HEADS

Positional skull deformation in infants

Heading towards evidence-based practice

Renske M. van Wijk

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POSITIONAL SKULL DEFORMATION IN INFANTS

HEADING TOWARDS EVIDENCE-BASED PRACTICE

DISSERTATION

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Paranymphs
Ank Ringoot
Marjon Rouwette

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CHAPTER 1

General introduction

GENERAL INTRODUCTION

Every day, young infants are presenting to child healthcare professionals with an odd shape of the skull. In few cases the odd shape is caused by malformation as the cranial sutures fuse prematurely (craniosynostosis). In most cases however, the shape of the infant's skull deforms as a result of prolonged prenatal or postnatal external forces. This condition is known as positional skull deformation. Two typical abnormalities of positional skull deformation can be identified: unilateral occipital flattening (deformational plagiocephaly) and symmetrical occipital flattening (deformational brachycephaly).[1, 2] A severe plagiocephalic flattening often presents with ipsilateral frontal bossing of the forehead and anterior shift of the ipsilateral ear (ear deviation) and cheek (figure 1.A).[2-4] A brachycephalic flattening can be accompanied by temporal bossing or an occipital lift (figure 1.B).[2]

A dramatic increase in the prevalence of positional skull deformation has been observed since the early nineties. This increase is likely caused by parents changing the positioning of their baby following the introduction of a large public campaign that recommended supine sleeping position for infants to effectively prevent sudden infant death syndrome (SIDS).[5-7]

Positional skull deformation: clinical background and epidemiology

Positional skull deformation is generally considered as a cosmetic condition. Naturally most parents are concerned for their infant's future appearance when a deformation is diagnosed.[8, 9] Some authors described associations of positional skull deformation with medical conditions like auditory processing disorders, mandibular asymmetry, and strabismus[10-12], but only developmental delays have consistently been related to the condition. Although their causal relation is not clear.[13-18]

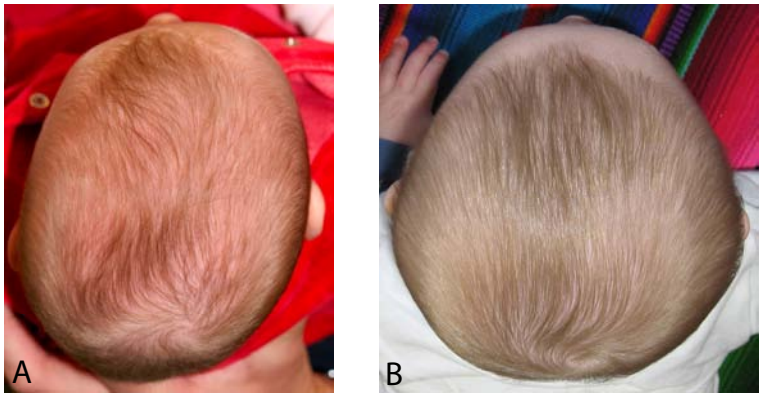

Figure 1. Positional skull deformation
A: Deformational plagiocephaly, B: Deformational brachycephaly

Epidemiology

As discussed, the prevalence of positional skull deformation increased dramatically after the start of the Back to Sleep campaign.[5, 6] Estimating prevalence rates of deformational plagiocephaly and deformational brachycephaly is complicated as most studies do not give uniform definitions of the outcomes they measured. This causes uncertainty whether only one of the types of skull deformation or both types are included. Also, different studies used different quantitative and qualitative approaches for defining skull deformation.

In the Netherlands, the prevalence was estimated by Boere-Boonekamp et al. at 10% under six months[19] in a cross-sectional study of 7609 infants in 1995. However this varies between age groups; the prevalence of deformational plagiocephaly and deformational brachycephaly in a birth cohort of 380 healthy infants as studied by van Vlimmeren et al. in 2004 and 2005 was up to 22% in 7-week-olds and 8% at 6 months, respectively.[20, 21] In New Zealand, Hutchison et al. found a prevalence of positional skull deformation of 16% at age 6 weeks and 20% at 4 months[22]. Littlefield et al. reported an estimated incidence of 15.2% in infants the US in 2004[23], whereas a considerable higher estimate of 45% was reported in infant at 7 to 12 months of age in Canada.[24] The degree of deformation diminishes after 6 months of age when infants grow older: in the Netherlands the prevalence of positional skull deformation at 24 months was 16%, in New Zealand this was 3%.[21, 22]

Risk factors

The dramatic increase of reported cases of skull deformation, made that many researchers began to study risk factors of positional skull deformation. Accordingly, the supine sleeping position was found as an important nursing risk factor for positional skull deformation[22, 25-29]. The most evident infant risk factor is positional preference.[18, 19, 22, 26, 30, 31] Positional preference affects up to 18% of Dutch infants younger than 4 months, and is defined by Boere-Boonekamp et al. as "the condition in which the infant, in supine position, shows head rotation to either the right or the left side for approximately three quarters of the time of observation. Active rotation of the head over a range of 180 degrees cannot be accomplished."[19] or when the infant, in supine position, shows limited rotation to either left or right and has its head in the mid position for approximately three quarters of the time.[21, 32] Other important infant risk factors are male sex[19, 25, 26, 28, 33] and infant neck problems (resulting from congenital muscular torticollis, birth trauma, consequence of intrauterine or postnatal head position).[3, 18, 22, 25, 27, 28, 31, 34] Obstetric factors include prematurity[19, 25, 27, 30, 35, 36], assisted delivery[25, 29], and being firstborn.[19, 22, 25, 26]

Tummy time when awake more than three times a day appears to be a protective factor.[25, 26, 28, 37]

Diagnosis and assessment of deformation

The diagnosis positional skull deformation is based on the history and clinical examination from the anterior, posterior and vertex position.[32, 38, 39] It is vital to distinguish positional skull deformational from craniosynostosis. Next to the clinical examination, healthcare professionals use various tools to determine the severity of deformation. Argenta developed a visual scale

to assess the degree of plagiocephaly and brachycephaly using pictures of 5 types or phases of deformation.[2] The Argenta scale proved to be a moderately reliable method.[40] but is often used in practice. Calipers are also often used as anthropometric measurement of the severity of skull deformation[4, 41-43], but contrasting outcomes for the interrater reliability were found.[40, 44, 45] Instead, measurements were developed that can be applied circumferentially around the infant's head , i.e. HeadsUp and Plagiocephalometry.[46-48] Both have been proven useful in clinical practice, Plagiocephalometry was determined to be a valid and reliable measurement instrument.[47, 48] Nowadays, also 3D measurements using laser or photo techniques are being used.[49-51] Although superior to capture 3D deformation, disadvantages of these 3D-instruments are their large size, costs and limited practical use outside craniofacial centers.

