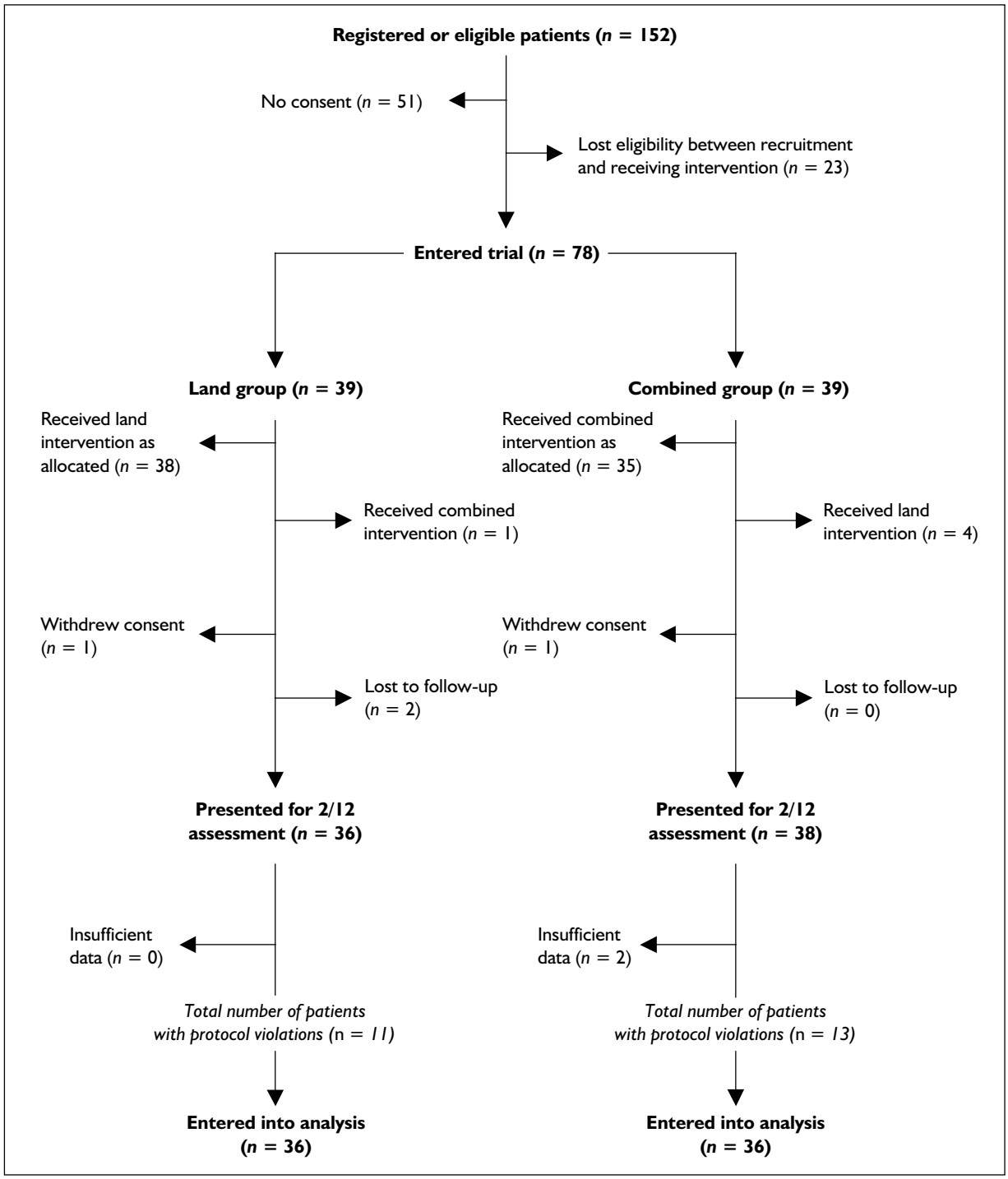

FIGURE 2 *Patient recruitment and flow and follow-up through the trial*

Patient clinical characteristics

The clinical characteristics of patients are shown later in *Table 6*. The only clinical imbalance between the two groups at baseline assessment that was significant ($p < 0.05$, not corrected for multiple testing) was a higher inflammatory index (ESR) in the **combined** group.

Clinical outcome

Primary outcome

Two months after intervention, 47% of patients allocated combined and 61% allocated land-based treatment had improved disease activity with 11 and 5% worsened, respectively (a 'disease flare' is

TABLE 3 *Patient characteristics at baseline by study group: data presented as mean (range)*

Characteristic	Land group (*n* = 39)	Hydrotherapy (*n* = 39)
Age (years)	11 (4–19)	12 (6–19)
Female	24	19
Male	15	20
Height (m)	1.42 (0.98–1.84)	1.40 (0.98–1.73)
Body mass (kg)	35.58 (13.20–82.70)	40.56 (17.50–85.90)
Disease duration (years)	5.77 (0.49–16.04)	5.15 (0.32–13.73)
Time from disease onset to diagnosis (years)	0.91 (0.00–7.10)	0.64 (0.00–4.73)
Systemic onset	5	5
Poly-articular	15	18
Oligo-articular	3	4
Extended oligo-articular	8	7
Enthesitis-related arthritis	8	4
Psoriatic arthritis with psoriasis	0	1
Disease course after 6 months is presented as opposed to disease onset.		

TABLE 4 *Change in disease status 2 months after intervention*

	Land (*n* = 36)	Combined (*n* = 36)
Number of patients who improved	22	17
Number of patients who did not improve	14	19
Proportion of patients who had a disease 'flare'	0.05	0.11
Proportion of patients who improved	0.61	0.47

TABLE 5 *Change in disease status 6 months after intervention*

	Land (*n* = 25)	Combined (*n* = 25)
Number of patients who improved	17	11
Number of patients who did not improve	8	12
Proportion of patients who had a disease 'flare'	0	0.08
Proportion of patients who improved	0.68	0.48

defined as a worsening of ≥ 30% in three or more of the six core outcome variables and a minimum of two active joints[62]) (*Table 4*).

The difference between the proportions of patients who improved in the two arms of the study was –0.14. The difference in proportions of patients who improved in the two arms of the study with continuity correction for observed differences was –0.11 (95% CI –0.34 to 0.12).

Sensitivity analysis of 2-month primary outcome data

The difference between the proportions of patients who improved in each arm of the study ranged from –0.07 to –0.16, well within the 95% CI of the primary result.

Six-month outcome data

Using the original definition of disease improvement 6 months after intervention, 48% of patients allocated combined and 68% of patients allocated land-based treatment had improved disease (*Table 5*). The difference in the proportions of patients who improved in the two arms of the study with continuity correction for observed differences was –0.16 (95% CI –0.43 to 0.11).

Core outcome measures

At the 2- and 6-month assessments, all core outcome measures improved in both groups, demonstrated by a reduction in mean scores (*Table 6*).

TABLE 6 *Difference between baseline and 2-month and baseline and 6-month core outcome measurements: data presented as mean (standard deviation)*

	Group	Change from baseline					
		n	Baseline value	*n*	2-month follow-up	*n*	6-month follow-up
No. of active joints[a]	**Land**	39	5 (4)	36	–3 (4)	25	–2 (3)
	Combined	39	7 (7)	38	–4 (6)	25	–3 (8)
No. of joints with loss of ROM[a]	**Land**	39	11 (10)	36	–4 (5)	25	–6 (6)
	Combined	39	13 (11)	38	–5 (5)	25	–5 (7)
CHAQ (0–3)[a]	**Land**	39	1.20 (0.8)	36	–0.20 (0.7)	25	–0.30 (0.7)
	Combined	39	1.21 (0.8)	38	–0.01(0.5)	25	–0.10 (0.7)
$VAS_{physician}$ (0–100 mm)[a]	**Land**	39	32 (20)	36	–10 (23)	25	–15 (22)
	Combined	39	35 (16)	38	–11 (17)	25	–13 (25)
$VAS_{well\text{-}being}$ (0–100 mm)[a]	**Land**	39	35 (24)	36	–7 (26)	25	–7 (24)
	Combined	39	40 (24)	38	–6 (25)	25	–3 (8)
ESR (mmHg)[a]	**Land**	38	14.2 (14)	34	–2.9 (13)	22	–6.6 (10)
	Combined	38	26.2 (28)	35	–3.5 (17)	23	–8.4 (19)

[a] A decrease in mean value signifies an improvement.

TABLE 7 *Difference between baseline and 2-month and baseline and 6-month scores for muscle strength, physical fitness and endurance by study group: data presented as mean (standard deviation)*

	Group	Change from baseline					
		n	Baseline value	*n*	2-month follow-up	*n*	6-month follow-up
Muscle strength (kg)							
Hip abductors	**Land**	31	7.08 (2.19)	31	2.75 (2.91)	20	2.21 (2.43)
	Combined	36	7.48 (3.93)	36	2.62 (2.47)	21	3.03 (2.53)
Knee extensors	**Land**	31	9.55 (3.87)	31	0.90 (4.70)	20	3.78 (4.42)
	Combined	37	11.48 (15.36)	37	2.79 (2.39)	21	4.40 (3.62)
Shoulder abductors	**Land**	31	5.80 (1.99)	31	0.83 (1.66)	20	1.12 (2.18)
	Combined	37	5.71 (2.61)	37	1.09 (1.93)	21	1.19 (2.03)
Physical fitness[a]							
Submaximal HR as a % of maximal HR (bpm)	**Land**	29	80.11 (11.48)	21	–10.2 (16.3)	14	–14.6 (10.7)
	Combined	23	82.80 (9.71)	18	–16.4 (12.8)	10	–20.2 (16.5)
Physical endurance							
Time (minutes)	**Land**	29	5.39 (2.01)	21	0.58 (2.25)	14	1.15 (2.15)
	Combined	23	5.18 (2.00)	18	1.71 (2.11)	10	1.84 (2.18)

bpm, Beats per minute; HR, heart rate.
[a] A decrease in mean value signifies an improvement.

Secondary outcome measures: muscle strength, physical fitness and endurance

Mean change in muscle strength, physical fitness and endurance improved at both the 2- and 6-month follow-ups in both groups. However, the standard deviations were wide in all assessments (*Table* 7).

There was little difference between the two intervention groups in shoulder abductor muscle strength, whereas the mean improvement in hip abductor strength was only maintained in the **combined** group at 6 months and knee extensor strength, fitness and endurance were greater in the **combined** than the **land** group at both time points.

