



CRYING, UNSETTLED, DISTRESSED INFANTS: EFFECTIVENESS STUDY

CUTIES-CH – Co-investigator version of protocol

IRAS ID268925-CH – v.1.4 23.06.2021

This document provides the main guidelines for procedures to follow by osteopathic clinicians who have received Good Clinical Practice Training for the CUTIES trial. It is a summary document that provide all the necessary information from the study protocol for co-investigators.

Additional information and documentation can be found at www.osteoresearch.org/cuties

Study details

Main Sponsor:	University College of Osteopathy, London UK
Co-Sponsors:	University of Applied Sciences and Arts Western Switzerland – Fribourg
Trial(s) name:	Crying, unsettled and distressed infants: Swiss arm of an international randomised controlled trial to test the effectiveness of osteopathic care
Registration	ACTRN12620000047998
Treatment(s):	Osteopathic light-touch manual care
Version:	1.4
Date:	25/06/2021
Principle investigator: (Switzerland)	Prof.Dr.Sci Paul Vaucher paul.vaucher@hes-so.ch +41 78 788 33 66 (available directly on Wednesdays and Thursdays)
Chief investigator:	Prof.Dress Dawn Carnes dawn.carnes@uco.ac.uk +44 20 7085 5330

Table of Content

STUDY DETAILS	1
TABLE OF CONTENT	2
SUMMARY	3
INTRODUCTION	4
HYPOTHESIS ON MECHANISMS OF ACTION	4
KNOWN EFFECTS OF SOFT TOUCH ON INFANTS	5
PROCEDURES AND GUIDANCE FOR CO-INVESTIGATORS	5
TRAINING AND RESEARCH AGREEMENT FORM	5
<i>Training</i>	5
<i>Criteria for being a co-investigator</i>	6
<i>Research agreement form</i>	6
SETTING UP RECRUITMENT	6
<i>Oral invitation</i>	6
<i>Advertising the trial</i>	6
<i>Personalising documents</i>	6
<i>Before recruiting</i>	6
INITIATING RECRUITMENT	7
INFORMATION LEAFLET	7
CONSENT	7
<i>Inclusion criteria for parents</i>	7
<i>Inclusion criteria for infants</i>	7
<i>Exclusion criteria for infants</i>	8
<i>Other verification</i>	8
<i>Consent form</i>	8
<i>Refusals</i>	8
CLINICAL INVESTIGATION	8
BASELINE DATA COLLECTION	9
<i>CastorEDC</i>	9
<i>1st questionnaire for parents (CastorEDC)</i>	9
ALLOCATION TO TREATMENT GROUP	9
DELIVERING THE INTERVENTION	9
<i>Targeted Tension Release (TTR)</i>	10
<i>Generic Tension Release (GTR)</i>	10
<i>Interactions with parents (both groups)</i>	10
<i>Parent education, counselling and support (both groups)</i>	11
<i>Follow-up and instructions (both groups)</i>	11
DOCUMENTING PATIENT MANAGEMENT	11
MONITORING AND REPORTING ADVERSE EVENTS	11
REPORTING PROTOCOL DEVIATIONS	11
END OF FOLLOW-UP	12
FINANCIAL RETRIBUTION	12
REFERENCES	12
CO-INVESTIGATOR SIGNATURE	14
REMINDERS OF PROCEDURES	15
<i>Pre-enrollment</i>	15
<i>1st visit</i>	15
<i>Follow-ups (optional)</i>	15
<i>>14 days</i>	15
CUTIES RECRUITMENT PROCESS	16
TYPES OF POSSIBLE MANUAL TREATMENT	17
RANDOM TABLE FOR LOCATION OF TREATMENT IN GTR GROUP	18

Summary

Background: Infants who excessively cry, are distressed and unsettled can have a marked impact on family life. Around 1 in 6 families are affected, it is associated with maternal depression, anxiety and loss of parenting confidence. These infant behaviors are usually self-limiting (subsiding around 12 weeks after birth) but during this difficult period many parents look for additional support. There is limited research and therefore much debate about the effectiveness of manual therapy and osteopathic care for these infants.

Aim: To evaluate the effectiveness and healthcare cost of osteopathic light touch manual therapy care for excessively crying, unsettled and distressed infants (< 10 weeks old).

Method: We propose a two-arm pragmatic randomised controlled trial to assess the effectiveness of osteopathic light touch manual therapy and best practice advice (the consultation). We will need to randomise 112 parent(s)/carers and their infants to either: i) Osteopathic light touch manual therapy with best practice advice and support or, ii) Non-specific light touch with best practice advice and support. Parents will be blinded to whether their infant receives the usual osteopathic therapy care or not. This design will enable us to test whether the osteopathic light touch manual therapy is superior to non-specific light touch and best practice advice alone. The cost of the delivery of the intervention will be determined and compared with data about the cost of other care.

Population: Healthy infants under 10 weeks old or under, reported by their parent(s)/carers as excessively crying, fussing, unsettled and distressed and difficult to console using a modified Rome IV criteria (> 3 hours of crying per day, for 3 days for 1 week or more). Infants with diagnosed health conditions for which they are receiving medical treatment, or who are unsuitable for osteopathic care will be excluded from the study.

Outcomes: The primary outcome is reduced infant crying time over 14 days, collected via parent reported diaries. Secondary outcomes are: i) Parental self-efficacy ii) Parent perceived global improvement iii) Satisfaction and experience with treatment and iv) Adverse events.