Next, in a cosmetic condition like positional skull deformation subjective outcomes are likewise important. Literature shows that objective measurements not always represent the perceived outcomes.[52-54] It has been advised to encompass parental satisfaction next to anthropometric assessment.[50]

Prevention and treatment of positional skull deformation

Prevention

General measures of prevention are taken to avoid developing and worsening of plagiocephaly. The main preventive advices are 1) alter the position of the infant's head every sleep, 2) vary sides when bottle feeding and 3) promote tummy time when the infant is awake and under supervision. In The Netherlands the vast majority (95%) of children are monitored by preventive child healthcare professionals during well-baby visits. Recently an integrated care guideline with regard to positional preference and positional skull deformation for preventive child health care was implemented in the Netherlands.[32] When preventive child healthcare professionals detect a case of positional preference or positional skull deformation, they provide parents with more detailed advice on handling and (re)positioning their infant. In cases that parental counselling during well-baby visits does not result in improvement of the positional preference or skull deformation, infants are to be referred for pediatric physical therapy at a young age (2-4 months) for the treatment of infant asymmetry.[20, 39, 55, 56]

Pediatric physical therapy

A pediatric physical therapy program based on Van Vlimmeren et al.[20] consists of positioning and handling opposite to the direction of the observed positional preference and activities or exercises that facilitate positions or movements opposite to the positional preference. Parents are taught how to incorporate this into daily activities such as playing, nursing, changing and dressing, feeding and sleeping. The aims of pediatric physical therapy include achieving a full active cervical range of motion and symmetrical motor development. As the majority of infants show symmetry in posture at 5-6 months of age[19, 20], no effects of continued pediatric physical therapy after this age may be expected.

Helmet therapy: description and available evidence

Often, orthotic helmets or headbands are considered for infants with persisting moderate to severe positional skull deformation at 5 to 6 months.[56-58] In 1979, Clarren et al. were the first to describe this treatment in scientific literature. Since the ancient Peruvians and Egyptians were successful in artificially altering infants skull shapes using external forces (fixed board or head wrapping) it was hypothesized that custom-made plastic helmets should be able to reshape the flattened infant head.[59-61]

The helmet is expected to redirect skull growth by fitting closely to the infant's head and leaving room for skull growth at the flattened area. Some companies claim to have developed a helmet that would apply active molding forces[43, 62], however this is questioned by others. Constant active pressure is expected to lead to pressure sores and would therefore not be possible.[63] This would make the difference between passive and active devices non-existing. Still helmets differ in construction, one type of helmets is manufactured as a solid unit, sometimes with a strap under the chin, while another type has a kind of a 'hinge' and the fit can be adjusted by Velcro-strap fastening (Figure 2). However, all types are constructed of a rigid plastic shell with a foam lining. It is generally recommended that the helmet is worn by the infant for 23 hours a day and therapy is started at 6 months of age.[56, 64, 65] The correction rate decreases when infants start with helmet therapy at a later age, and reaches a plateau rate of change in 8-months-old infants.[63, 64]
Side effects are generally considered to be mild, but have hardly been studied systematically. Wilbrand et al. found 104 complications of treatment in 410 infants in a separate study. The most prevalent complications were pressure sores (11%), ethanol erythema (6%), and deficient fitting (6%). Helmet treatment costs anywhere from $180-4000.[56, 66, 67]

Figure 2. Infants wearing a helmet

Clinical evidence for helmet treatment

In the Netherlands 1% to 2% of all infants (176.000 newborns in 2012[68]) received helmet therapy for positional skull deformation in the recent years. Although the treatment is often prescribed, conclusive evidence on its effectiveness from randomized controlled trials remains lacking. The few prospective studies comparing helmet therapy to no helmet or another treatment tend to show positive results in favor of helmet therapy after three to five months of treatment.[4, 50, 57, 66, 69] However these studies have several limitations; treatment allocation was not at random, long term outcomes and assessment of side effects are missing and the clinical relevance of the reported effect is questionable.[56, 58, 65, 67, 70, 71]

Health policy issues: is helmet treatment justified?

The dramatic increase of positional skull deformation caused a higher awareness of the problem among professionals and media. Even more infants were diagnosed when parents became increasingly concerned. Some craniofacial centers organized screening days.[8] Because of the cosmetic nature of the condition and the resulting parental concern with their infant's future appearance[9, 72], parent can induce a demand for treatment.[8] In most countries parents can receive repositioning advice in the first half year of life, but thereafter treatment options are limited to helmet therapy or continuing repositioning and awaiting natural course. Yet, in an atmosphere where costs of healthcare are rising, and at the same time, budgets are getting more tight, treatments need to be proven to be value for money. This is not only to justify the costs for society when the treatment is being covered by insurance, but also to justify the out of pocket costs for parents when they have to pay for the helmet themselves.

As mentioned previously, there is a lack of good evidence for the (cost-)effectiveness of helmet therapy. Accordingly, there is variation in clinical practice and in healthcare professionals' preferences.[73] The unclear policy of professionals with regard to the prescription of helmet therapy makes parents more uncertain and leads to "shopping" to find proper treatment. At the same time, orthotics companies promote treatment, the internet provides information concerning possible consequences of skull deformation and success stories of parents who choose for helmet therapy for their child, while most of the time information about the natural course of positional skull deformation is lacking. Knowledge on the costs and effects of helmet therapy compared to the natural course is therefore important to help both healthcare professionals and parents make decisions.

However, to influence healthcare practice, providing data on cost-effectiveness alone is not sufficient.[74, 75] Haynes et al described how evidence based clinical decisions are made. The clinical state and circumstances of the patient, research evidence and patients' preferences and actions are interrelated. It is up to the healthcare professional to 'read' the three fields and combine the information.[75] In the case of positional skull deformation, it is essential for the professional to be able to determine the clinical state of the infants, have knowledge of the best available evidence for treatment, and understand the infants' parents' preferences. Thus, they can support parents in decision making by balancing medical information with parents' expectations and preferences.

To influence healthcare practice on an international level with new evidence, the health system of a country can play a vital role; is the treatment being covered or does a patient need to pay out of pocket? Therefore, it is important to get insight into professionals' treatment preferences and decisions in various countries with different health systems.