TABLE 8 *Difference between baseline and 2-month and baseline and 6-month pain and CHQ scores by study group: data presented as mean (standard deviation)*

	Group	Change from baseline					
		n	Baseline value	*n*	2-month follow-up	*n*	6-month follow-up
Pain (0–100 mm)[a]	**Land**	39	36.9 (28)	36	–0.6 (35)	25	–4.6 (40)
	Combined	39	33.3 (30)	38	7.3 (36)	25	2.6 (47)
CHQ physical (0–100)	**Land**	31	27.8 (15)	28	4.0 (13)	17	1.8 (16)
	Combined	33	24.2 (16)	33	2.7 (15)	21	8.0 (18)
CHQ psychological (0–100)	**Land**	31	44.8 (10)	28	–0.7 (13)	17	1.8 (16)
	Combined	33	44.3 (11)	30	1.2 (9)	21	1.4 (7)

[a] A decrease in mean value signifies an improvement.

TABLE 9 *Difference between baseline and 2-month and baseline and 6-month EQ-5D scores by study group: data presented as mean (standard deviation)*

	Combined group		Land group	
	n	Health state value	*n*	Health state value
Baseline	38	0.63 (0.24)	36	0.54 (0.29)
2 months	38	0.68 (0.24)	36	0.68 (0.27)
6 months	25	0.62 (0.38)	25	0.69 (0.33)

Secondary outcome measures – pain and HRQoL

Change in pain was negligible in both arms of the trial at the 2- and 6-month assessments. The CHQ was incomplete in ~20% of cases, because parents did not understand or were uncomfortable answering questions. CHQ scores improved at 2 months, with further improvement at 6 months in the **combined** group. The **land** group showed an initial worsening of the psychological profile, which improved at 6 months, and an improvement in physical profile, not maintained at 6 months (*Table 8*).

Mean HRQoL scores measured using the EQ-5D were worse for the **land** group (health state utility = 0.54) than the **combined** group (health state utility = 0.63) at baseline. These values are on a scale from 0 (dead) to 1 (good health). The **land** group showed an improvement between baseline and 6-month assessment, but there was no significant difference between the groups, $p < 0.5$ (*Table 9*).

Patient satisfaction

About 88% (23/26) of patients and their parents preferred hydrotherapy to land-based exercises in the **land** group. The three patients who preferred land treatment stated that they 'didn't like chlorine, found the hydrotherapy pool inconvenient to travel to and didn't feel that it worked'. About 90% (26/29) patients and their parents preferred hydrotherapy to land-based exercises in the **combined** group. The three patients who preferred land treatment gave their reasons as 'didn't have to get changed, were bored and the pool kept breaking down'. In total, 89% (49/55) preferred hydrotherapy; the three key themes that emerged as reasons for liking hydrotherapy better than land-based exercise were adherence with exercise, easier and less painful to exercise and fun and enjoyment.

Economic outcome

Some 68% of patients received a 6-month assessment, with mean follow-up 162 days (range 60–272 days) in the **combined** group and 175 days (range 54–294 days) in the **land** group. Twenty-five patients received complete baseline and 2- and 6-month assessments in each group. Data from the 74 patients who presented for 2-month assessment were used in the economic analysis (*Figure 2*) (the two patients with insufficient data for clinical analysis were not excluded).

TABLE 10 *Individual patient resource use during follow-up: data presented by study group as mean (standard deviation)*

	Combined group (*n* = 38)	Land group (*n* = 36)
Inpatient days		
Intervention to 2 months	0.08 (0.36)	0.36 (1.29)
2 to 6 months	0.4 (1.44)	0.44 (2.00)
Outpatient referrals		
Intervention to 2 months	0	0.19 (0.58)
2 to 6 months	0.2 (0.5)	0.47 (0.22)
Diagnostic tests		
Intervention to 2 months	1.10 (1.46)	1.22 (1.85)
2 to 6 months	0.48 (0.91)	1.08 (0.70)
Interventions		
Intervention to 2 months	0.52 (1.17)	1.61 (3.78)
2 to 6 months	1.44 (5.00)	0.72 (2.05)
GP visits		
Intervention to 2 months	1.16 (1.92)	1.08 (2.25)
2 to 6 months	1.48 (2.02)	2.04 (3.59)
Physiotherapy sessions[a]		
Intervention to 2 months	4.57 (4.73)	5.11 (4.40)
2 to 6 months	3.4 (4.93)	3.24 (8.25)
Parents' days off work due to child's health		
Intervention to 2 months	2.97 (6.86)	4.16 (8.93)
2 to 6 months	3.2 (6.41)	5.41 (12.16)

[a] During this follow-up period, patients randomised to the **combined** group received hydrotherapy only and those randomised to the **land** group received land-based treatment only. These were both on an outpatient basis.

Resource use

The main areas of resource use are summarised in *Table 10*. The **combined** group had a smaller mean number of days as inpatients (0.48 versus 0.80 days) during the follow-up period, and required fewer outpatient referrals, investigations and GP visits. Mean days lost from work by parents because of their child's illness were higher in the **land** than the **combined** group (mean of 9.57 versus 6.17 days).

The proportion of patients taking disease-modifying medication was 69% in both groups between intervention and 2 months. Between 2 and 6 months, the proportions were 82 and 66% in the **combined** and **land** groups, respectively. One patient in the combined group took anti-TNF (tumour necrosis factor) therapy (cost ~£8000 per annum). Non-steroidal anti-inflammatory drugs (NSAIDS) were taken by 92% of patients in the **combined** and 91% of patients in the **land** group between intervention and 2 months, and 82% of patients in the **combined** and 77% of patients in the **land** group between the 2- and 6-month follow-ups. Steroidal medication was similar in both groups. The use of other medication, which included antibiotics and mild pain-killers, was more common in patients in the **combined** group between intervention and 2 months (23 versus 17%), but similar between 2 and 6 months (11%). The use of complementary medication, which included cod liver oil and aromatherapy, was relatively uncommon in both groups, being used by only one patient in the **combined** and two patients in the **land** group (*Table 11*).

Patients received a similar number of outpatient physiotherapy sessions in each group between intervention and the 6-month follow-up. Patients in the **land** group had more individual sessions than those in the **combined** group (123 versus 39), but fewer group sessions (238 versus 324). A superintendent physiotherapist was present during 20 (5.5%) of the hydrotherapy sessions and 13 (3.6%) of the land-based sessions. Hydrotherapy sessions required less staff time (29 versus 34 minutes). A larger number of staff were involved in the hydrotherapy sessions, with 51 (14.1%) sessions having more than two members of staff compared with 46 (12.6%) sessions in the land-based therapy group (*Table 12*).

TABLE 11 *Medication use during follow-up: data presented by study group*

	Group	Intervention to 2-month follow-up		2- to 6-month follow-up	
		No. of patients	Proportion of patients	No. of patients	Proportion of patients
Anti-TNF therapy	**Combined**	1	0.02	0	0
	Land	0	0	0	0
DMARDs	**Combined**	27	0.71	23	0.92
	Land	25	0.69	18	0.72
NSAIDs	**Combined**	36	0.94	23	0.92
	Land	33	0.91	21	0.84
Steroids	**Combined**	8	0.21	4	0.16
	Land	7	0.19	4	0.16
Complementary	**Combined**	1	0.03	0	0
	Land	2	0.05	2	0.08
Other	**Combined**	9	0.23	3	0.12
	Land	6	0.16	3	0.12

DMARD, disease-modifying antirheumatic drug.
[a] Data were available from 38 patients in the **combined** group and 36 patients in the **land** group between intervention and 2 months. Data were available from 25 patients in each group between 2 and 6 months.

TABLE 12 *Outpatient physiotherapy resource use between intervention and 6-month follow-up*

	Combined group: hydrotherapy sessions (n = 361)	Land group: land-based sessions (n = 363)
Numbers of one-to-one sessions	238 (66%)	324 (89%)
Number of group sessions	123 (34%)	39 (10.7%)
Superintendent present during session	20 (5.5%)	13 (3.6%)
More than 2 members of staff	51 (14.1%)	46 (12.6%)
Average length of session (minutes)	29	34

Costs

Mean costs per patient during the trial and follow-up were based on resource use and unit costs (*Tables 1* and *2*). Mean costs per patient are summarised in *Table 13*. Total mean physiotherapy costs were lower in the **land** than the **combined** group owing to higher costs of hydrotherapy facilities. For some resource use items, patients in the **combined** group had lower mean costs than those in the **land** group. The mean cost of parents' time away from work between intervention and 2 months was £98.77 in the **combined** group compared with £150.86 in the **land** group, and £114.42 versus £200.48 between 2- and 6-month follow-up. Mean inpatient stay costs were also lower for the **combined** group patients, £139.54 compared with £256.35 for **land** group patients over 6 months. The mean cost of **land** group outpatient referrals was more than double that of the **combined** group between intervention and 2 months at £17.92 compared with £6.41, but costs between 2 and 6 months were similar, £16.18 for the **land** group and £15.98 for the **combined** group. Investigations were also more common in the **land** group. The mean total cost of investigations was £3.78 for patients in the **combined** group; this was lower than for the **land** group at £116.89. The cost of interventions was lower in the **combined** group between intervention and 2 months, £10.89 versus £45.07. However during 2- and 6-month follow-ups, the mean cost of interventions in the **combined** group was £172.13 compared with £78.75 in the **land** group.

Although total mean physiotherapy staff costs during the follow-up period were higher for patients in the **land** group (£182.43 compared

TABLE 13 *Comparison of costs per patient between* ***combined*** *and* ***land*** *groups (1999–2000 prices, UK £): data presented as mean (standard deviation)*

	Combined group[a]	Land group[a]
Drug costs		
Intervention to 2 months	398.58 (494.43)	394.53 (390.04)
2 to 6 months	342.38 (457.44)	235.44 (337.82)
Inpatient stay costs		
Intervention to 2 months	25.26 (114.81)	115.55 (413.01)
2 to 6 months	128.00 (461.88)	140.80 (640.53)
Outpatient referral costs		
Intervention to 2 months	6.41 (32.15)	17.92 (57.49)
2 to 6 months	15.98 (56.03)	16.18 (56.22)
Interventions costs		
Intervention to 2 months	10.89 (29.77)	45.07 (96.31)
2 to 6 months	40.87 (88.57)	88.31 (193.24)
GP visits costs		
Intervention to 2 months	29.60 (47.52)	27.08 (56.49)
2 to 6 months	37.00 (50.57)	49.00 (86.75)
Time costs to parents		
Intervention to 2 months	98.77 (228.93)	150.86 (319.87)
2 to 6 months	114.42 (222.69)	200.48 (511.26)
Outpatient physiotherapy costs		
Staff	53.14 (79.69)	64.33 (167.26)
Facilities	36.39 (63.51)	6.45 (28.40)
Total cost	2065.07	
Differential mean cost[b] (95% CI[c])	20.9 (–870.50 to 750.93)	

[a] Data were available from 39 patients in each group between intervention and 2 months and 25 patients in each group between 2 and 6 months.
[b] Combined minus land.
[c] 95% non-parametric CI based on 1000 bootstrap replications.

with £149.32), reflecting the lower proportion of physiotherapist's time per patient during group sessions, the facilities cost of hydrotherapy (e.g. the pool and its maintenance) were higher than for land-based treatments (£142.52 compared with £11.22). A similar difference in physiotherapy staff and facilities costs was seen during the 2-week hospital-based intervention. Mean drug costs were higher in the **combined** group at £740.96 for the 6-month follow-up compared with £629.97 in the **land** group.