This international parallel multicentric pragmatic randomized controlled trial will provide information about the clinical and social relevance of osteopathic care for excessively crying, unsettled and distressed infants and their parents.

Introduction

Infants who excessively cry and are perceived as unduly distressed and unsettled may be otherwise healthy and thriving. However, these symptoms can have a marked impact on family life. Around 1 in 6 families are affected by excessive infant crying [1]. It is associated with maternal issues such as depression, anxiety and loss of parenting confidence [2,3]. The peak age for crying in infants, at week six, is the same as the peak age for severe infant injury or death as a result of abuse [4,5]. Health care resource use by parents is higher in an infant's first 6 months of life, indicating a greater need for support during this period [2]. One of the major reasons for this increase includes unsettled infant behaviour and problems with sleeping and feeding [6].

While this behaviour is relatively common, there is a lack of consensus about its nature and cause which is compounded by limited research regarding the effectiveness of treatments currently used to manage the condition [7]. Excessive crying, undue distress and/or unsettled behaviour are often grouped together under the heading 'colic'.

Many parents seek alternative care such as osteopathy for their 'colicky' infants. In Switzerland, one infant in two are seen by an osteopath during its first year of life [8]. One of the most frequent motives is unsettled crying. Osteopathic care is therefore perceived as usual care for infants with colic even if there is no evidence of the added value of hands-on treatment with the intention of altering tissues. Osteopathic treatment for 'colicky' infants commonly involves gentle touch and movement [9]. The intention is to relieve soft tissue tension in the infant's body, improve range of motion and function and promote better feeding and/or gut motility [10]. Treatment includes gentle application of light tactile pressure to areas that are perceived to demonstrate palpably increased soft tissue tone. The osteopath maintains manual light pressure with the infant's body until the tension is felt to decrease and may also use gentle techniques to encourage movement in areas where movement is restricted [10].

It is recognised that parents/carers are often in crisis when they seek support and care for their 'colicky' infants and that they expect the outcome of that care to have an almost immediate effect. This study has therefore been designed to look at only the short-term impact of care. The reasons for this are two-fold: i) to limit the stress on the parent/carer (the peak time for crying is during the infants first six to eight weeks of age), and ii) because normally the symptoms of excessive crying, unsettledness and distress are self-limiting and start resolving around nine to 12 weeks of age [11]. Parents/carers in both groups will receive recommended advice and information drawn from national clinical guidelines (NICE 2017). The inclusion of a 'non-touch' control group was not possible due to the inability to blind the parents/carers of infants in such a group.

The aim of this study is therefore to evaluate the effectiveness of osteopathic manual therapy care for excessively crying, unsettled and distressed infants under 10 weeks old. The study will compare the effect of osteopathic specific light touch manual therapy care delivered with therapeutic intent with a non-specific light touch manual intervention. The trial will provide data regarding the belief of both osteopaths and parents/carers, that the 'therapeutic intent' associated with the directed osteopathic light touch is the active element in delivering benefits.

Hypothesis on mechanisms of action

There is little evidence to support the mechanism of action underpinning this approach with the rationale for treatment theoretically driven. Proposed physiological explanations include altered

parasympathetic activity resulting from compression of the vagus nerve [12,13] and/or cranial bone movement dysfunction [14], both attributed to birth trauma, with neither having been verified experimentally. [15] postulated that infants with colicky crying were less able to regulate their responses to everyday stimuli. This led to the hypothesis that osteopathic affective touch may be able to modulate stimuli produced within the gut and other internal organs (interoceptive stimuli) in a direction that reduced symptoms such as crying and distress [16,17].

Known effects of soft touch on infants

There is limited, low to moderate quality evidence to show that osteopathic and chiropractic care can help to reduce crying time in infants [9,18,19]. There is evidence to show that this type of gentle light touch therapy has a low risk of harm [20] and that adverse events reported were transient and low to moderate in severity [9].

A survey in the Netherlands collected information on adverse events following manual treatment in 785 children seeing by 27 osteopathic practitioners. 13% of paediatric patients experienced side effects which were recognised as being non-serious and with minor consequences of short duration (i.e. crying, changes in sleeping habits, restlessness). No serious or mild adverse events were observed [21]. When broadening investigations of adverse events to all forms of manual treatment, a systematic review identified 9 cases of severe adverse events following paediatric spinal manipulation over a 58-year period [22]. Spinal manipulation in infants is however not part of what is proposed to infants during osteopathic paediatric care. No serious adverse events associated to osteopathic care were observed in small clinical trials studying effects of osteopathic care on colic, representing 116 infants who received treatment [18]. To our knowledge, there are but two reported cases of severe fatal complications following manual therapy with excessive force. Both were due to respiratory depression. One took place following spinal manipulation [23], the other following cranio-sacral therapy [24]. Both cases were related to negligence, unusual osteopathic paediatric manual care, and due to the use of techniques that are against actual recommendations. The incidents of such events remain very rare and are believed to occur in less than one infant in 2.5 million.

As exposed in the previous paragraph, the reported incidence and prevalence of moderate and serious adverse events is very low with this form of gentle light touch therapy. Manipulation using manual thrust techniques are contra-indicated in this patient population and none will be used in this study.