The HEADS study and this thesis

Summarizing, we do not know what the best treatment plan is for infants with positional skull deformation; pediatric physical therapy is proven to be effective, however not all infants show full recovery. Helmet therapy is a very popular, but also controversial and expensive without convincing evidence for its effectiveness. This lack of clear evidence is represented in contradictory opinions and preferences of parents and professionals. It is unknown on what basis healthcare professionals prescribe helmet therapy. Furthermore we do not know which parents start helmet therapy in their infant; they might be more anxious or concerned than parents who do not choose for treatment.
Against these backgrounds, the HEADS (HElmet therapy Assessment in Deformed Skulls) study was designed. The HEADS study was funded by ZonMw and consisted of two parts; the main study investigating the clinical evidence and an ancillary study focusing on patients' and healthcare professionals' preferences. The HEADS had a unique design **(chapter 2)**, integrating a randomised controlled trial (RCT) in a cohort study while systematically evaluating patients' decisions to take helmet therapy. The chapters in this thesis represent the key findings of this comprehensive study (Figure 3).
The main aims of the HEADS study are to A) provide a stronger evidence base for the treatment of positional skull deformation **(chapter 3, 5 and 6)** and B) gain a better understanding of the decision making for treatment by parents **(chapter 4)** and professionals **(chapter 7)** in a situation where high quality evidence on the best treatment is lacking. This should lead to evidence based decision making regarding treatment for infants with positional skull deformation by parents and professionals, more evidence based care, less infants with persistent skull deformation and less concerned parents.

Chapter 2 provides an extensive description of the study protocol of the complete HEADS study. The study starts as a cohort study in infants of 2 to 4 months of age who start pediatric physical therapy for a positional preference or positional skull deformation. Then, at 5 months, eligible infants are invited to participate in a nested RCT comparing effects and costs of 6 months of helmet therapy and natural course at 24 months. Non-participants of the RCT are invited to stay enrolled for follow-up in a non-randomised controlled trial (nRCT) until 24 months. Data of the first part of the cohort study are analyzed in **chapter 3**. All infants started pediatric physical therapy between 2 to 4 months of age, however not all show full recovery at age 5 months. This study aims to identify predictors of poor response to the pediatric physical therapy. Infants who present with persistent moderate or severe skull deformation are eligible to start helmet therapy

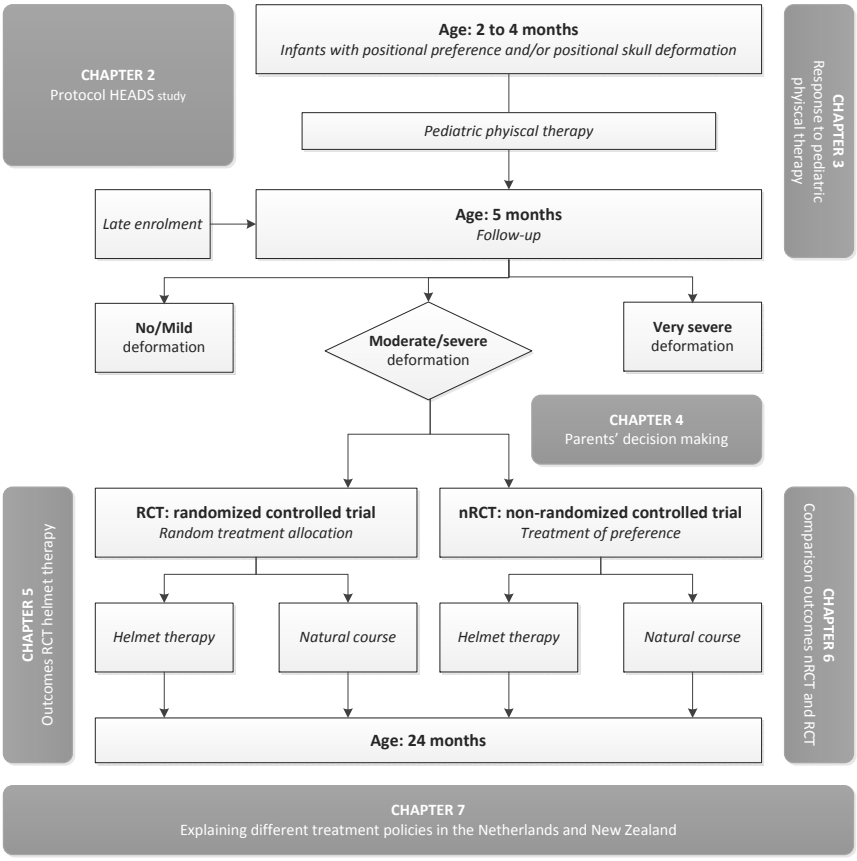

Figure 3. Flow chart HEADS study and thesis chapters

at 5 to 6 months of age. The study described in **chapter 4** aims to assess the relation between parents' decision for treatment of positional skull deformation in their infant and their level of anxiety, decisional conflict, expectations of treatment effect, perceived severity of deformation and perceived adverse events.

Chapter 5 presents outcomes of the RCT comparing helmet therapy started at 5 to 6 months of age with the natural course of positional skull deformation in infants at 24 months. Results of the parallel nRCT comparing helmet therapy to natural course are described in **chapter 6**. Results of the RCT and real world data from the nRCT are combined to strengthen conclusions. Finally, we analyze differences in treatment policy for positional skull deformation between The Netherlands and New Zealand. Infants with positional skull deformation undergo extensive treatment regimens in The Netherlands, including the use of helmet therapy, while in New Zealand hardly any helmet therapy is being prescribed. In **chapter 7**, beliefs, attitudes and expectations of clinicians involved in infant healthcare in The Netherlands are compared with those of New Zealand in an attempt to explain the difference in treatment policy in both countries. The societal impact and implications of the results of this dissertation are discussed in **chapter 8.**

REFERENCES

1. Meyer-Marcotty P, Bohm H, Linz C, et al. Spectrum of positional deformities - Is there a real difference between plagiocephaly and brachycephaly? *J. Craniomaxillofac. Surg.* 2014.

2. Argenta L, David L, Thompson J. Clinical classification of positional plagiocephaly. *J. Craniofac. Surg.* 2004;15(3):368-372.

3. Clarren SK. Plagiocephaly and torticollis: etiology, natural history, and helmet treatment. *J. Pediatr.* 1981;98(1):92-95.

4. Mulliken JB, Vander Woude DL, Hansen M, LaBrie RA, Scott RM. Analysis of posterior plagiocephaly: deformational versus synostotic. *Plast. Reconstr. Surg.* 1999;103(2):371-380.