Total mean costs during the 6-month follow-up period were slightly lower in the **land** group by £20.90 per patient (95% CI –870.50 to 750.93). This difference is not statistically significant.

Health outcomes

Patients in the **combined** group had lower mean QALYs gained (0.01734) than those in the **land** group (0.06516) over 6 months of follow-up. The difference between QALYs gained in each of the groups was 0.0478 (95% CI –0.11294 to 0.0163 based on 1000 bootstrap replications).

Cost-effectiveness

Patients in the combined group had slightly higher mean costs (£20.90) and lower mean QALYs (–0.0478). *Figure 3* shows the uncertainty in mean differences in costs and QALYs gained between the two groups (that is, it shows mean costs and QALY differences based on the 1000 bootstrap replicates).

Figure 4 represents this uncertainty in the form of a cost-effectiveness acceptability curve, which shows the probability that combined treatment is more cost-effective than land-based treatment for a range of maximum values that decision-makers may place on generating an additional QALY. When society's willingness to pay for a QALY gained is close to 0 (which is where QALY gain is not valued so the focus is difference in mean costs only), combined treatment is associated with a

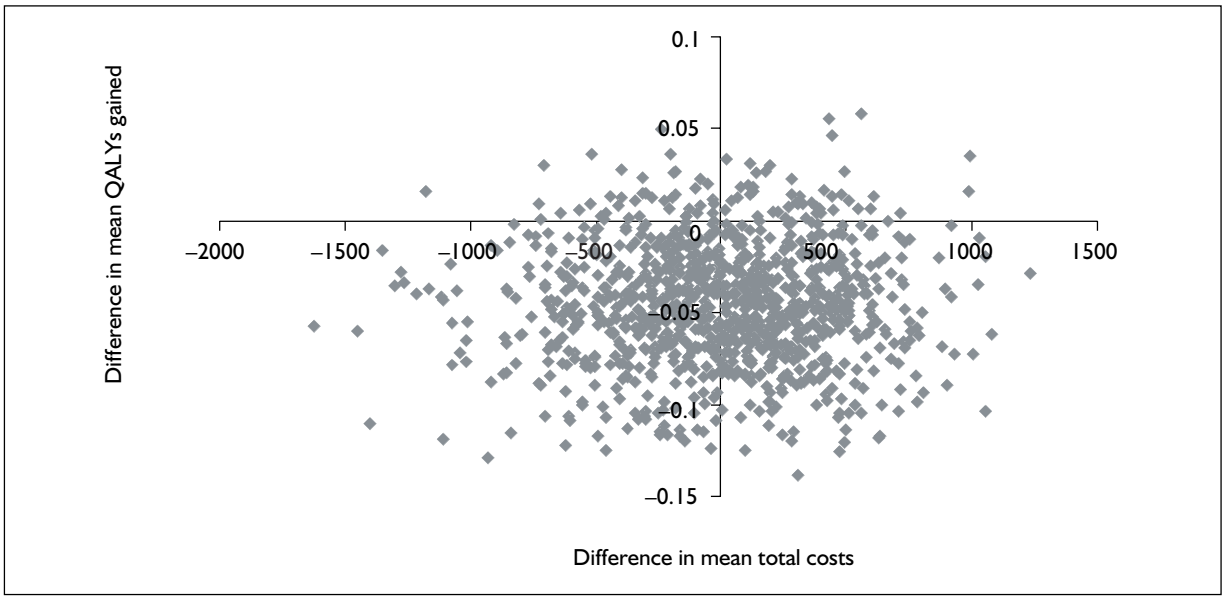

FIGURE 3 *Representation of the uncertainty in differential mean costs and QALYs gained showing 1000 bootstrap replicates. The vertical axis shows differential mean QALYs gained (combined minus land) and the horizontal axis shows differential mean costs (combined minus land).*

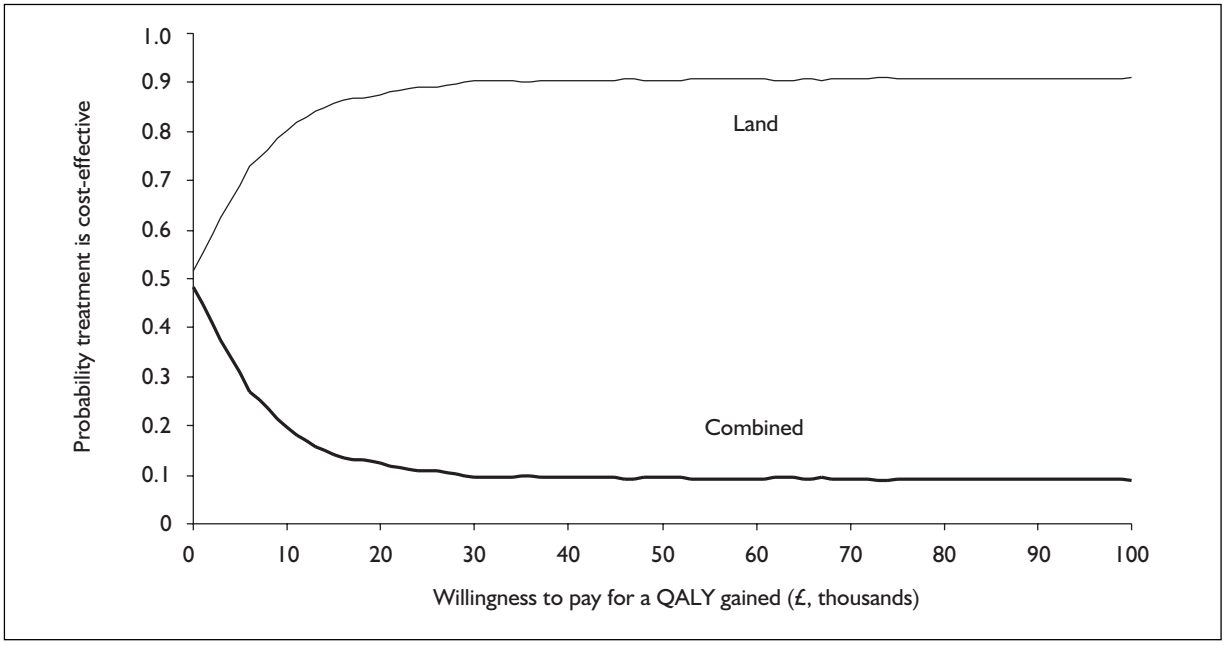

FIGURE 4 *Cost-effectiveness acceptability curve showing the probability of combined treatment being more cost-effective for a range of maximal values that society might be willing to pay for an additional QALY*

lower probability of being cost-effective than land-based treatment. As the willingness to pay for a QALY gained increases, land treatment has a higher probability of being cost-effective. If society is willing to pay £29,000, the probability of land-based therapy being the more cost-effective form of management reaches 90%.

Sensitivity analysis

Using only complete case results (excluding those without 6-month data) made no difference to QALY results (mean QALY differential –0.054, 95% CI –0.13 to 0.02) but increased the cost differential between combined and land-based interventions (mean cost differential £58.80,

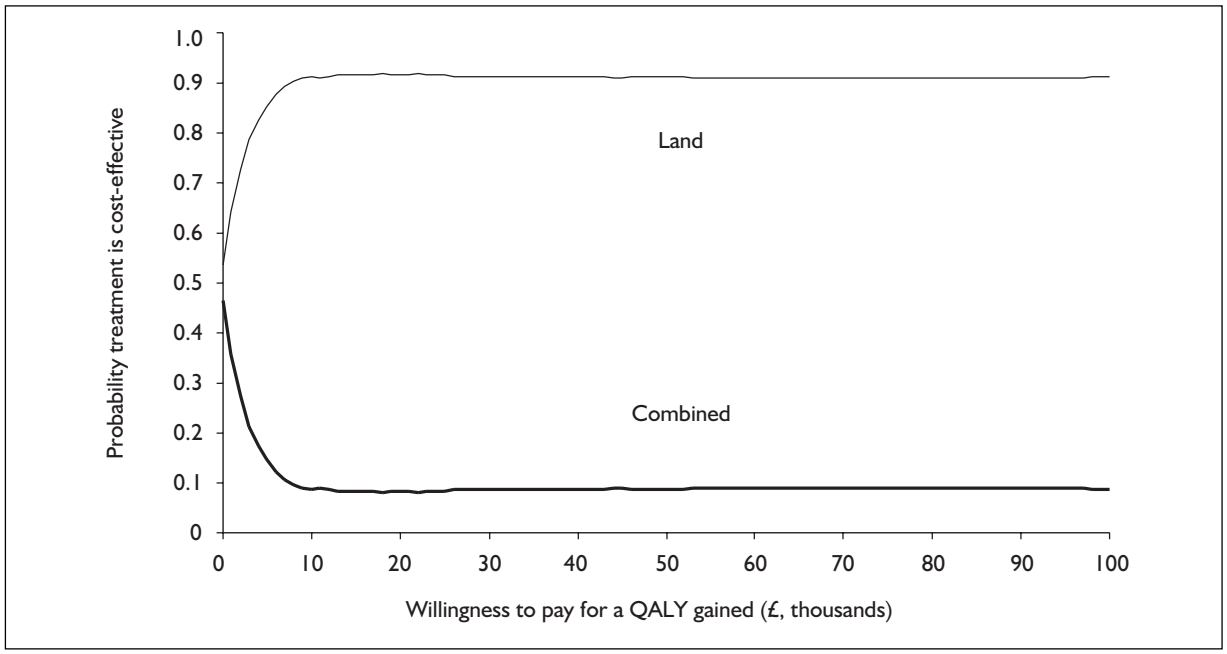

FIGURE 5 *Cost-effectiveness acceptability curve with only complete follow-up data at 6 months*

95% CI –£32 to £14). The uncertainty in the differences in costs and QALYs is represented in a cost-effectiveness acceptability curve (*Figure 5*). This analysis did not affect conclusions drawn from primary analysis.

Similarly using PSSRU fixed costs for land-based sessions, £0.0841 per minute (instead of costs from Staffordshire, the only hospital with any cost data) did not influence the outcome of this trial, as cost per patient in the **combined** group was increased to £2042.38 and cost per patient in the **land** group was increased to £2092.88, mean cost differential £50.50. Relating this difference in total costs to the incremental gain in QALYs gained associated with land-based treatment gave an incremental cost per additional QALY gained of £1052.