Procedures and guidance for co-investigators

Training and research agreement form

Training

Each co-investigator is to follow two training sessions to make sure you are familiar with the study procedure and Good Clinical Practice standards for clinical trials. These trainings are organised in advanced. The dates are communicated by the Principle Investigator.

Criteria for being a co-investigator

To be eligible, osteopaths have to be Swiss registered osteopaths (NAREG), have at least 1 year of post-graduate working practice, follow at least one infant per week, and master English well enough to understand written documents and follow the two-day training organised within the study.

Research agreement form

Please complete and sign the Research Agreement Form before recruiting the first participant. The form should be sent to paul.vaucher@hes-so.ch who will sign it and send it back to you.

Setting up recruitment

Oral invitation

Participants can be recruited by a receptionist, the osteopath or any other person at the office if their appointment for their 1st consultation is set at least 24h after being informed of the study.

Advertising the trial

Please use the poster given to you to advertise the trial. Please add your contact details at the bottom but do not change the wording or layout of the poster. The poster can be used at the clinician's office or by other health professionals (midwives, paediatricians, GPs, birth clinics, etc.).

Once you have adapted the Advertisement for Recruitment document for your office, please send a version back to paul.vaucher@hes-so.ch for archiving.

Personalising documents

For each participant, a printed version of the information form and two consent forms with your details need to be printed before the first visit. The Information and consent form therefore needs to be completed and a copy of your version sent back to paul.vaucher@hes-so.ch.

You will also need to plan a local logging system that will link the true participant's ID to their study ID. This document will also serve to document refusals. An Excel template called "Study log file" has been provided. You can see with the investigator how to best use this file and adapt it to your settings and recruitment procedure.

Before recruiting

You need to send the following documents to paul.vaucher@hes-so.ch to then receive your CASTOR login:

- The signed Osteopath Agreement Consent Form
- The signed Co-investigator version of the protocol (this document)
- The completed Advertisement and Recruitment Form for your office
- The completed Information and Consent Form for your office

Initiating recruitment

You can print the summary recruitment flow chart showing the process and procedures for recruiting participants (CUTIES Recruitment process).

Please ask ALL eligible parents to join the study. Please do not pick and choose who to invite. We have to give all potential participants an equal opportunity to take part in the trial. When possible, you can however only invite parents who's infant fit the recruitment criteria (<10 weeks old, excessive crying, otherwise healthy and thriving).

If the parent is interested in being in the trial, they will be receiving:

- An invitation letter in French, German, Italian or English
- A template of the Participant Information Leaflet and Consent Form in French, German, Italian or English
- The Crying Diary Form in French, German, Italian or English

These are sent automatically by on the electronic capturing software (CastorEDC) once you have registered them. To do so, click on one of the following link, add a new entry, and add the parent's E-mail address in the system.

- [CastorEDC](#)

Information leaflet

Participant's parents will automatically receive a generic information form that does not contain your contact details. It is therefore important to have a printed copy available for when they are to give their consent.

Consent

Before obtaining consent, please verify that the potential participants meet recruitment criteria.

Inclusion criteria for parents

- Legal representative of an infant responding to inclusion criteria.
- Age of 18 years or above.
- Mastery of French, German or English to understand the information and consent form, and answer questionnaires.
- Able to give informed consent as documented by signature.

Inclusion criteria for infants

- Infants aged from 1 to 10 weeks (8 to 70 days). This timeframe is important as unsettled crying usually resolves spontaneously after 12 weeks of age and the treatment period is to last two weeks.
- Infants are healthy and thriving.
- Excessively crying, distressed or unsettled for more than 3 hours per day, more than 3 days per week for 1 week or more. This definition is adapted from the Rome IV criteria used in the postnatal clinical classification of infants with difficulties settling, distress and excessive crying

Exclusion criteria for infants

- Active co-morbidities that require medical attention or treatment. This is to limit serious confounders and ensure that the infants recruited are healthy and thriving and that osteopathic care is not inappropriate.
- Priorly or under treatment with an osteopath for similar reasons.
- Already in a clinical trial.

Other verification

Before commencing with the consultation please make sure that the parent has received the study invitation, participant information leaflet, crying diary and consent form. At this point it is essential to ask the parent if they have had the time to read the information and ask them if they are interested in being part of the study. Please invite them to ask any questions they may have.

Answer any questions as per the information in the participant leaflet.

To avoid the potential to induce the parent to participate by offering free treatment please ensure that you mention it may not be costing the parent money, but they will be required to complete 2 questionnaires and the crying diary over 14 days. This will incur time and probably travel costs.

To avoid the potential of coercion, when asking if the parent is interested or not in the trial it is essential that you use the following type of wording:

'It is up to you whether you decide to join the study. If you choose not to be part of the study, this is fine, and will not affect the quality of care you and your baby will receive. If you agree to take part, I will ask you to sign a consent form and if you change your mind about participating, at any time, this will also not affect the quality of care that you or your baby are given in the future.'

Consent form

If the parent is interested, please ask them to initial and sign the trial consent form (2x). Add the participant ID from CastorEDC, sign the forms and give a copy with your personalised Information Form to the parent.

Complete the log file and archive the signed consent form with the patient's health record or in a secured place. This document needs to be made accessible for the next 25 years.

Refusals

If they are not interested, please gently ask why if they have not given a reason already.

Please record this in your recruitment log (Participation List).