5. Argenta LC, David LR, Wilson JA, Bell WO. An increase in infant cranial deformity with supine sleeping position. *J. Craniofac. Surg.* 1996;7(1):5-11.

6. Kane AA, Mitchell LE, Craven KP, Marsh JL. Observations on a recent increase in plagiocephaly without synostosis. *Pediatrics.* 1996;97(6 Pt 1):877-885.

7. Turk AE, McCarthy JG, Thorne CH, Wisoff JH. The "back to sleep campaign" and deformational plagiocephaly: is there cause for concern? *J. Craniofac. Surg.* 1996;7(1):12-18.

8. Collett B, Breiger D, King D, Cunningham M, Speltz M. Neurodevelopmental implications of "deformational" plagiocephaly. *J. Dev. Behav. Pediatr.* 2005;26(5):379-389.

9. Hutchison BL, Stewart AW, Mitchell EA. Deformational plagiocephaly: a follow-up of head shape, parental concern and neurodevelopment at ages 3 and 4 years. *Arch. Dis. Child.* 2011;96(1):85-90.

10. Balan P, Kushnerenko E, Sahlin P, Huotilainen M, Naatanen R, Hukki J. Auditory ERPs reveal brain dysfunction in infants with plagiocephaly. *J. Craniofac. Surg.* 2002;13(4):520-525; discussion 526.

11. Rekate HL. Occipital plagiocephaly: a critical review of the literature. *J. Neurosurg.* 1998;89(1):24-30.

12. St John D, Mulliken JB, Kaban LB, Padwa BL. Anthropometric analysis of mandibular asymmetry in infants with deformational posterior plagiocephaly. *J. Oral Maxillofac. Surg.* 2002;60(8):873-877.

13. Collett BR, Gray KE, Starr JR, Heike CL, Cunningham ML, Speltz ML. Development at age 36 months in children with deformational plagiocephaly. *Pediatrics.* 2013;131(1):e109-115.

14. Hutchison BL, Stewart AW, Mitchell EA. Characteristics, head shape measurements and developmental delay in 287 consecutive infants attending a plagiocephaly clinic. *Acta Paediatr.* 2009;98(9):1494-1499.

15. Kennedy E, Majnemer A, Farmer JP, Barr RG, Platt RW. Motor development of infants with positional plagiocephaly. *Phys Occup Ther Pediatr.* 2009;29(3):222-235.

16. Kordestani RK, Panchal J. Neurodevelopment delays in children with deformational plagiocephaly. *Plast. Reconstr. Surg.* Sep 2006;118(3):808-809; author reply 809-810.

17. Panchal J, Amirsheybani H, Gurwitch R, et al. Neurodevelopment in children with single-suture craniosynostosis and plagiocephaly without synostosis. *Plast. Reconstr. Surg.* 2001;108(6):1492-1498; discussion 1499-1500.

18. Pollack IF, Losken HW, Fasick P. Diagnosis and Management of Posterior Plagiocephaly. *Pediatrics.* 1997;99(2):180-185.

19. Boere-Boonekamp MM, van der Linden-Kuiper LT. Positional preference: prevalence in infants and follow-up after two years. *Pediatrics.* 2001;107(2):339-343.

20. van Vlimmeren LA, van der Graaf Y, Boere-Boonekamp MM, L'Hoir MP, Helders PJ, Engelbert RH. Effect of pediatric physical therapy on deformational plagiocephaly in children with positional preference: a randomized controlled trial. *Arch. Pediatr. Adolesc. Med.* 2008; 162(8):712-718.

21. Van Vlimmeren LA, Helders PJM. Het afgeplatte babyhoofd: meten van de afplatting en volgen van het beloop. *Praktische Pediatrie.* 2009;2:129-133.

22. Hutchison BL, Hutchison LA, Thompson JM, Mitchell EA. Plagiocephaly and brachycephaly in the first two years of life: a prospective cohort study. *Pediatrics.* 2004;114(4):970-980.

23. Littlefield TR, Saba NM, Kelly KM. On the current incidence of deformational plagiocephaly: an estimation based on prospective registration at a single center. *Semin. Pediatr. Neurol.* 2004;11(4):301-304.

24. Mawji A, Vollman AR, Hatfield J, McNeil DA, Sauve R. The incidence of positional plagiocephaly: a cohort study. *Pediatrics.* 2013;132(2):298-304.

25. Hutchison BL, Thompson JM, Mitchell EA. Determinants of nonsynostotic plagiocephaly: a case-control study. *Pediatrics.* 2003;112(4):e316.

26. van Vlimmeren LA, van der Graaf Y, Boere-Boonekamp MM, L'Hoir MP, Helders PJ, Engelbert RH. Risk factors for deformational plagiocephaly at birth and at 7 weeks of age: a prospective cohort study. *Pediatrics.* 2007;119(2):e408-418.

27. Littlefield TR, Kelly KM, Pomatto JK, Beals SP. Multiple-birth infants at higher risk for development of deformational plagiocephaly. *Pediatrics.* 1999;103(3):565-569.

28. McKinney CM, Cunningham ML, Holt VL, Leroux B, Starr JR. A case-control study of infant, maternal and perinatal characteristics associated with deformational plagiocephaly. *Paediatr. Perinat. Epidemiol.* 2009;23(4):332-345.

29. Peitsch WK, Keefer CH, LaBrie RA, Mulliken JB. Incidence of cranial asymmetry in healthy newborns. *Pediatrics.* 2002;110(6):e72.

30. Oh AK, Hoy EA, Rogers GF. Predictors of severity in deformational plagiocephaly. *J. Craniofac. Surg.* 2009;20 Suppl 1:685-689.

31. Rogers GF, Oh AK, Mulliken JB. The role of congenital muscular torticollis in the development of deformational plagiocephaly. *Plast. Reconstr. Surg.* 2009;123(2):643-652.

32. Nederlands Centrum Jeugdgezondheid. *JGZ-richtlijn Preventie, signalering en aanpak van voorkeurshouding en schedelvervorming.* Utrecht: TNO innovation for life;2012.

33. Joganic JL, Lynch JM, Littlefield TR, Verrelli BC. Risk factors associated with deformational plagiocephaly. *Pediatrics.* 2009;124(6):e1126-1133.

34. Littlefield TR, Kelly KM, Pomatto JK, Beals SP. Multiple-Birth Infants at Higher Risk for Development of Deformational Plagiocephaly: II. Is One Twin at Greater Risk? *Pediatrics.* 2002;109(1):19-25.