Chapter 4
Discussion

Hydrotherapy is an expensive modality of treatment often prescribed in JIA to reduce pain and improve physical function, fitness and HRQoL, and might improve the long-term health outcome of this population.[21,22,26,92] However only three studies have examined the effectiveness of hydrotherapy in JIA,[30–32,93] and there are no published studies of the costs or cost-effectiveness of hydrotherapy in this population.

This trial was designed to compare combined hydrotherapy and land-based physiotherapy with land-only physiotherapy. As the interventions lasted the same time (1 hour in each group), it was hypothesised that differences in outcome between the groups would reflect the effects of hydrotherapy, and that resource and societal costs would be greater in the **combined** group owing to the fixed costs of hydrotherapy pools.

Clinical and cost-effectiveness

Greater improvements were expected in disease outcome following combined treatment. Advantageous hydrodynamic and physiological effects of immersion and exercise in water allow greater freedom of movement and more effective rehabilitation.[24,33,34,45,46,54,55,94,95] Improvement in disease would presumably lead to improved HRQoL and increased QALYs gained, which would offset high fixed costs. However, the gains in disease improvement during intervention were insufficient to affect HRQoL meaningfully (based on results from the EQ-5D) and have QALYs gained in either group, and although more patients improved in the **land** than the **combined** group, the difference was neither clinically or statistically significant. These results are similar to previous studies with no difference between land-based therapy and hydrotherapy in patients with arthritis.[24,30,50]

That no differences were apparent may be a consequence of the small sample size giving an underpowered trial, or the additional effects of exercise in water do not improve disease outcome any more than land exercise only. Nevertheless, disease improved in both groups and, most important, there was little evidence of exacerbated disease activity during intervention, indicating that the treatments are safe.

Unfortunately, there are no studies available for comparison to help resolve some of the contradictive findings of this trial. A reduction in many of the resource use items implies improved health, which would be expected to be reflected in increased HRQoL, yet HRQoL did not change. It may be that the use of the EQ-5D was inappropriate because it was not designed to measure children's health status, uses adult population preferences and may not be responsive to real change in this population.

Furthermore, outliers could have affected costs and outcomes, which is a very real concern given the small sample size (as was demonstrated by one patient taking Enbrel, a new and very expensive drug, given as twice-weekly injections at 0.4 mg/kg; this drug costs £95.46 per injection). In addition, estimates of mean QALYs gained may have been affected by the difference in mean EQ-5D scores at baseline, which was greater in the **combined** group (0.63) than the **land** group (0.54). The mean additional QALYs gained in the **land** group might have been overestimated because HRQoL was worse and therefore improvement could be greater when compared with the **combined** group (the most a score could increase was 0.37 in the **combined** group but 0.46 in the **land** group).

Furthermore, fixed costs for land-based physiotherapy were based on just one hospital, which was not actually involved in the study (Staffordshire), and there were no data on capital costs. A sensitivity analysis was undertaken to explore the impact of using alternative fixed costs for land-based physiotherapy which resulted in lower mean costs in the **combined** group (–£50.5); however, this did not change the primary outcome.

In cost-effectiveness analysis, it is now widely agreed that uncertainty in differences in mean costs and QALYs should be presented in terms of cost-effectiveness acceptability curves.[89,90] A cost-effectiveness acceptability curve is shown in *Figure 4* for the base-case analysis. It shows the probability that combined treatment will be more

cost-effective than land-based treatment at different maximum values that society might be willing to pay for an additional QALY. Based on the results of this analysis, there seems to be little case for replacing standard land-based physiotherapy with combined land-based physiotherapy and hydrotherapy for patients with JIA who are stable. This conclusion may not apply to patients with unremitting active disease who could not be entered into the trial because of the exclusion criteria specified. For this group, physiotherapy incorporating hydrotherapy may still be the only option. Until further research is undertaken, both in this population and other diseases, it is not possible to determine whether the initiation and costs of building new hydrotherapy pools is justifiable or cost-effective in the long term.

Nonetheless, this is the first economic evaluation of combined land-based physiotherapy and hydrotherapy ever conducted for this or any other paediatric population, and as such represents an important advance from both economic and methodological perspectives.

Secondary outcomes

Although the analysis of secondary outcome data was exploratory, both groups demonstrated an improvement in all outcomes except pain following intervention, which supports the findings of studies in JIA whereby strength, endurance and contraction of the knee extensors,[53,96,97] fitness[17,98] and HRQoL[32] improved following physiotherapy interventions. Physical HRQoL improved more in the **combined** group using the CHQ, but more in the **land** group using the EQ-5D. Although only exploratory secondary outcomes, the results from the CHQ-PF50 (which asks 50 questions) are given more credence in this trial than the EQ-5D (which asks five questions) as, unlike the EQ-5D, the CHQ has been validated in JIA[69] and was developed for paediatric populations.[70,72] Therefore, comparing groups, greater improvement was found in both endurance, fitness and the physical aspects of HRQoL in the **combined** than the **land** group, in line with findings of smaller hydrotherapy studies in paediatric and adult rheumatological populations.[24,31,42,48–50,54,55] These improvements might be explained by the reduced weightbearing through joints in water, which allows patients to exercise strenuously without pain, risk of injury or stress on articular and soft tissue structures.[45–47] Furthermore, deep water running requires less aerobic metabolism and shorter stride length (less strain on joints, especially if articular movement is restricted) than running in shallow water or on land.[99]

This information will provide baseline data for future trials. The results of this study show a potentially beneficial effect from both land-based physiotherapy and hydrotherapy that should be explored further in a chronic disease with few non-pharmaceutical treatment options.

Methods

Sample size calculation

The original sample size estimate was 100 patients in each arm to detect a statistically significant difference between land-only physiotherapy and a combination of hydrotherapy and land-based physiotherapy at the 5% level with a power of 57% within the trial. A 40% improvement in the **land** group was estimated using data from adult studies because no information was available for JIA. However, 61% patients improved in the **land** group and, even if 200 patients had been recruited into the trial, the power would be reduced to 31% (excluding any effects of deviation from randomised allocation). It is estimated that 400–450 patients were needed to reach the original power of 57%.

Recruitment and selection

One of the problems when recruiting patients for non-medical trials from tertiary centres is that new drugs are being researched all the time. The patients most eligible for physiotherapy research are also those most eligible for drugs trials, they have ongoing disease and benefit from further medical and therapeutic interventions. Furthermore, patients at the severe end of the disease spectrum tend to be excluded as their management is not stable, yet these are the patients who probably gain most benefit from physiotherapy and hydrotherapy interventions. In addition, many community physiotherapists could not provide any treatment, or were not prepared to offer land-based physiotherapy as an alternative to hydrotherapy. Several children and their parents would not consent to being in the **land** group as they enjoyed hydrotherapy when in hospital. Other families were satisfied with outpatient hydrotherapy and would not commit to 2 weeks of intensive treatment because it would be too disruptive to family life, other children would need to be cared for and they could not afford to take time off work. Additionally, adolescents who

had spent much of their earlier years attending hospitals were reluctant to miss school at a crucial time in their education. All these factors in combination with rapidly changing medical advances led to a lower than expected recruitment level and a study population not necessarily most representative of the most common JIA users of hydrotherapy.

Retention

Further difficulties were encountered owing to the practicalities of this type of study. The centres involved in the trial care for patients throughout the UK, and patients need to stay in hospital for intensive physiotherapy if daily commuting is not practical. At the time of designing the trial, this practice was commonplace, but as patient care has become more community-, school- and home-based, hospital wards tend to be occupied by those children who are very ill or have complex disorders. Although children are still admitted to hospital wards for intensive physiotherapy, it is often combined with other medical or healthcare interventions that would exclude them from the trial. Some patients lost eligibility owing to the need for other interventions, or improvement or deterioration of their disease when time lapsed between recruitment and intervention. Furthermore, emergency admissions to wards or the need for a child to stay longer in hospital than expected often led to trial patients being cancelled.

Protocol, standardisation and primary end-point

Protocol violations are inevitable in any clinical trial of this nature because it is unethical to withhold treatments from patients if their condition deteriorates. In addition, hydrotherapy availability cannot be guaranteed because pool equipment and maintenance (such as chlorine pumps and temperature regulators) can fail, leading to pool closures. For these reasons, there were more protocol violations in the **combined** group (10/39) than the **land** group (4/39), which could have affected the results of the trial because patients in the **combined** group received land-based physiotherapy and fewer (by 50% in some cases) treatments.

The study was originally designed so that patients would receive outpatient physiotherapy or hydrotherapy once per week from the end of the intervention period until the 6-month follow-up, the primary end-point. However, questionnaires sent to local physiotherapists prior to the start of this trial revealed that staffing levels, waiting lists or funding might prevent them from providing weekly treatment and that it was not ethically acceptable to parents or physiotherapists to withhold hydrotherapy from patients in the control arm of the study for more than 2 months. The minimum amount of outpatient treatment required for the study was therefore reduced to four or five alternate week sessions and the primary end-point was reduced to 2 months. Nevertheless, the amount of treatment was variable owing to patients not attending, inconvenient treatment times, increased waiting lists and staff absences. Furthermore, although physiotherapists were requested to continue with the patient's randomised allocations, the principal investigator was aware of deviations occurring on at least three occasions. It is therefore not known if the amount of physiotherapy treatment or potential allocation deviation during the follow-up period could have influenced results.

Follow-up assessments could not be performed exactly 2 months after intervention owing to patient, clinic and consultant availability. Patients in the **land** group were poorer attendees than those in the **combined** group, which led to appointments being rearranged and delays in assessment.

Clinical relevance of the trial

Rapid advances in pharmaceutical treatments occurred during the course of this trial, which may have led to the inclusion of patients who no longer required intensive land-based physiotherapy or hydrotherapy treatment. Nonetheless, disease improved in both groups with no exacerbation of symptoms, indicating that physiotherapy treatments are both beneficial and safe. Furthermore, most secondary measures showed mean improvement, which continued at the 6-month follow-up.

However, these results are not generalisable to the whole JIA population owing to selection criteria (patients with unremitting active disease were excluded) and sample size. Until further research is undertaken, in both this population and other diseases, it is not possible to determine whether the additional capital and running costs of hydrotherapy are cost-effective and hence justifiable in the long term.

However, JIA is a disease in which the pathogenesis is unknown and a cure is not available, therefore any treatment that has a

beneficial effect on disease and outcome should be continued. In addition, parents and children reported a preference and greater compliance with hydrotherapy treatment and they perceived treatment as fun and enjoyable. It would therefore be inappropriate to withdraw hydrotherapy from physiotherapy treatments because there was no difference between the two arms of this trial.

Chapter 5
Conclusion

The combination of problems with recruitment, retention and sample size means that recruiting enough patients to be confident that a trial of this design could detect a statistically significant difference between combined hydrotherapy and land-based physiotherapy and land-based physiotherapy only would not be feasible in the UK alone. Furthermore, the trial was only possible for patients who are in a stable condition.