Clinical investigation

- Take the case history of the infant, the pregnancy and birth.
- Do a health screening of the infant.
The standard health screening should assess the infants: weight, temperature, respiration, pulse, overall muscle tone, symmetry and movement. All parents will be informed of the findings from their infant's health screening.
- Evaluate the infant's osteopathic functional situation as you would usually.

After the initial case history and health screening the parents will be informed that the infant is healthy where appropriate and therefore still suitable to join the trial. If the osteopath feels that there are health concerns about the infant, they must refer as appropriate, for example to their GP, health visitor or midwife or if in exceptional emergency circumstances to A&E, for example signs of a fever, sustained rash under pressure, infection and or severe mental health issues in the parent.

If the osteopath thinks the infant or parent is 'at risk' with any safeguarding concerns, then appropriate action must be taken to contact the local social services. Please ensure that the help line number is known and accessible, as per normal good clinical practice.

If no tensions in the infant are palpated during the osteopathic examination and the osteopath feels that the baby does not require treatment, then the baby should not be enrolled in the trial (exclusion criteria).

Baseline data collection

CastorEDC

The first step is to complete baseline data on the electronic capturing software (CastorEDC).

To do so, use your personal ID and password to access the system. Confirm eligibility in the Cuties Health Screening. Then, record all information in the Infants Notes (patient record) and in the Case History section.

1st questionnaire for parents (CastorEDC)

Verify that parents have already completed baseline data on their questionnaire. If they have not, ask them to do so on their mobile phone (CastorEDC) using the link that was sent to them.

Allocation to treatment group

Using the CastorEDC section dedicated to revealing the participant's allocated treatment, randomise the baby to one of the study groups. Both arms involve the use of light touch which is thought to modulate parts of the brain involved in sensation recognition (interoception).

The infant will either be allocated to the Targeted Tension Release (TTR) Group or to the Generic Tension Release (GTR) Group. Write the group allocation in the patient record for future use.

PLEASE DO NOT TELL THE PARENT WHICH GROUP THEY HAVE BEEN RANDOMISED INTO

- Discuss the findings of the examination and the proposed treatment plan followed by parental consent for treatment.

The osteopath should inform the parent that the infant might have some underlying tension in their soft tissues and restricted movement/s which might explain some of the distress that the infant is displaying.

The osteopath should then explain to the parent/guardian that they would like to gently touch the infant to feel for restrictions and then aim to address them using very soft light touch.

Delivering the intervention

All participants will be scheduled to receive up to a maximum of 4 consultations over a 2-week period as deemed appropriate by the parent and the treating osteopath. The Targeted Tension Release arm involves usual light osteopathic touch intended to target specific areas of the baby's

body to reduce tension in the soft tissues and promote circulation. The Generic Tension Release arm involves light touch alone which is not targeted at specific areas of the baby's soft tissues.

Targeted Tension Release (TTR)

The osteopathic manual therapy treatment should be given as appropriate for around 10-20 minutes.

Under no circumstances should any invasive and or high velocity techniques be administered to the infants.

The osteopath must note the techniques used and on which part of the infant's body for what purpose. Osteopaths may deliver treatment to any of the following areas: cranium, neck, face, thorax, abdomen and sacral area in any order as deemed appropriate. Treatment using gentle touch only should be applied to the infants, techniques which may be used are listed in the printable section (**Types of possible manual treatment**).

Generic Tension Release (GTR)

The infants in the control intervention arm will be touched lightly, with no osteopathic therapeutic treatment intent to move tissues or fluids. The infant will be given a non-specific light touch attention control intervention for around 10-20 minutes.

The non-specific light touch can be given to the cranium, thorax, pelvis and abdomen only. Place your hands globally on the region without any intent of bringing any change. Print and use the random table to decide in which order regions should be addressed (**Random table for location of treatment in GTR group**).

To prevent any treatment intent, we will ask the osteopaths to do a secondary cognitive task whilst holding the infants, this will involve the osteopath counting backwards in 6s, 7s or 8s from 200 [16] or name animals or vegetables for each letter of the alphabet

During the treatment the parent or guardian will be present at all times and able to observe the treatment.

Interactions with parents (both groups)

During the treatment the parent or guardian will be present at all times and able to observe the treatment.

During the treatment phase the osteopath should use the following types of phrases to communicate with the parent or guardian:

- "your baby is doing very well",
- "I have nearly finished",
- "a couple more minutes",
- "we have now finished the treatment"

The osteopath can make soothing and or playing noises with the infant.

Should the parent ask any questions about the treatment during the treatment they will be able to answer with non-committal statements such as:

- “I am focusing on your baby, the touch triggers responses in the brain that can modulate tissue reactions”
- “This touch component of care is targeted at tension release in the soft tissues”
- “I am making manual contact in this area because this is a common area to find tension”

Parent education, counselling and support (both groups)

At the end of the manual component of the intervention the osteopath and the parents/guardians can discuss any issues about parenting and managing a newborn infant. Best practice advice should be given, and the supporting information given to the parent should they want it.

The non-manual contextual components of the intervention will be delivered with therapeutic intent in both groups. This includes reassurance, listening, advice and any other psychological support.

Follow-up and instructions (both groups)

At the end of the 1st visit, you must decide with parents on whether follow-up visits are to be planned and when they are to take place. Remind parents to complete the crying diary daily and ask them if they have met any difficulties. Set new appointments as you find it best depending on parents’ distress, the importance of symptoms, availabilities, and the evolution of the situation.