35. Teichgraeber JF, Ault JK, Baumgartner J, et al. Deformational posterior plagiocephaly: diagnosis and treatment. *Cleft Palate. Craniofac. J.* 2002;39(6):582-586.

36. Nuysink J, van Haastert IC, Eijsermans MJ, et al. Prevalence and predictors of idiopathic asymmetry in infants born preterm. *Early Hum. Dev.* 2012;88(6):387-392.

37. Lennartsson F. Developing Guidelines for Child Health Care Nurses to Prevent Nonsynostotic Plagiocephaly: Searching for the Evidence. *J. Pediatr. Nurs.* 2011;26(4):348-358.

38. SIDS AAoPTFoISPa. Changing concepts of sudden infant death syndrome: implications for infant sleeping environment and sleep position. . *Pediatrics.* 2000;105(3 Pt 1):650-656.

39. Persing J, James H, Swanson J, Kattwinkel J, Comm Practice Ambulatory M. Prevention and management of Positional skull deformities in infants. *Pediatrics.* 2003;112(1):199-202.

40. Spermon J, Spermon-Marijnen R, Scholten-Peeters W. Clinical classification of deformational plagiocephaly according to Argenta: a reliability study. *J. Craniofac. Surg.* 2008;19(3):664-668.

41. Graham JM, Jr., Gomez M, Halberg A, et al. Management of deformational plagiocephaly: repositioning versus orthotic therapy. *J. Pediatr.* 2005;146(2):258-262.

42. Lee RP, Teichgraeber JF, Baumgartner JE, et al. Long-term treatment effectiveness of molding helmet therapy in the correction of posterior deformational plagiocephaly: a five-year follow-up. *Cleft Palate. Craniofac. J.* 2008;45(3):240-245.

43. Littlefield TR, Beals SP, Manwaring KH, et al. Treatment of craniofacial asymmetry with dynamic orthotic cranioplasty. *J. Craniofac. Surg.* 1998;9(1):11-17; discussion 18-19.

44. Mortenson PA, Steinbok P. Quantifying positional plagiocephaly: reliability and validity of anthropometric measurements. *J. Craniofac. Surg.* 2006;17(3):413-419.

45. Wilbrand JF, Wilbrand M, Pons-Kuehnemann J, et al. Value and reliability of anthropometric measurements of cranial deformity in early childhood. *J. Craniomaxillofac. Surg.* 2011;39(1):24-29.

46. Hutchison BL, Hutchison LA, Thompson JM, Mitchell EA. Quantification of plagiocephaly and brachycephaly in infants using a digital photographic technique. *Cleft Palate. Craniofac. J.* 2005;42(5):539-547.

47. van Adrichem LNA, van Vlimmeren LA, Cadanova D, et al. Validation of a simple method for measuring cranial deformities (Plagiocephalometry). *J. Craniofac. Surg.* 2008;19(1):15-21.

48. van Vlimmeren LA, Takken T, van Adrichem LN, van der Graaf Y, Helders PJ, Engelbert RH. Plagiocephalometry: a non-invasive method to quantify asymmetry of the skull; a reliability study. *Eur. J. Pediatr.* 2006;165(3):149-157.

49. Atmosukarto I, Shapiro LG, Starr JR, et al. Three-dimensional head shape quantification for infants with and without deformational plagiocephaly. *Cleft Palate. Craniofac. J.* 2010;47(4):368-377.

50. Lipira AB, Gordon S, Darvann TA, et al. Helmet versus active repositioning for plagiocephaly: a three-dimensional analysis. *Pediatrics.* 2010;126(4):e936-945.

51. Plank LH, Giavedoni B, Lombardo JR, Geil MD, Reisner A. Comparison of infant head shape changes in deformational plagiocephaly following treatment with a cranial remolding orthosis using a noninvasive laser shape digitizer. *J. Craniofac. Surg.* 2006;17(6):1084-1091.

52. Feijen M, Schuckman M, Habets E, van der Hulst R. Positional plagiocephaly and brachycephaly: is there a correlation between subjective and objective assessment of cranial shape? *J. Craniofac. Surg.* 2012;23(4):998-1001.

53. Govaert B, Michels A, Colla C, van der Hulst R. Molding therapy of positional plagiocephaly: subjective outcome and quality of life. *J. Craniofac. Surg.* 2008;19(1):56-58.

54. Katzel EB, Koltz PF, Sbitany H, Emerson C, Girotto JA. Real versus perceived improvements of helmet molding therapy for the treatment of plagiocephaly. *Plast. Reconstr. Surg.* 2010;126(1):19e-21e.

55. Hutchison BL, Stewart AW, De Chalain TB, Mitchell EA. A randomized controlled trial of positioning treatments in infants with positional head shape deformities. *Acta Paediatr.* 2010;99(10):1556-1560.

56. Flannery AB, Looman WS, Kemper K. Evidence-based care of the child with deformational plagiocephaly, part II: management. *J. Pediatr. Health Care.* 2012;26(5):320-331.

57. Kluba S, Kraut W, Calgeer B, Reinert S, Krimmel M. Treatment of positional plagiocephaly - Helmet or no helmet? *J. Craniomaxillofac. Surg.* 2014;42(5):683-8.

58. Xia JJ, Kennedy KA, Teichgraeber JF, Wu KQ, Baumgartner JB, Gateno J. Nonsurgical treatment of deformational plagiocephaly: a systematic review. *Arch. Pediatr. Adolesc. Med.* 2008;162(8):719-727.

59. Ayer A, Campbell A, Appelboom G, et al. The sociopolitical history and physiological underpinnings of skull deformation. *Neurosurg. Focus.* 2010;29(6):E1.

60. Clarren SK, Smith DW, Hanson JW. Helmet treatment for plagiocephaly and congenital muscular torticollis. *J. Pediatr.* 1979;94(1):43-46.

61. Lekovic GP, Baker B, Lekovic JM, Preul MC. New World cranial deformation practices: historical implications for pathophysiology of cognitive impairment in deformational plagiocephaly. *Neurosurgery.* 2007;60(6):1137-1146; discussion 1146-1137.

62. Lee WT, Richards K, Redhed J, Papay FA. A pneumatic orthotic cranial molding helmet for correcting positional plagiocephaly. *J. Craniofac. Surg.* 2006;17(1):139-144.

63. Seruya M, Oh AK, Taylor JH, Sauerhammer TM, Rogers GF. Helmet treatment of deformational plagiocephaly: the relationship between age at initiation and rate of correction. *Plast. Reconstr. Surg.* 2013;131(1):55e-61e.