However, the results of this study have determined the proportion of children with JIA who will improve at 2 and 6 months following hydrotherapy and land-based physiotherapy treatments, the standard deviation of that treatment effect, and that adult surrogate measures are not appropriate in paediatric sample size calculations.

In the present study, there was no statistical difference in primary outcome between either group, and both treatments have the potential to be beneficial to the child with JIA. Exploratory analysis of secondary outcome data suggests that HRQoL (measured using the CHQ), fitness and endurance may be more appropriate outcomes for future studies of different modalities of physiotherapy treatment, and until further research is undertaken it is not possible to determine if the initiation and costs of building new hydrotherapy pools is justifiable or cost-effective in the long term.

Recommendations for further study

Based on the results of this study, any similarly sized RCT would be seriously underpowered and inappropriate. It is therefore recommended that a larger study be conducted with less restrictive inclusion and exclusion criteria or that a European study be considered. It is not ethically acceptable to offer 'no treatment' as a substitute for hydrotherapy, and pragmatic studies may be the only logical alternative to a larger study. Although these methodologies are not considered as scientifically robust as well-designed controlled trials, they do reflect current practice, which would improve recruitment and retention, and facilitate the implementation of results. Studies of methodologies in complex interventions such as physiotherapy and hydrotherapy should be considered to improve recruitment and ensure protocol is acceptable to patients and carers in JIA and other diseases.

Future studies should explore the outcomes that physiotherapy aims to improve, such as impairment, physical function, fitness and HRQoL. Comparative studies of hydrotherapy and land-based physiotherapy could use the outcomes that improved more in the **combined** than the **land** group, such as HRQoL and fitness. However, there are currently no measures of impairment, physical function and fitness that have been rigorously tested for reliability, validity and responsiveness to meaningful change in JIA. It is therefore recommended that studies of outcome measurement precede any future trials measuring the effectiveness of any physiotherapy intervention in JIA.

Further research considering the effectiveness of hydrotherapy to the general paediatric population should focus on larger groups that use hydrotherapy more frequently than those with musculoskeletal disease, such as children with neurological dysfunction.

Acknowledgements

We are grateful to all the patients, parents and staff from Great Ormond Street and Birmingham Children's Hospitals, and the Middlesex Adolescent unit, University College London Hospitals, whose collaboration made this research possible. We wish to thank the HTA for their financial support. We also wish to thank the members of the Trial Management Committee, S Maillard, J Scott, S Philips, and Y Rogers; the Data Monitoring and Ethics Committee, B Ansell, B Newman and P Hollingworth; the Trial Steering Committee external members, A Nunn and M Tottman; and also M Hurley, physiotherapy research fellow, for advice and support. In addition, we thank J Granger for recruitment concealment and allocation, C Lucas, L Gerschwitz and N Eagling for their assistance in coordinating the trial, K Murray, C Pilkington, N Hassan, C Ryder and J Gardner Medwyn for their assistance in assessment and recruitment and S Sawhney, K Davies and E Crawley for their assistance in recruitment. We also thank the R & D Department at University College London Hospitals and Rheumatology Department at University College London.

We thank all physiotherapists at participating centres and outpatient departments as listed below for providing physiotherapy treatment for patients in the study. Ysguol Crug Glas Croft Childrens Centre; Bury St Edmonds; Queens, Burton on Trent; Brierley Health Centre, Wordesley; Northwick Park, Middlesex; Ipswich; Horsham, Sussex; Rivers, Herts; West Middlesex; Southend; Hillingdon, Middlesex; Royal Alexander, Brighton; Wordesley, Dudley; Ashford, Isleworth; Princess Royal, Haywards Heath; St Georges, Essex; Bedford; Queen Elizabeth, Herts; Dartford and Livingstone; Queen Marys, Sidcup; Luton and Dunstable; Basildon; Royal Gwent; St Heliers, Surrey; Conquest, Sussex; Chelmsford; Richard Clousley School, London; Queen Marys, Surrey; Finchley Memorial, London; Mile End, London; Tadworth Court, Surrey; Darent Valley, Kent; Maple Down School, Cricklewood; Sheldon Centre, London; Frimley, Guildford; Chase Farm, London; Dover Health Centre; St Leonards on Sea.

Contribution of authors

Heather Epps (Specialist Paediatric Physiotherapist and Consultant in Hydrotherapy) was the principal investigator, responsible for designing, organising, coordinating and managing the trial, designing treatment protocol, training therapists, recruitment, assessment, data collection, data input, reporting, administration and writing all sections in the final report except the cost-effectiveness analysis. Laura Ginnelly (Research Fellow) was responsible for the cost-effectiveness analysis and wrote the economics sections in the final report. Martin Utley (Deputy Director) was the trial statistician, liaised with DMEC, and assisted in drafting the final report. Taunton Southwood (Professor of Paediatric Rheumatology) was coapplicant on the NHS grant, a member of the steering committee, responsible for the recruitment of patients at Birmingham Children's Hospital, assisted in drafting the interim and final reports, and provided strategic and clinical support for Dr Epps. Steve Gallivan (Professor of Operational Research) was coapplicant on the NHS grant, provided statistical advice and assisted in drafting the final report. Mark Sculpher (Professor of Health Economics) provided overall supervision for the cost-effectiveness analysis and wrote the economics sections in the final report. Patricia Woo (Professor of Paediatric Rheumatology) was the coapplicant on the NHS grant, a member of the steering committee, was involved in the recruitment of patients, assisted in drafting the interim and final reports and publications, and provided strategic and clinical support for Dr Epps.

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Appendix 1

Stable on medication

Medication inclusion criteria for trial patients:

1. No patient may enter the study within 1 month of intravenous or intra-articular steroids.
2. No patient may enter the study within 2 months of starting disease-modifying antirheumatic drugs.
3. No more than 20% variability in the dose of disease-modifying antirheumatic drugs is acceptable during the intervention period.
4. A change from oral to subcutaneous disease-modifying antirheumatic drugs is acceptable only if there is no additional increase in dosage. A change to subcutaneous represents an effective 20% increase in bioavailability of methotrexate.
5. No more than 25% variability in the dose of steroids is acceptable during the intervention period.
6. To remain eligible for the study, there can be no more than one change in non-steroidal anti-inflammatory drugs.

Appendix 2

Standard land exercises

Hold relax and stretches

All stretches except for the neck whereby the patient assists the movement incorporate the use of slight traction. The stretches are performed three times each at each joint with limited movement in every restricted anatomical direction.

Upper limbs

Shoulder stretches

Abduction

Patient position	Supine on a plinth with the shoulder abducted and elbow flexed.
Therapist position	Standing at the side of the patient, hands on the anterior proximal aspect of the upper arm and the shoulder girdle. Forearm supporting the patient's forearm.
Action	The patient pushes against the therapist's distal hand. This position is held for a count of 5. The arm is relaxed and the physiotherapist moves the shoulder into abduction or flexion until limited by discomfort or anatomical restriction occurs.

Flexion (>90°)

Patient position	Supine on a plinth with the shoulder abducted and elbow flexed.
Therapist position	Standing at the head of the plinth, hands on the posterolateral proximal aspect of the upper arm and the scapula. Forearm supporting the patient's forearm.
Action	The patient pushes against the therapist's distal hand. This position is held for a count of 5. The arm is relaxed and the physiotherapist moves the shoulder into flexion while mobilising the scapula to assist scapulothoracic motion until limited by discomfort or anatomical restriction occurs.

Flexion (<90°)

As above but the therapist faces the patient, standing at the side of the plinth. During passive movement the therapist uses the other hand to prevent shoulder girdle elevation rather than mobilising the scapula.

Extension

Patient position	Supine with the arm over the end of the plinth in extension with the elbow flexed.
Therapist position	Facing the patient, standing at the side of the plinth. Hands on the anterolateral proximal aspect of the upper arm and the shoulder girdle. Forearm supporting the patient's forearm.
Action	The patient pushes against the therapist's distal hand. This position is held for a count of 5. The arm is relaxed and the physiotherapist moves the shoulder into extension until limited by discomfort or anatomical restriction occurs.

Internal rotation

Patient position	Supine on a plinth with the elbow flexed to approximately 90° and the arm away from the body as close to 90° abduction as possible.
Therapist position	Facing the patient, standing at the side of the plinth supporting the posterior distal aspects of the forearm with one hand. The shoulder girdle and upper arm supported by the therapist's other upper arm over the shaft of the humerus.

Action	The patient pushes against the therapist's distal hand. This position is held for a count of 5. The arm is relaxed and the physiotherapist moves the shoulder into internal rotation until limited by discomfort or anatomical restriction occurs.

External rotation

Patient position	Supine on a plinth with the elbow flexed to approximately 90° and the arm away from the body as close to 90° abduction as possible.
Therapist position	Facing the head of the plinth, standing at the side of the patient supporting the anterior distal aspects of the forearm with one hand. The shoulder girdle and upper arm supported by the therapist's other upper arm over the shaft of the humerus.
Action	The patient pushes against the therapist's distal hand. This position is held for a count of 5. The arm is relaxed and the physiotherapist moves the shoulder into internal rotation until limited by discomfort or anatomical restriction occurs.

Elbow stretches

Flexion

Patient position	Supine on a plinth with the arm by the trunk.
Therapist position	Facing the patient, standing to the side with hands on the posterior distal aspects of the arm and forearm.
Action	The patient pushes against the therapist's distal hand. This position is held for a count of 5. The arm is relaxed and the physiotherapist moves the elbow into flexion until limited by discomfort or anatomical restriction occurs.

Extension

Patient position	Supine on a plinth with the arm by the trunk.
Therapist position	Facing the patient, standing to the side with hands on the anterior distal aspect of the forearm. The shoulder girdle and upper arm supported by the therapist's other upper arm over the shaft of the humerus.
Action	The patient pushes against the therapist's distal hand. This position is held for a count of 5. The arm is relaxed and the physiotherapist moves the elbow into extension until limited by discomfort or anatomical restriction occurs.

Radio-ulna stretches

Supination

Patient position	Supine on a plinth with elbow flexed to approximately 90°, the arm by the trunk and the forearm in supination.
Therapist position	Facing the patient, standing to the side. One hand on the distal anterior upper arm and the palm of the other hand over the anterolateral aspect of the wrist and carpus.
Action	The patient pushes against the therapist's distal hand. This position is held for a count of 5. The forearm is relaxed and the physiotherapist moves the forearm into supination until limited by discomfort or anatomical restriction occurs.

Pronation

Patient position	Supine on a plinth with elbow flexed to approximately 90°, the arm by the trunk and the forearm in pronation.
Therapist position	Facing the patient, standing at their side. One hand on the distal anterior upper arm and the palm of the other hand over the posterolateral aspect of the wrist and carpus.
Action	The patient pushes against the therapist's distal hand. This position is held for a count of 5. The forearm is relaxed and the physiotherapist moves the forearm into pronation until limited by discomfort or anatomical restriction occurs.