Documenting patient management

All treatment administered must be recorded by the treating osteopath and completed and submitted online using the Health Screening Case History Tracking Form.

Anonymised copies of clinical notes will be accessed by the study team for further scrutiny (with prior permission and consent of the parent or guardian, see parent participant consent form).

Monitoring and reporting adverse events

An Adverse Event (AE) is any untoward medical occurrence in a patient or a clinical investigation subject which does not necessarily have a causal relationship with the trial procedure. An AE can therefore be any unfavourable or unintended finding, symptom, or disease temporally associated with a trial procedure, whether or not related to it. All AEs must be reported in the Health Screening Case History Tracking Form.

A Serious Adverse Event (SAE) is any untoward medical occurrence that

- Results in death or is life-threatening,
- Requires in-patient hospitalisation or prolongation of existing hospitalisation,
- Results in persistent or significant disability or incapacity, or
- Causes a congenital anomaly or birth defect

SAEs must be reported to the Principal Investigator immediately by E-mail (paul.vaucher@hes-so.ch) with the subject heading “CUTIES-TRIAL – URGENT SAE”. The Principal Investigator will then get in touch with you to document the situation within 24h. In the initial E-mail, please report the nature of the event, the date,

Reporting protocol deviations

Any protocol deviation must be reported within 24h to the Principal Investigator by E-mail (paul.vaucher@hes-so.ch).

End of follow-up

15 days after randomisation (the first consultation) please telephone or email the parent to ask if they have completed and submitted their follow up questionnaire and diary. If they have, you can inform the parent which treatment arm their infant was allocated to. If they have not completed the follow up questionnaire and the crying diary, please can you gently remind them and once completed they can ring you for the allocation information. If you do not hear from the parent, please ring or email them a reminder between 16- and 20-days post randomisation.

If the parent does not or has not completed the follow up questionnaire or submitted their crying diary within 21 days of the first treatment, please ask if they require additional support. If the parent would like some additional support, a person independent of the running of the trial and blind to allocation will be made available to help the parent by phone or email (please contact paul.vaucher@hes-so.ch to arrange). If they still do not wish to or can't complete the follow up information and still wish to know their allocation, we will reveal it to the parent after 21 days, and they will be recorded as a non-responder.

Any treatment offered after this point is subject to usual practice in accordance with osteopathic practice standards and conditions of your registration.

Financial retribution

In Switzerland, the SOSF has agreed to financially compensate a part of the time you are dedicating to this trial. Each of you should receive an amount depending on the number of patients you are able to recruit:

- 1 participant 300.-,
- 2 participants 500.-,
- 3 participants 700.-,
- 4 participants 900.-,
- 5 participants 1'100.-
- 6 participants 1'300.-

If you were to recruit over 6 participants, you should receive 200.- per extra participants after receiving the approbation to recruit more than 6 infants and parent from the local investigator (Paul Vaucher)

References

- 1 Hiscock H, Jordan B. Problem crying in infancy. *Med J Aust* 2004;**181**:507–12. doi:10.5694/j.1326-5377.2004.tb06414.x
- 2 Johnson JD, Cocker K, Chang E. Infantile Colic: Recognition and Treatment. *Am Fam Physician* 2015;**92**:577–82.
- 3 Kurth E, Spichiger E, Cignacco E, *et al.* Predictors of Crying Problems in the Early Postpartum Period. *J Obstet Gynecol Neonatal Nurs* 2010;**39**:250–62. doi:10.1111/j.1552-6909.2010.01141.x
- 4 Berkowitz CD. Physical Abuse of Children. *N Engl J Med* 2017;**376**:1659–66. doi:10.1056/NEJMcp1701446