64. Kluba S, Kraut W, Reinert S, Krimmel M. What is the optimal time to start helmet therapy in positional plagiocephaly? *Plast. Reconstr. Surg.* 2011;128(2):492-498.

65. Robinson S, Proctor M. Diagnosis and management of deformational plagiocephaly. *J. Neurosurg. Pediatr.* 2009;3(4):284-295.

66. Loveday BP, de Chalain TB. Active counterpositioning or orthotic device to treat positional plagiocephaly? *J. Craniofac. Surg.* 2001;12(4):308-313.

67. Goh JL, Bauer DF, Durham SR, Stotland MA. Orthotic (helmet) therapy in the treatment of plagiocephaly. *Neurosurg. Focus.* 2013;35(4):E2.

68. Statistics Netherlands. Population; sex, age, origin and generation, 1 January. 2013; http://statline.cbs.nl/StatWeb/publication/?VW=T&DM=SLEN&PA=37325eng&D1=0-2&D2=0&D3=0&D4=0&D5=0-1,3-4,139,145,210,225&D6=4,9,(l-1)-l&HD=090611-0858&LA=EN&HDR=G3,T&STB=G5,G1,G2,G4. Accessed 13-11-2013.

69. Vles JS, Colla C, Weber JW, Beuls E, Wilmink J, Kingma H. Helmet versus nonhelmet treatment in nonsynostotic positional posterior plagiocephaly. *J. Craniofac. Surg.* 2000;11(6):572-574.

70. Bialocerkowski AE, Vladusic SL, Howell SM. Conservative interventions for positional plagiocephaly: a systematic review. *Dev. Med. Child Neurol.* 2005;47(8):563-570.

71. Singh A, Wacogne I. What is the role of helmet therapy in positional plagiocephaly? *Arch. Dis. Child.* 2008;93(9):807-809.

72. Steinbok P, Lam D, Singh S, Mortenson PA, Singhal A. Long-term outcome of infants with positional occipital plagiocephaly. *Childs Nerv. Syst.* 2007;23(11):1275-1283.

73. Lee A, Van Pelt AE, Kane AA, et al. Comparison of perceptions and treatment practices between neurosurgeons and plastic surgeons for infants with deformational plagiocephaly. *Journal of Neurosurgery: Pediatrics*. 2010;5(4):368-374.

74. Hoffmann C, Stoykova BA, Nixon J, Glanville JM, Misso K, Drummond MF. Do health-care decision makers find economic evaluations useful? The findings of focus group research in UK health authorities. *Value Health*. 2002;5(2):71-78.

75. Haynes RB, Devereaux PJ, Guyatt GH. Physicians' and patients' choices in evidence based practice. *BMJ*. 2002;324(7350):1350.

CHAPTER 2

HElmet therapy Assessment in infants with Deformed Skulls (HEADS): protocol for a randomised controlled trial

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ABSTRACT

Background – In The Netherlands, helmet therapy is a commonly used treatment in infants with skull deformation (deformational plagiocephaly or deformational brachycephaly). However, evidence of the effectiveness of this treatment remains lacking. The HEADS study (HElmet therapy Assessment in Deformed Skulls) aims to determine the effects and costs of helmet therapy compared to no helmet therapy in infants with moderate to severe skull deformation.

Methods/Design – Pragmatic randomised controlled trial (RCT) nested in a cohort study. The cohort study included infants with a positional preference and/or skull deformation at two to four months (first assessment). At 5 months of age, all children were assessed again and infants meeting the criteria for helmet therapy were asked to participate in the RCT. Participants were randomly allocated to either helmet therapy or no helmet therapy. Parents of eligible infants that do not agree with enrolment in the RCT were invited to stay enrolled for follow up in a non-randomised controlled trial (nRCT); they were then free to make the decision to start helmet therapy or not. Follow-up assessments took place at 8, 12 and 24 months of age. The main outcome will be head shape at 24 months that is measured using plagiocephalometry. Secondary outcomes will be satisfaction of parents and professionals with the appearance of the child, parental concerns about the future, anxiety level and satisfaction with the treatment, motor development and quality of life of the infant. Finally, compliance and costs will also be determined.

Discussion – HEADS will be the first study presenting data from an RCT on the effectiveness of helmet therapy. Outcomes will be important for affected children and their parents, health care professionals and future treatment policies. Our findings are likely to influence the reimbursement policies of health insurance companies.
Besides these health outcomes, we will be able to address several methodological questions, *e.g.* do participants in an RCT represent the eligible target population and do outcomes of the RCT differ from outcomes found in the nRCT?

BACKGROUND

Infants have malleable and fast-growing cranial bones, and are therefore at risk of developing skull deformation if their head often remains in the same position. When a child turns its head toward one side most of the time, this is defined as positional preference.[1] Skull deformation due to such prolonged external forces (non-synostotic) must be distinguished from skull malformation due to premature fusion of the cranial sutures (synostotic).[2] Deformational brachycephaly refers to a symmetric occipital flattening of the skull that is sometimes accompanied by temporal bossing or an occipital lift.[3] The term deformational plagiocephaly is used to describe a unilateral occipital flattening of the skull. More severe cases often present with ear misalignment and facial asymmetry.[2, 4]

Skull deformation is generally considered a purely cosmetic disorder. Yet parents worry that the deformation might be permanent and might influence the child's attractiveness with the risk of, for example, being teased.[5] Some studies suggest long-term developmental delays due to skull deformity, but no causal relationships have been found.[5-7].

The prevalence of skull deformation can be up to 21.5% in infants younger than 6 months, but decreases within the first years of life.[8-10]. A low parental level of education, ethnicity, male gender, primiparity, prematurity, birth factors, delayed (motor) development, low activity level and several positioning and dietary factors have been reported as risk factors, while placing a child in the prone position when awake appears to be a protective factor.[1, 11-17]

Prevention or treatment of positional preference and skull deformation include parental counselling, counter-positioning and physical therapy.[10, 18] Children with persisting severe skull deformation at the age of 5 to 6 months are commonly treated using orthotic devices (redression helmets or headbands).[4, 19] In the Netherlands, a redression helmet costs about €1,200 and is reimbursed by health insurance companies as well as the accompanying visits to the (paediatric) physician. However, until now, no randomised controlled trials (RCTs) have been performed to study the effectiveness of this therapy.[20, 21] The few non-randomised studies tend to show positive results, but have several limitations. To start with it is unknown whether the reported differences in effectiveness are clinically relevant. Furthermore, follow-up in these studies was short-term (either directly after treatment or just a few months afterwards), there was a lack of blinding or information about blinding and often no validated outcome measures were used. Finally, data about complications were not collected in a structural way in these studies.[2, 4, 20, 22, 23] Although the known complications of helmet therapy are mild and do not seem to occur often, the treatment burdens both parents and their young children.[22] Next to the lack of scientific evidence, experience shows differences in beliefs and referral policies of health care professionals regarding helmet therapy. Some advocate the use of helmets to treat skull deformation, while others are reluctant to prescribe this intensive treatment for a cosmetic condition without knowing its effectiveness.[21, 24] This makes parents very uncertain when they have to decide whether to start helmet therapy or not.