Wrist stretches

Flexion

Patient position	Sitting at a table with the elbow flexed to approximately 90° with the forearm supinated.
Therapist position	Facing the patient, with one hand supporting the posterior and lateral surfaces of the distal forearm and the thumb of the other hand over the anterior carpus to correct any subluxation.
Action	The wrist is flexed.

Extension

Patient position	Sitting at a table with the elbow flexed to approximately 90° with the forearm supinated.
Therapist position	Facing the patient, with one hand supporting the posterior and lateral surfaces of the distal forearm and the thumb of the other hand over the anterior carpus to correct any subluxation.
Action	The wrist is extended.

Thumb and finger stretches

Note: if flexor tendons are involved the holds may be adapted to either side of the joint.

MCP I movements

Patient position	Sitting at a table with the elbow flexed to approximately 90° with the forearm midway between supination and pronation.
Therapist position	Sitting facing the patient. Stabilise the first metacarpal with the thumb and index finger of one hand while moving the first proximal phalanx with the thumb and index finger of the other hand.
Action	The joint is moved into flexion, extension, abduction, adduction and circumduction.

PIP I–V. Flexion and extension

Patient position	Sitting at a table with the elbow flexed to approximately 90° with the forearm midway between supination and pronation.
Therapist position	Sitting facing the patient. Stabilise the proximal phalanxes with the thumb and index finger of one hand while moving the middle phalanxes with the thumb and index finger of the other hand.
Action	The joints are moved into flexion and extension.

DIP II–V

Patient position	Sitting at a table with the elbow flexed to approximately 90° with the forearm midway between supination and pronation.
Therapist position	Sitting facing the patient. Stabilise the middle phalanxes with the thumb and index finger of one hand while moving the distal phalanxes with the thumb and index finger of the other hand.
Action	The joints are moved into flexion and extension.

Lower limbs

Hip stretches

Abduction

Patient position	Supine on a plinth with the knees extended and the hip abducted. The opposite lower leg is placed over the end of the plinth with a stool supporting the foot to stabilise the pelvis.
Therapist position	Facing the patient, standing to the side, hands on the medial distal aspect of the upper leg and the opposite iliac crest. The patient then pushes against the therapist's distal hand.
Action	This position is held for a count of 5. The leg is relaxed and the physiotherapist moves the hip into abduction until limited by discomfort or anatomical restriction occurs.

Extension

Patient position	Lying on the side on a plinth with knees flexed and the hip to be stretched extended. The opposite hip is flexed.
Therapist position	Standing behind the patient with one hand on the anterior distal aspect of the upper leg supporting the lower leg on the trunk (iliac crest) and using the other hand to stabilise the trunk. The thigh may be used to stabilise the trunk.
Action	The patient pushes against the therapist's distal hand. This position is held for a count of 5. The leg is relaxed and the physiotherapist moves the hip into extension until limited by discomfort or anatomical restriction occurs.

Flexion

Patient position	Supine on a plinth with the knee and hip flexed. The opposite hip and knee extended. A seatbelt or sandbag may be placed over the opposite proximal upper leg.
Therapist position	Standing facing the patient with one hand on the posterior distal aspect of the upper leg supporting the lower leg on their trunk (iliac crest) and the other hand on the iliac crest.
Action	Using an assistant, sandbag or seatbelt to prevent the opposite hip from lifting off the plinth. The patient pushes against the therapist's distal hand. This position is held for a count of 5. The leg is relaxed and the physiotherapist moves the hip into flexion until limited by discomfort or anatomical restriction occurs.

Internal rotation

Patient position	Prone with the knee flexed to as close to 90° as possible.
Therapist position	Standing facing the patient with one hand on the medial distal aspect of the lower leg and the other hand keeping the pelvis in contact with the plinth.
Action	The patient pushes against the therapist's distal hand. This position is held for a count of 5. The leg is relaxed and the physiotherapist moves the hip into internal rotation until limited by discomfort or anatomical restriction occurs.

External rotation

Patient position	Supine or sitting on a plinth with the knee and hip flexed.
Therapist position	Standing facing the patient with hands on the medial distal aspects of the upper legs.
Action	The patient pushes against the therapist's hands. This position is held for a count of 5. The legs are relaxed and the physiotherapist moves the hip into external rotation until limited by discomfort or anatomical restriction occurs.

Knee stretches

Flexion

Patient position	Prone on a plinth with the knee flexed (the stretch may be performed sitting).
Therapist position	Standing facing the head of the plinth, hands on the anterior aspect distal aspects of the upper and lower leg.
Action	The patient pushes against the therapist's distal hand. This position is held for a count of 5. The leg is relaxed and the physiotherapist moves the knee into flexion until limited by discomfort or anatomical restriction occurs.

Extension

Patient position	Prone on a plinth with the knee extended and a small towel folded under the thigh.
Therapist position	Standing facing the patient, hands on the posterior distal aspects of the upper and lower leg.
Action	The patient then pushes against the therapist's distal hand. This position is held for a count of 5. The leg is relaxed and the physiotherapist moves the knee into extension until limited by discomfort or anatomical restriction occurs.

Patello-femoral

Medial transverse

Patient position	Supine on a plinth or in half lying with the knee slightly flexed on a folded towel.
Therapist position	Standing at the side of the knee with the pads of the thumbs against the lateral borders of the patella.
Action	Displace the patella medially.

Lateral transverse

Patient position	Supine on a plinth or in half lying with the knee slightly flexed on a folded towel.
Therapist position	Standing at the side of the knee with the pads of the thumbs against the medial borders of the patella.
Action	Displace the patella laterally.

Cephalad and caudad

Patient position	Supine on a plinth or in half lying with the knee slightly flexed on a folded towel.
Therapist position	Standing at the side of the knee with the heel of one hand against the superior margin of the patella. The other hand points proximally over the patella (taking care not to apply any compressive forces) with the fingers and thumb passing over the heel of the proximal hand.
Action	Displace the patella in a caudad and/or cephalad direction.

Ankle and foot stretches

Dorsiflexion

Patient position	Supine on a plinth or in half lying with the knee slightly flexed on a folded towel.
Therapist position	Standing beyond the foot, facing the patient with one hand on the distal posterior aspect of the lower leg and the other hand under the heel with the forearm along the plantar surface of the foot.
Action	The therapist dorsiflexes the ankle foot until limited by discomfort or anatomical restriction occurs.

Plantarflexion

Patient position	Supine on a plinth or in half lying with the knee slightly flexed on a folded towel.
Therapist position	Standing beyond the foot, facing the patient with one hand on the distal posterior aspect of the lower leg and the web between the thumb and index finger of the distal hand over the neck of the talus adjacent to the ankle.
Action	The therapist plantarflexes the ankle until limited by discomfort or anatomical restriction occurs.

Intertarsal movements

Patient position	Supine or in half lying with the hip and knee slightly flexed on a plinth.
Therapist position	Standing beyond the foot, facing it, the therapist stabilises the transverse tarsal joint by placing the hand beneath the calcaneus and talus.
Action	The therapist adducts, internally and externally rotates the forefoot from the navicular and cuboid.

Subtalar movements

Patient position	Supine or in half lying with the hip and knee slightly flexed on a plinth.
Therapist position	Standing beyond the foot, facing it with the heel of one hand under the patient's heel. The therapist then stabilises the ankle and talus by placing the other hand posteriorly around the talus and malleolli.
Action	The calcaneus is then moved into adduction and abduction.

MTP and toes

Patient position	Supine or in half lying with the hip and knee slightly flexed on a plinth.
Therapist position	Standing beyond the foot, facing it with the thumb and index finger of one hand proximal to the joint while moving the joint with the thumb and index finger of the other hand.
Action	The joint is moved into flexion and extension.

Trunk and neck

Neck auto-assisted movement

Flexion and extension

Patient position	Supine on a plinth with arms by the side and head over the end of the plinth.
Therapist position	Supporting the head in the hands.
Action	The head is moved into flexion or extension by the patient supported by the therapist.

Rotation

Patient position	Sitting with arms by the side and one hand in front of the ear with the palm flat.
Therapist position	Prevents rotation of the trunk.
Action	The patient rotates the neck and applies own overpressure to the movement.

Side flexion

Patient position	Sitting with arms by the side and one hand in front of the ear with the palm flat.
Therapist position	Prevents elevation of the shoulder girdle.
Action	The patient side flexes the neck and applies own overpressure to the movement.

Trunk stretches

Flexion and extension

Patient position	Sitting with the side resting on the elevated portion of a plinth.
Therapist position	Standing at the side of the patient with one arm around the patient's thoracic cage and the other hand on the near iliac crest.
Action	The therapist flexes and extends the patient's trunk.

Rotation

Positions used will be determined by the lower and upper limb joints that are restricted and or tender.

Patient position	Sitting on the end of a plinth.
Therapist position	Standing on the same side as the rotation at the end of the plinth with legs at a right angle to, and against, the patient's thighs. One hand is placed on the posterior aspect of one shoulder and the other hand on the anterior aspect of the opposite shoulder away from the joint surfaces.
Action	The therapist rotates the patient's trunk.

Patient position	Supine with hips and knees flexed.
Therapist position	Standing facing the patient with hands on the posterior iliac crest and the opposite anterior shoulder or the forearm on the thoracic cage. The therapist prevents shoulder elevation.
Action	The patient rotates the trunk with the assistance of the therapist.

Side flexion

Patient position	Sitting on the end of a plinth.
Therapist position	Standing on the opposite side to the side flexion at the end of the plinth with legs at a right angle to and against the patient's thighs. One hand is placed on the thoracic cage and the other hand on the iliac crest.
Action	The therapist side flexes the trunk.

Active movements and strengthening – stage 1

Active movements will be performed between 10 and 30 times as the patient's strength and mobility improves.

Upper limbs

Shoulder movements

Abduction/adduction and elevation

The patient lifts arms out to the side in standing or supine. Then elevates them above the head aiming for both hands to touch with elbows extended. The patient then returns arms to the side and crosses them over in front of the body.

The patient lies prone and lifts the arm above the head.

Internal rotation and extension

In standing, the patient reaches up behind the back as far as possible.

External rotation

In sitting, the patient reaches up to behind the neck and then takes the hands as far down the back as is possible.

Elbow movements

Flexion and extension

In supine, the patient stretches arms out as straight as possible and then tries to bend them up to touch the shoulders with the hands.

Radio-ulna movements

Supination and pronation

The patient sits with forearm resting on a table and elbow bent and at the side. Then turns the hand over so that it is as flat as possible on the table with the palm facing upwards. Then turns the hand in the other direction so that it is facing the table.