- 5 Kato N. Prevalence of Infant Shaking Among the Population as a Baseline for Preventive Interventions. *J Epidemiol* 2016;**26**:2–3. doi:10.2188/jea.JE20150321
- 6 Morris S, James-Roberts IS, Sleep J, *et al.* Economic evaluation of strategies for managing crying and sleeping problems. *Arch Dis Child* 2001;**84**:15–9.
- 7 Sung V. Infantile colic. *Aust Prescr* 2018;**41**:105–10. doi:10.18773/austprescr.2018.033
- 8 Vaucher P, Macdonald RJD, Carnes D. The role of osteopathy in the Swiss primary health care system: a practice review. *BMJ Open* 2018;**8**:e023770. doi:10.1136/bmjopen-2018-023770
- 9 Parnell Prevost C, Gleberzon B, Carleo B, *et al.* Manual therapy for the pediatric population: a systematic review. *BMC Complement Altern Med* 2019;**19**:60. doi:10.1186/s12906-019-2447-2
- 10 Jäkel A, von Hauenschild P. A systematic review to evaluate the clinical benefits of craniosacral therapy. *Complement Ther Med* 2012;**20**:456–65. doi:10.1016/j.ctim.2012.07.009
- 11 Wolke D, Bilgin A, Samara M. Systematic Review and Meta-Analysis: Fussing and Crying Durations and Prevalence of Colic in Infants. *J Pediatr* 2017;**185**:55–61.e4. doi:10.1016/j.jpeds.2017.02.020
- 12 Cowie J. Managing infant colic: a literature review: Interventions available to cope with this condition are discussed by Jean Cowie, with an overview of potential problems if parents are not supported. *Prim Health Care* 2013;**23**:16–20. doi:10.7748/phc2013.03.23.2.16.e759
- 13 Lim KW. Infantile colic: A critical appraisal of the literature from an osteopathic perspective. *Int J Osteopath Med* 2006;**9**:94–102. doi:10.1016/j.ijosm.2006.07.001
- 14 Kotzampaliris PV, Chou KJ, Wall SP, *et al.* The Cranial Rhythmic Impulse and Excessive Crying of Infancy. *J Altern Complement Med* 2009;**15**:341–5. doi:10.1089/acm.2007.0579
- 15 Leuchter RH-V, Darque A, Hüppi PS. Brain Maturation, Early Sensory Processing, and Infant Colic: *J Pediatr Gastroenterol Nutr* 2013;**57**:S18–25. doi:10.1097/01.mpg.0000441929.05684.78
- 16 Cerritelli F, Chiacchiaretta P, Gambi F, *et al.* Effect of Continuous Touch on Brain Functional Connectivity Is Modified by the Operator's Tactile Attention. *Front Hum Neurosci* 2017;**11**:368. doi:10.3389/fnhum.2017.00368
- 17 D'Alessandro G, Cerritelli F, Cortelli P. Sensitization and Interoception as Key Neurological Concepts in Osteopathy and Other Manual Medicines. *Front Neurosci* 2016;**10**:100. doi:10.3389/fnins.2016.00100
- 18 Carnes D, Plunkett A, Ellwood J, *et al.* Manual therapy for unsettled, distressed and excessively crying infants: a systematic review and meta-analyses. *BMJ Open* 2018;**8**:e019040. doi:10.1136/bmjopen-2017-019040
- 19 Dobson D, Lucassen PLBJ, Miller JJ, *et al.* Manipulative therapies for infantile colic. *Cochrane Database Syst Rev* 2012;**12**:CD004796. doi:10.1002/14651858.CD004796.pub2
- 20 Carnes D, Mars TS, Mullinger B, *et al.* Adverse events and manual therapy: a systematic review. *Man Ther* 2010;**15**:355–63. doi:10.1016/j.math.2009.12.006

- 21 Kales S. *Adverse events in pediatric osteopathy*. 2011.<http://rgdoi.net/10.13140/2.1.3506.4649> (accessed 26 Nov 2020).
- 22 Vohra S, Johnston BC, Cramer K, *et al*. Adverse Events Associated With Pediatric Spinal Manipulation: A Systematic Review. *PEDIATRICS* 2007;**119**:e275–83. doi:10.1542/peds.2006-1392
- 23 Holla M, Ijland MM, van der Vliet AM, *et al*. Death of an infant following “craniosacral” manipulation of the neck and spine. *Ned Tijdschr Geneeskd* 2009;**153**:828–31.
- 24 Brand PLP, Engelbert RHH, Helders PJM, *et al*. Systematic review of the effects of therapy in infants with the KISS-syndrome (kinetic imbalance due to suboccipital strain). *Ned Tijdschr Geneeskd* 2005;**149**:703–7.

Co-investigator signature

I attest having read the entire document, to have obtain clarifications to questions I might have had, and to understand the procedures.