Both helmet therapy and no helmet therapy (allowing natural recovery) are standard approaches in The Netherlands. To compare the effectiveness of these two approaches a pragmatic RCT study design is required.[25] Pragmatic trials are designed to find out the effectiveness of a treatment in routine, everyday practice and thereby have a high external validity.[26, 27] A high external validity can be achieved by recruiting a broad study population that is representative of the target population, studying interventions that approach a real world delivery of care, applying blinding to neither participants nor specialists and selecting a wide range of outcome measures.[28, 29]

Since the condition of interest changes over time and the decision-making is time-dependent, the RCT needs to be nested in a cohort study.[30-32] The decision to start helmet therapy is usually taken at 5 to 6 months of age. Recruitment at that stage is complicated as the children tend to be scattered among various institutes if their parents prefer helmet therapy or are outside the health care system if their parents choose not to start helmet therapy. As the cohort study recruits children at risk of disease progression before helmet therapy can be prescribed, we tackle this problem and we are also able to predict the number of children that ultimately will be eligible for helmet therapy and identify prognostic factors.
Additionally, nesting the RCT in a prospective cohort study makes it possible to present information on the representativeness of the RCT population, by comparing this population with non-participants.[33, 34] Furthermore, outcomes of the randomised trial can be compared with the parallel non-randomised trial that employs the same types of intervention.

The main goal of the Helmet Therapy Assessment in Deformed Skulls (HEADS) study is to investigate the effects and costs of six months of helmet therapy compared to no helmet therapy in children with moderate to severe skull deformation. This article describes how this study is designed and reports the recruitment scheme so far. We provide a description of the statistical analysis plan to be used after data collection is completed and conclude with general recommendations on study design.

METHODS/DESIGN

Study design

The HEADS study is a two-armed pragmatic RCT nested in a cohort study (Figure 1). The intervention is redression helmet therapy; the control condition is no helmet therapy (allowing natural recovery). The study starts as a cohort study for children aged two to four months with a positional preference and/or skull deformation (T0). At five months of age (T5), follow-up assessments are performed and parents of children with a moderate to severe skull deformation are invited to participate in the RCT. Eligible children whose parents do not wish to enrol in the RCT are invited to join the non-randomised controlled trial (nRCT) that runs parallel to the RCT.

In both studies, follow-up assessments are performed at eight (T8), twelve (T12) and twenty-four months (T24) of age.

Ethics approval for the study was given on the 8th January 2009 (ref: NL24352.044.08) by the Medical Ethics Committee of the Medisch Spectrum Twente hospital in Enschede, The Netherlands.

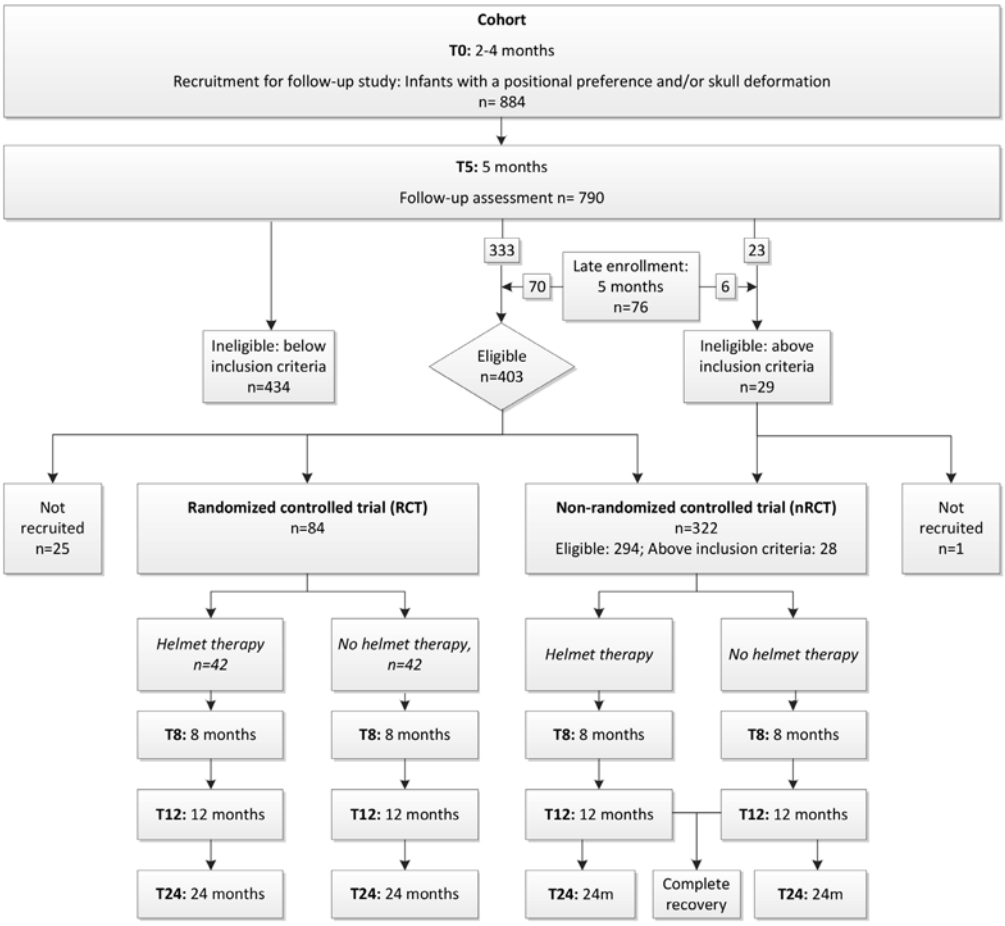

Figure 1. Flow chart participants HEADS. Provisional data at January 2012

Recruitment & Setting

Participants were recruited (April 2009 to present) and measured by specially trained paediatric physical therapists (HEADS PPTs) in the Eastern part of the Netherlands (in the provinces of Drenthe, Overijssel and parts of Gelderland). In The Netherlands, all infants are screened in the first months of life for positional preference and skull deformation at well-baby clinics. Youth Health Care professionals working at well-baby clinics in the region where the study is carried

out have been informed about this study, reminded to look for this condition and asked to refer cases to HEADS PPTs.