Wrist and fingers

Flexion and extension wrist

The patient sits with forearm resting on a table and elbow bent and at the side. The patient puts hands together with palms facing and tries to lift the elbows up without the hands losing contact (as if praying). Then repeats the exercise but with the backs of the hands in contact and the fingers pointing towards the floor.

The patient then holds the forearm distally and bends the wrist forwards and backwards.

Flexion and extension fingers

The patient sits with the forearm resting on a table and elbow bent and at the side. Patient then makes a fist as tight as possible (with the thumb on the outside) and then stretches fingers out as straight as possible.

Thumb movements

The patient sits with forearm resting on a table and elbow bent and at the side. The forearm is positioned with the palm facing upwards. Patient then moves thumb across palm aiming to touch the base of the fifth finger. The patient then moves the thumb out as far away from the palm as possible.

Lower limbs

Hip movements

Abduction

The patient starts this movement in supine progressing to side lying. Then lifts the leg about 6 inches above the plinth keeping the body straight and the head in line with the body and leg. The underneath leg is flexed for comfort.

Flexion
The patient lies supine and lifts the knee up towards the chest keeping the other leg straight on the plinth if possible.

The patient then lifts the leg just above the plinth keeping the knee as straight as possible.

Extension
The patient lies on the side and then progresses to prone. Then lifts the leg towards the ceiling keeping the knee straight and the pelvis in contact with the plinth.

External rotation
The patient sits on a plinth and lifts the foot up to touch the opposite knee. Patient then lies supine and lets the legs fall outwards keeping the hips and knees bent and the feet as close together as possible.

Knee movements
Flexion
The patient lies prone and bends the knee and tries to touch the buttocks with the foot.

Extension
The patient lies supine and tries to push the knee straight so that it touches the plinth.

The patient then sits on a plinth with the knee flexed and lifts the foot until the knee is straight.

Foot and ankle
Dorsiflexion and plantarflexion
The patient sits with knees slightly flexed and pulls toes up towards the ceiling. Patient then pushes toes down towards the plinth.

Inversion and eversion
The patient sits with knees slightly flexed and turns the foot in towards the other foot and then out away from the other foot. Younger children will circle their ankles.

Neck and trunk

Neck movements
Flexion and extension
The patient sits and bends head forwards trying to touch chest with the chin and then backwards to look at the ceiling until a stretch is felt at the back and then the front of the neck.

Rotation
The patient turns head to look over one shoulder and then the other.

Side flexion
The patient tries to touch shoulder with ear without lifting the shoulder. Then repeat this to the other side.

Trunk movements
Flexion
The patient lies supine with hips and knees bent. Patient then lifts pelvis off the plinth.

The patient lies supine with hips and knees bent. Then flattens the back onto the plinth (pelvic tilt).

The patient lies supine with hips and knees bent. Then lifts head off the plinth and reaches forwards with the hands if possible (sit up).

The patient lies supine with hips and knees bent and lifts bottom off the plinth (bridging).

Extension
The patient lies prone and lifts head (and feet if possible) off the plinth.

Rotation
The patient lies supine with hips and knees bent. Then lets knees fall to one side of the body and then the other.

Active movements and strengthening – stage 2

Weights will only be used if the joints are assessed to be inactive by the treating physiotherapist.

All exercises are then reduced to 10 times each and a 1-pound weight is attached to the wrist or ankle. The exercises are then increased up to 30 times each.

Active movements and strengthening – stage 3

All exercises are then reduced to 10 times each and a 2-pound weight is attached to the wrist or ankle. The exercises are then increased up to 30 times each.

Active movements and strengthening – stage 4

All exercises are then reduced to 10 times each and a 3-pound weight is attached to the wrist or ankle. The exercises are then increased up to 30 times each.

Functional activity

- Sit to stand and vice versa.
- Up and down on tip toes.
- Step ups.
- Marching on the spot.
- Getting up and down off the floor.

Aerobic activity

The time will gradually be increased from 5 min up to a maximum of 20 min within the session depending on the patient's level of fitness.

- Static bike.
- Step machine.
- Side steps.
- Walking forwards and backwards.
- Skipping.
- Hopping.
- Bunny jumps.
- Cycling legs in the air with concurrent arm punches into the air.

Appendix 3

Standard hydrotherapy exercises

Stretches

Stretches may be performed with floats if the patient's joints are inactive. The same stretches will be performed without floats if the patient has active or unstable joints or if specific ligament laxity or joint deformity is present, for example stretching into hip abduction with a valgoid knee. Stretches will be performed three times in each restricted anatomical movement. If the wrist is involved then floats will be placed above the wrist rather than held in the hand for upper limb stretches.

Upper limbs

Shoulder stretches

Abduction flexion up to 90°

Patient position	Standing with the water at shoulder level and the arm abducted or flexed as high as possible with the elbow extended and holding a float in the hand.
Therapist position	Behind the patient stabilising the shoulder girdle.
Action	Push the float down into the water. The position is held for a count of 5. The arm is then relaxed allowing it to move up in the water producing a stretch until limited by discomfort or anatomical restriction occurs.

Any range

Patient position	In supine float with the body supported with the relevant flotation with the arm elevated and abducted.
Therapist position	At the side of the patient with one hand on the distal anteromedial aspect of the upper or lower arm depending on comfort and the other stabilising the trunk.
Action	The patient pushes against the therapist's distal hand. The position is held for a count of 5. The arm is then relaxed and the therapist moves the limb into elevation or abduction until discomfort or anatomical restriction occurs.

Patient position	Prone on a half plinth with the shoulder elevated and the elbow extended with a float in the hand.
Therapist position	Standing at the side of the patient, stabilising the pelvis.
Action	Push the float down into the water. The position is held for a count of 5. The arm is then relaxed allowing it to move up in the water producing a stretch until limited by discomfort or anatomical restriction occurs.

Patient position	In prone float with the body supported with the relevant flotation and the shoulder flexed.
Therapist position	In front of the patient with one hand on the distal anterior aspect of the upper or lower arm. The other hand is placed on the shoulder girdle.
Action	The patient pushes against the therapist's distal hand. The position is held for a count of 5. The arm is then relaxed and the therapist moves the limb into flexion until discomfort or anatomical restriction occurs.

End-of-range elevation

Patient position	Side lying with a large ring around the neck and underneath the arm with a float in the hand.
Therapist position	Supporting the patient's pelvis on the hip.

Internal and external rotation

Patient position	In prone on a plinth with the elbow flexed to about 90° and the shoulder abducted as much as possible holding a float in the hand.

Therapist position	Standing at the side of the patient with one hand fixing the trunk and the other on the distal upper arm maintaining the degree of abduction achieved.
Action	Move the shoulder into internal or external rotation. Push the float down into the water. The position is held for a count of 5. The arm is then relaxed allowing it to move up in the water producing a stretch until limited by discomfort or anatomical restriction occurs.

Elbow stretches

Flexion/extension

Patient position	Inclined standing or sitting with the arm by the side for flexion and the shoulder abducted for extension with a float in the hand.
Therapist position	Standing behind the patient stabilising the position of the upper arm.
Action	Flex or extend the elbow and then push the float down into the water. The position is held for a count of 5. The arm is then relaxed allowing it to move up in the water producing a stretch until limited by discomfort or anatomical restriction occurs.

Wrist stretches

Flexion and extension

Patient position	Standing holding a small float.
Therapist position	Stabilises the distal forearm.
Action	Flex the wrist with the forearm supinated and under the water. Extend the wrist with the forearm pronated and under the water.

Thumb and finger stretches

Note: if flexor tendons are involved the holds may be adapted to either side of the joint.

MCP I movements

Patient position	Sitting on a plinth or step or stands with the elbow flexed to approximately 90° with the forearm midway between supination and pronation.
Therapist position	Facing the patient. Stabilise the first metacarpal with the thumb and index finger of one hand while moving the first proximal phalanx with the thumb and index finger of the other hand.
Action	The joint is moved into flexion, extension, abduction, adduction and circumduction.

PIP I–V. Flexion and extension

Patient position	Sitting on a plinth or step or standing with the elbow flexed to approximately 90° with the forearm midway between supination and pronation.
Therapist position	Facing the patient. Stabilise the proximal phalanxes with the thumb and index finger of one hand while moving the middle phalanxes with the thumb and index finger of the other hand.
Action	The joints are moved into flexion and extension.

DIP II–V

Patient position	Sitting on a plinth or step or standing with the elbow flexed to approximately 90° with the forearm midway between supination and pronation.
Therapist position	Facing the patient. Stabilise the middle phalanxes with the thumb and index finger of one hand while moving the distal phalanxes with the thumb and index finger of the other hand.
Action	The joints are moved into flexion and extension.

Lower limbs

Hip stretches

Abduction

Patient position	Standing facing the wall with a float around the knee and the hip in abduction.

Therapist position	Stand behind the patient and stabilise the pelvis and trunk.
Action	Push the float down into the water. The position is held for a count of 5. The leg is then relaxed allowing it to move up in the water producing a stretch until limited by discomfort or anatomical restriction occurs.

Extension

Patient position	Standing facing the wall holding the rail, the patient flexes one knee against the wall to stabilise the pelvis. A float is placed on the other knee.
Therapist position	Stand behind the patient and stabilise the pelvis and trunk.
Action	Push the float down into the water. The position is held for a count of 5. The leg is then relaxed allowing it to move up in the water producing a stretch until limited by discomfort or anatomical restriction occurs.

Flexion up to 50°

Patient position	Supine float.
Therapist position	Facing the patient with the patient's knees over the shoulder.
Action	Therapist moves the patient in a caudad/cephalad direction.

Flexion beyond 50°

Patient position	Standing (inclined standing for the last 20°) facing the rail with a float around the knee.
Action	Push the float down into the water. The position is held for a count of 5. The leg is then relaxed allowing it to move up in the water producing a stretch until limited by discomfort or anatomical restriction occurs.

Rotation

Patient position	Standing facing the rail with the hip and knee flexed to 90° and a float around the ankle.
Action	Push the float down into the water. The position is held for a count of 5. The leg is then relaxed allowing internal or external rotation to occur until limited by discomfort or anatomical restriction occurs.

Knee stretches

Flexion

Patient position	Standing facing the wall holding the rail with a float placed above the ankle with the hip extended and knee flexed. The hip is slightly flexed for the last 20° of movement.
Action	Push the float down into the water. The position is held for a count of 5. The leg is then relaxed allowing flexion to occur until limited by discomfort or anatomical restriction occurs.

Extension

Patient position	Sitting on a step, plinth or submerged stool with the knee extended and stabilising the thigh with the hand. A float is placed on the ankle.
Therapist position	The therapist may need to stabilise the thigh.
Action	Push the float down into the water. The position is held for a count of 5. The leg is then relaxed allowing extension to occur until limited by discomfort or anatomical restriction occurs.
Patient position	Squatting with the back against the wall and one leg extended out in front. A float on the knee.
Action	Raise the leg as far as possible without flexing the knee. The position is held for a count of 5 and the patient then attempts to raise the leg further until limited by discomfort or anatomical restriction occurs.