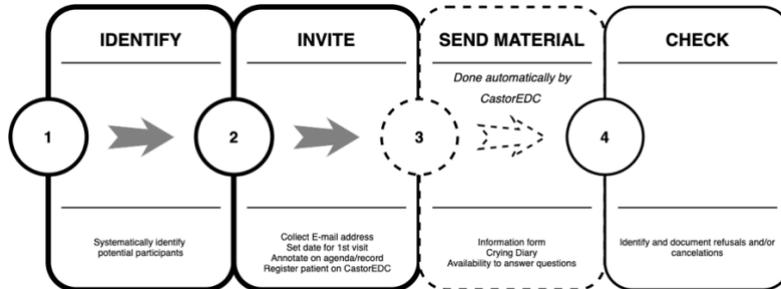
Place and date

Name

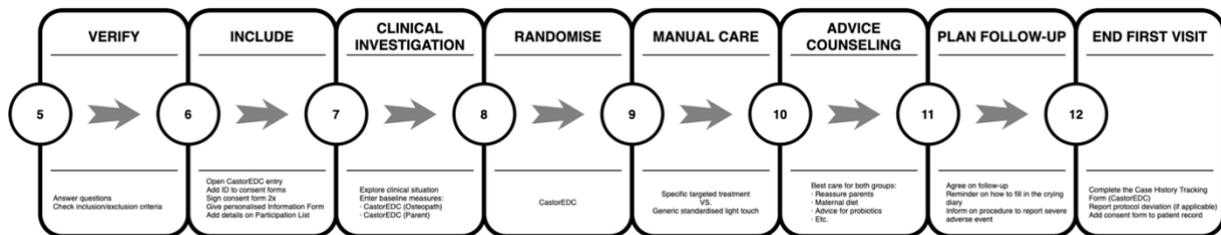
Signature

Reminders of procedures

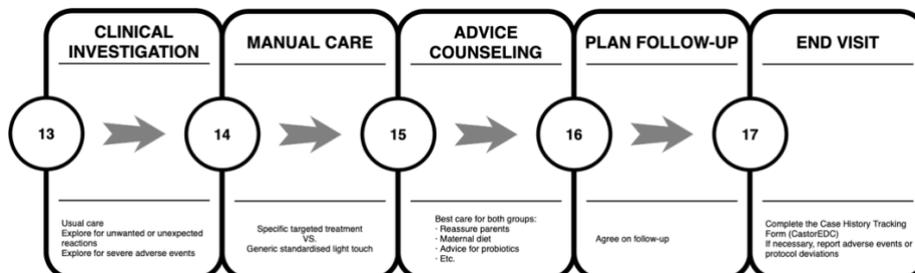
Pre-enrollment



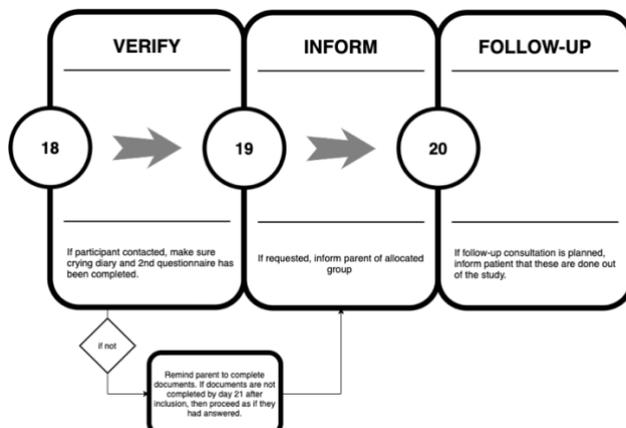
1st visit



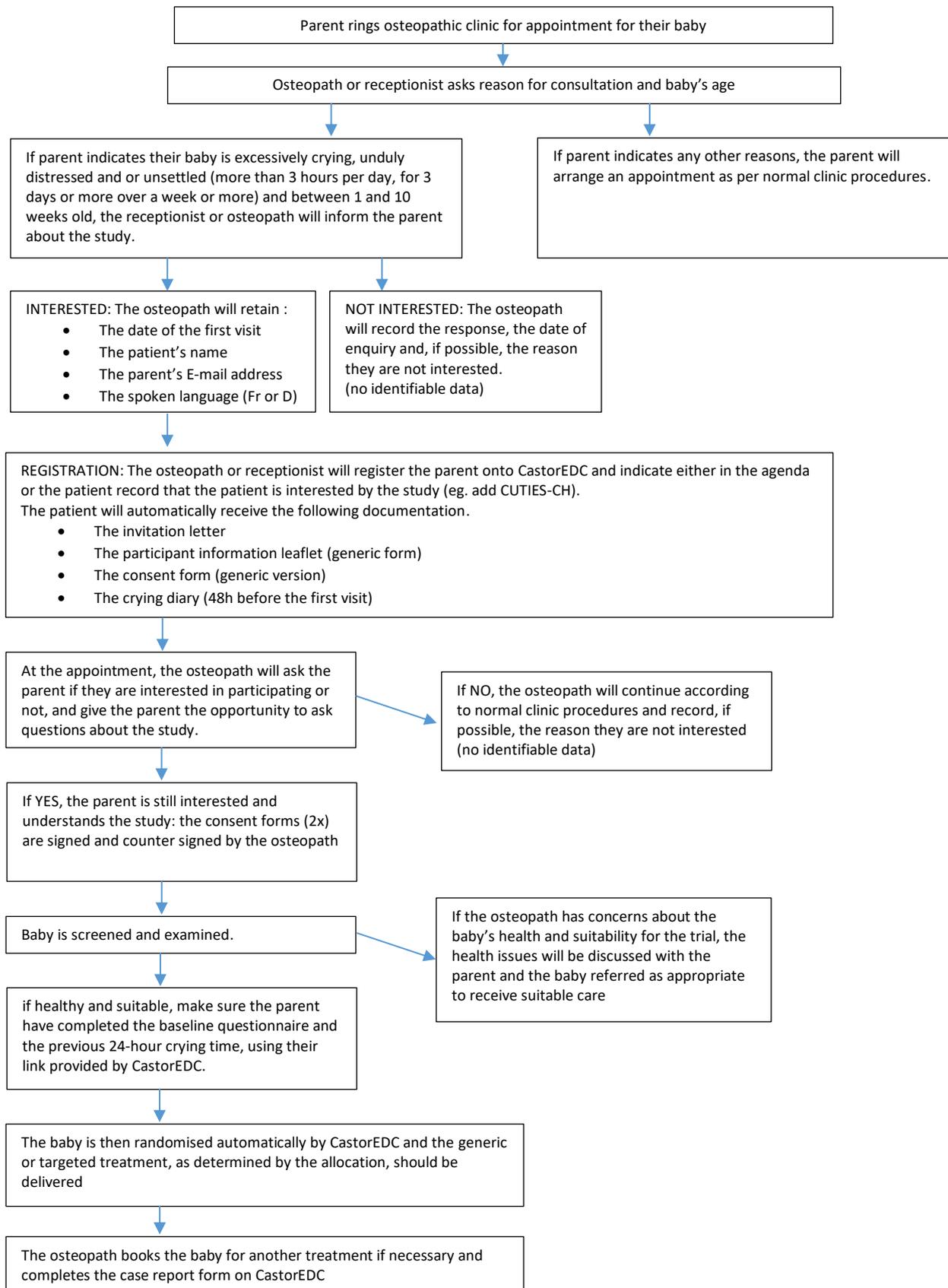
Follow-ups (optional)



>14 days



CUTIES Recruitment process



Types of possible manual treatment

Acronym	Full name	Description
ART	Articulation	A technique where a joint is carried through a range of motion with the therapeutic goal of increased freedom of the range of movement. The activating force is either a springing motion or repetitive concentric movement of the joint.
BLT	Balanced ligamentous tension	Practitioner uses process of active engagement with tissues and patient positioning towards disengagement, respiratory co-operation may be used as an adjunct.
BTTcr	Balanced tissue tension [at cranium]	Practitioner uses tissue engagement / active engagement of treatment principles of sutural disengagement (eg: V-spread, membranous pattern exaggeration, compression and disengagement, opposite physiological motion etc. leading to a point of balanced membranous tension).
BTTpl	Balanced Tissue tension [to trunk pelvis or limbs]	Practitioner uses tissue engagement / active engagement of treatment principles of sutural disengagement (eg: V-spread, membranous pattern exaggeration, compression and disengagement, opposite physiological motion etc. leading to a point of balanced membranous tension at any other site of the body other than the cranium
BTTvis	Balanced Tissue tension [to the viscera]	Practitioner uses tissue engagement / active engagement of treatment principles of tissue disengagement leading to a point of balanced membranous tension to the viscera.
BTTother	Balanced Tissue tension [to other structures]	Practitioner uses tissue engagement / active engagement of treatment principles of tissue disengagement leading to a point of balanced membranous tension to other tissues than ligaments, cranium, trunk, pelvis, limbs or viscera.
CFF	Central fluid fluctuation management	Cranial-sacral technique focused on modulating central fluid fluctuation [eg CV4,EV4 lateral fluctuation, Directing the Tide].
PFF	Peripheral fluid fluctuation management	Peripheral fluid fluctuation management: practitioner engages with the fluids / fluid field in peripheral tissues, or directs the Tide to peripheral tissues.
Lymph	Lymphatic pumping	Drainage techniques
CS/FPR	Counterstrain/Facilitated Positional Release	A system of diagnosis and treatment that considers the dysfunction to be a continuing, inappropriate strain reflex, which is inhibited by applying a position of mild strain in the direction exactly opposite to that of the reflex; this is accomplished by specific directed positioning about the point of tenderness to achieve the desired therapeutic response. A system of indirect myofascial release treatment. The component region of the body is placed into a neutral position, diminishing tissue and joint tension in all planes, and an activating force (compression or torsion) is added.
IND	Indirect functional method	A technique where the restrictive barrier is disengaged; the dysfunctional body part is moved away from the restrictive barrier until tissue tension is equal in one or all planes and directions. An indirect treatment approach that involves finding the dynamic balance point and one of the following: applying an indirect guiding force, holding the position or adding compression to exaggerate position and allow for spontaneous readjustment. The osteopathic practitioner guides the manipulative procedure while the dysfunctional area is being palpated in order to obtain a continuous feedback of the physiologic response to induced motion. The osteopathic practitioner guides the dysfunctional part to create a decreasing sense of tissue resistance.
MFR	Myofascial release	Technique using continual palpatory feedback to achieve release of myofascial tissues.
ST	Soft tissue	A system of diagnosis and treatment directed toward tissues other than skeletal or arthroal elements. A direct technique that usually involves lateral stretching, linear stretching, deep pressure, traction and/or separation of muscle origin and insertion while monitoring tissue response and motion changes by palpation.
VIS	Visceral manipulation	Treatment directed to the viscera to improve physiologic function. Typically, the viscera are moved toward their fascial attachments to a point of fascial balance.
Other		Any technique performed that does not fit into one of the above categories that involves light touch only

Random table for location of treatment in GTR group

Spend 3 minutes on each region identified in the table by a letter. If the same letter appears twice, spend 6 minutes on the region. Place your hands in the following manner:

- Abdominal:** One hand and arm holding the baby, your dominant hand placed broadly on the abdomen.
- Cranium:** Infant laying on their back. Both hands placed on the cranium in a global hold with indexes on frontal region and little fingers on occipital regions.
- Thorax:** One hand placed in the back and one placed transversally on the front over the sternum.
- Pelvis:** Infant sits in one hand resting against the osteopath's arm, the other transversely covering superior anterior spines of the ilium and symphysis.

If all techniques have been done under 10 minutes, start the sequence again until at least 10 minutes are reached.

Days	Monday	Tuesday	Wednesday	Thursday	Friday	Saturday
1, 11, 21, 31	PCCTP	TATPA	CTPTT	PATCA	TPTAT	TCPCT
2, 12, 22	AACAP	PCCAC	CATT	PPACC	TTPPA	CTCCT
3,13,23	ATATA	PCPPC	PPTPT	CTTTC	APTTA	AACAC
4,14,24	CPAPC	ACCAP	AAPPT	CCPPP	TPCCT	CATAP
5, 15, 25	CATCP	PCAPC	PAPPC	CTACA	CCTAA	TAPCA
6, 16,26	PAPPC	ACPCA	PAPCC	TTPCT	PCTPP	PTCAA
7, 17, 27	PCPTT	AATAT	PPCTT	AATAT	PAATT	PPACT
8, 18, 28	PAPAC	ATTTA	TTPAA	PCTCA	TAPTC	CATTA
9, 19, 29	PAAAC	ATPPP	CCAPT	CPTAP	PTCPC	AAAPC
10, 20, 30	TPACT	AACTC	PCCPC	TCACT	PP TTC	APAAA

A=Abdominal, C=Cranium, T=Thorax, P=Pelvis