Ankle and foot stretches

Dorsiflexion

Patient position	Sitting on a plinth, step or submersed stool with the knee slightly flexed.
Therapist position	Facing the patient. Hand under the heel and forearm along the plantar aspect of the foot.
Action	Stretch the ankle and foot into dorsiflexion.

Plantarflexion

Patient position	Sitting on a plinth, step or submersed stool with the knee slightly flexed.
Therapist position	Facing the patient. Hand under the heel and web space between thumb and index finger of other hand over the neck of the talus.
Action	Stretch the ankle and foot into dorsiflexion.

Inversion and eversion

Patient position	Sitting on a plinth, step or submersed stool with the knee slightly flexed.
Therapist position	Facing the patient. One hand beneath the calcaneus and talus and the other along the cuboid and navicular.
Action	Therapist adducts, internally and externally rotates the forefoot from the navicular and cuboid.

Subtalar movements

Therapist position	Standing beyond the foot, facing it with the heel of one hand under the patient's heel. The therapist then stabilises the ankle and talus by placing the other hand posteriorly around the talus and malleolli.
Action	The calcaneus is then moved into adduction and abduction.

MTP and toes

Patient position	Supine or in half lying with the hip and knee slightly flexed on a plinth.
Therapist position	Standing beyond the foot, facing it with the thumb and index finger of one hand proximal to the joint while moving the joint with the thumb and index finger of the other hand.
Action	The joint is moved into flexion and extension.

Trunk and neck

Neck stretches

Rotation

Patient position	In supine float.
Therapist position	Supporting the head with the arm.
Action	The therapist lifts or pushes the shoulder down to rotate the body on the head.

Side flexion

Patient position	In supine float.
Therapist position	Supporting the head with the arm.
Action	The therapist pushes down on the shoulder girdle to move the body away from the head.

Extension and flexion

Patient position	In supine float.
Therapist position	Supporting the head with the arm.
Action	The therapist flexes and extends the neck by moving the head.

Trunk stretches

Flexion and extension

Patient position	Standing facing the wall.
Action	Walks feet up the wall allowing the hips and knees to bend until a stretch is felt on the back. Push the legs away from the wall allowing the patient to lift up towards the surface of the water.

Flexion

Patient position	Side float.
Therapist position	Stand behind the patient and support the pelvis.
Action	Flex the trunk by the therapist moving the patient into extension and the 'drag' and momentum of the movement enabling a stretch into flexion.

Thoracic extension

Patient position	Facing the wall, holding the rail with the feet enough paces away from the wall to allow the shoulders to be in the water.
Action	The patient lifts alternative legs up in the water for a count of 5. The patient then pushes the body away from the wall keeping the pelvis down in the water until a stretch is felt. Then hold the position for a count of 5.

Rotation

Patient position	Supine float with the body and the patient holding the rail. A float is placed above both ankles and the knees are flexed to approximately 90°.
Therapist position	May need to stabilise the upper trunk.
Action	The patient allows the float to move towards the surface of the water into either right or left rotation. Then pushes the float down into the water. The position is held for a count of 5. The legs are then relaxed allowing them to move up in the water producing a stretch until limited by discomfort or anatomical restriction occurs.

Side flexion

Patient position	Facing the wall holding the rail. A float is placed around the knees. The knees are then either flexed or extended depending on the depth of the pool.
Therapist position	Stabilising the upper trunk.
Action	The patient allows the legs to move up in the water. Then pushes the float down into the water. The position is held for a count of 5. The legs are then relaxed allowing them to move up in the water producing a stretch until limited by discomfort or anatomical restriction occurs.

Seaweeding may be used for very young children.

Strengthening – stage one

Starting positions are adapted so that buoyancy is counterbalanced. Each exercise is performed up to 30 times each for the movements that are anatomically restricted or where muscle weakness has been identified.

Upper limbs

Shoulder

Abduction

In supine float with the body supported with the relevant flotation (with a float above the wrist) and the feet under the rail or lying supine on a plinth.

Flexion and extension

Floating on the side with support from the physiotherapist and a float around the wrist.

Rotation

In standing with the arm by the side and elbow flexed to 90°.

Elbow

Flexion and extension

In supine float with the body supported with the relevant flotation (with a float above the wrist) and the feet under the rail or lying supine on a plinth.

Wrist and fingers
All movements
In standing or sitting on a plinth, step or submersed stool.

Lower limbs
Hip
Flexion and extension
Floating on the side with support from the physiotherapist or holding the rail with a float around the ankle.

Abduction
In supine float holding the rail with the body supported with the relevant flotation with a float around the ankle.

Rotation
In standing facing the wall holding the rail. The knee is flexed to about 90° and the hip in neutral.

Knee
Flexion and extension
Floating on the side holding the rail with a float around the ankle. The physiotherapist stabilises the hip.

Ankle and foot
All movements
Incorporated into the knee movements.

Trunk
Flexion and extension
Floating on the side with support from the physiotherapist or holding the rail with a float around the ankle and pelvis.

Rotation
The patient faces the wall holding the rail. The knees are then flexed to approximately 90°.

Side flexion
In supine float holding the rail with the body supported with the relevant flotation with a float around the ankle. The physiotherapist stabilises the upper body if necessary.

Strengthening – stage two

Starting positions are adapted so that buoyancy is resisted, speed of the movement is increased and/or bats/flippers are used. The exercises are increased up to 30 times. The upper limb exercises do not need to be incorporated if there is no upper limb involvement.

Upper limbs
Shoulder
Abduction
Use buoyancy counterbalanced position or standing and increase speed, then add a bat if wrist is unaffected.

Flexion and extension
Use standing position and increase speed, then add a bat if wrist is unaffected. Can also be performed in prone float.

Elbow
Flexion and extension
Use standing position and increase speed, then add a bat if wrist is unaffected.

Wrist and fingers

All movements

In standing or sitting on a plinth, step or submersed stool. Keep the arm by the side with the elbow flexed to about 90°. Increase speed of movements or use a bat.

Lower limbs

Hip

Flexion

In prone float or on a plinth. Standing increase speed and use flippers if ankles are unaffected.

Extension

In supine float (preventing the trunk from extending). Standing increase speed and use flippers if ankles are unaffected.

Abduction

Floating on the side with support from the physiotherapist or holding the rail. Standing, increase speed and use an armband at the knee.

Knee

Flexion

In supine float up to 90° and prone float beyond 90°. Use speed sitting on a submersed stool or step. Alternatively incorporate into the hip flexion and extension exercise in standing.

Extension

In prone float or on a plinth with the hip stabilised. Alternatively incorporate into the hip flexion and extension exercise in standing.

Ankle and foot

All movements

Incorporate into the hip flexion and extension exercise in standing. Increase speed and use a flipper.

Trunk

Flexion

In prone float. Alternatively use the buoyancy counterbalanced position on the side and increase the speed of movement/deflate the float around the ankle.

Extension

Supine float holding the rail. Alternatively use the buoyancy counterbalanced position on the side and increase the speed of movement/deflate the float around the ankle.

Rotation

In supine float with the knees flexed to approximately 90°. Increase the speed of movement/deflate the float around the ankle.

Side flexion

Floating on the side with support from the physiotherapist. Alternatively in supine float holding the rail with a float around the ankle, increase the speed of movement/deflate the float around the ankle.

Strengthening – stage three

Add floats to all positions whereby speed can be increased as above. The amount of inflation will depend on the size of the child and their muscle strength. All exercises will be increased up to 30 times each. The upper limb exercises do not need to be incorporated if there is no upper limb involvement.

General aerobic

Time will gradually be increased from 5 min up to a maximum of 20 min within the session depending on the patient's level of fitness.

Include general games for young children. Younger children will perform the same movements with a ring around their trunk so that they are free floating. The programme will depend on the child's level of exercise tolerance and joint involvement.

Leg movements:

- Jogging on the spot.
- High knee raises.
- Scissor kicks.
- Star jumps.
- Various forms of bobbing and jumping.

Concurrent arm movements below the water:

- Punching.
- Flexion/extension at the elbows.
- Flexion/extension at the shoulders.
- Abduction/adduction at the shoulders.
- Clapping.

Simulated or real functional activity

Only if the child is unable to perform them on land:

- Supine to sitting and vice versa.
- Supine to prone and vice versa.
- Sitting to standing and vice versa.

If the depth of the water allows or on a step if necessary:

- Two-point kneeling and one-point kneeling to standing and vice versa.
- Running, jumping, skipping, hopping, steps and walking.

Appendix 4

Protocol violations

	Allocated treatment	Treatment changed beyond protocol	Number of treatments	Drugs changed beyond protocol
1	Combined	6 hydrotherapy and 6 land	12	IAS joint injection
2	Combined	5 hydrotherapy and 10 land	15	
3	Combined	All hydrotherapy in same week	16	Intravenous steroids and DMARDs
4	Combined	4 hydrotherapy and 12 land	16	
5	Combined	7 hydrotherapy and 9 land	16	
6	Combined	7 hydrotherapy and 8 land	15	
7	Combined	6 hydrotherapy and 9 land	15	
8	Combined	6 hydrotherapy and 9 land	15	
9	Combined	8 land (cross over)	8	
10	Combined	4 hydrotherapy and 4 land	8	
11	Combined	16 land (cross over)	16	
12	Combined	16 land (cross over)	16	
13	Combined	8 land (cross over)	8	
14	Land	15 land	15	
15	Land	13 land	13	
16	Land	15 land	15	
17	Land	14 land	14	
18	Land	13 land	13	
19	Land	26 land	26	
20	Land	14 land	14	
21	Land	26 land	26	Intravenous steroids
22	Land	8 land (withdrew consent)	8	
23	Land	8 hydrotherapy and 8 land (withdrew consent /cross over)	16	
24	Land			IAS joint injection

IAS, intra-articular steroidal.

Appendix 5

Steps taken to boost recruitment

The following steps were taken:

1. A questionnaire was sent to physiotherapists to determine hydrotherapy availability and requesting support for the trial.
2. The British Paediatric Rheumatology group, Chartered Society of Physiotherapy, Frontline, and Hydrotherapy and Paediatric Physiotherapy SIGs (special interest groups) published letters requesting support from physiotherapists treating children with JIA.
3. Physiotherapists and heads of department were contacted by telephone and given trial details.
4. Information sheets were sent to physiotherapists to distribute to patients.
5. Letters were sent to the Chronic Children's Arthritis Association and Young Arthritis Care asking parents and children interested in the trial to contact one of the centres. Posters and information sheets were posted in clinics.
6. Local rheumatology consultants were contacted to help with recruitment.

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We look forward to hearing from you.

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ISSN 1366-5278