There are 96 HEADS PPTs involved in the study, working in 73 physical therapist practices. They all received three instruction sessions from the researchers of the HEADS study, including theory lessons on positional preference and skull deformation, a refresher course about plagiocephalometry (PCM) assessment and training in recruiting patients for RCTs. Based on their experience and performance in the HEADS study, six HEADS PPTs were selected to perform the assessments at T24 (T24-HEADS PPTs) and received an extra instruction session.

Children could be treated with helmet therapy at ProReva (Zwolle), Deventer Hospital/LIVIT (Deventer) and Slingeland Hospital/Roessingh Rehabilitation Technique (Doetinchem). At the start of the HEADS study, these were the only institutions providing helmet therapy within the region in which the project is carried out, and therefore they were asked to collaborate in the RCT. Parents of children in the nRCT could also choose institutions outside of this region or newer institutes that provide helmet therapy within the region.

Eligibility criteria

Cohort study

Children aged two to four months with a positional preference and/or skull deformation are eligible for the cohort study. Premature children (gestational age below 36 weeks), children with congenital muscular torticollis, craniosynostosis and/or dysmorphic features are all excluded.

Randomised controlled trial

Children aged 5 months with a moderate to severe skull deformation, measured by PCM are eligible for the RCT. PCM is a reliable, valid, non-invasive and easy-to-use method for measuring the shape of the skull.[35, 36] To determine the severity of deformational plagiocephaly, the oblique diameter difference index (ODDI) is used. This is the ratio between the longest and the shortest oblique diameter, multiplied by 100%. Both diameters are located at 40° from the anterior-posterior line. A moderate to severe plagiocephaly is defined as 108%≤ODDI≤113%. The severity of deformational brachycephaly is established with the cranio proportional index (CPI). This is the ratio between the width and the length of the skull and is considered to be moderate to severe when 95%≤CPI≤104%. Mixed forms with ODDI>106% and CPI>92% are also included. Exclusion criteria are similar to those at T0.

At T5, children meeting RCT eligibility criteria can still enrol in the study (late-enrolment)

Non-randomised controlled trial

Children eligible for the RCT, but whose parents declined participation, are invited to participate in the nRCT for follow-up. Children with PCM outcomes above the upper thresholds of the inclusion criteria for the RCT are also asked to participate in the nRCT.

Population

Figure 1 shows that 883 infants enrolled at T0 for baseline measurement. At T5, 808 infants had a follow-up assessment; 477 did not meet the inclusion criteria for the RCT. Of these 477 infants, 26 infants had PCM outcomes above the upper thresholds of the inclusion criteria for the RCT and were eligible to participate in the nRCT. Seventy-five infants enrolled at T5 via late-enrolment, of whom 5 infants had PCM outcomes above the upper thresholds of the inclusion criteria for the RCT and were eligible to participate in the nRCT. Of the eligible 401 infants, 84 (21%) were recruited for the RCT, 296 did not participate in the RCT because their parents declined to enrol them, but were recruited for the nRCT (74%) and 21 (5%) were not recruited to either of the studies. Parents signed an informed consent form before participation in the cohort study, as well as before participation in the RCT.

Randomisation

A computer-generated blocked randomisation plan with blocks of eight participants is used to allocate treatment in the RCT. After a HEADS PPT enrols a child for the RCT, he or she informs the researcher (RMW) who contacts the parents. Both parents and researcher are unaware of allocation until the parents have signed the informed consent form and confirmed participation. The researcher performs the allocation and informs the parents about group allocation. The child's HEADS PPT, general practitioner and Youth Health Care professional are also informed about the allocation afterwards.

Blinding

Blinding of parents and professionals to allocation is not possible during the intervention period, including the T8 and T12 assessment. To ensure unbiased long-term outcomes, the T24 assessments are blinded. These assessments are carried out by T24-HEADS PPTs, who are unfamiliar with the history of the infants they are measuring. Furthermore, we instruct parents in the invitation letter and a poster at the assessment location, not to mention group allocation to the assessor.

Interventions

Randomised controlled trial

Helmet therapy: parents of participants allocated to the helmet therapy group were asked to make an appointment at one of the three collaborating institutes for helmet therapy. First a (paediatric) physician was consulted to confirm diagnosis and exclude contraindications.

Subsequently, the orthotist provided care as usual; he constructed the custom-made helmet, supplied information about introducing the helmet to the infant, regular wearing instructions and instructions about cleaning of the helmet and general care. The helmet has to be worn for at least 23 hours per day from six to twelve months of age.
No helmet therapy: Parents of participants allocated to the no helmet therapy group were asked not to start any treatment for the skull deformation of their child. In this group, recovery of deformation of the head was awaited by allowing spontaneous growth of the skull.

Non-randomised controlled trial

In the nRCT, parents were able to select a treatment for their child, that is, either helmet therapy or no helmet therapy. The choice was recorded afterwards when the child was twelve months old (T12).

Data collection

The cohort study started with a baseline measurement at two to four months of age (T0). A follow-up measurement was performed in all children at 5 months of age (T5).

In the RCT, assessments took place at the age of 8 months (T8), 12 months (T12) and 24 months (T24) (Figure 1). In the nRCT the same assessments took place at T12 and T24. At T8 only a parental questionnaire was collected by mail. Data were collected by the HEADS PPTs. During every assessment, the shape of the skull was measured, a motor assessment was carried out and both the parents and the HEADS PPTs were asked to complete a questionnaire. The HEADS PPT sent the data about each child to the researcher (RMW).

Baseline characteristics

Through the parental questionnaire at T0 and the parental questionnaire for late-enrolment at T5, information about background characteristics, medical characteristics and other possible prognostic factors were collected.

Primary outcome

The primary outcome is the transverse shape of the skull at 24 months, measured with PCM. The severity of deformational plagiocephaly was determined using the ODDI, and ear deviation (ED) was calculated to determine ear misalignment. The severity of deformational brachycephaly was determined by the CPI. A continuous outcome variable (change in score from pre- to post-test) as well as a dichotomous outcome variable will be used for analysis. The dichotomous variable distinguishes full recovery from no full recovery with a cut-off for full recovery of ODDI < 104% and CPI < 90%.

Secondary outcomes

Secondary outcomes are 1) satisfaction of the parents and HEADS PPT with skull shape, face and body (5-point Likert scale); 2) psychomotor development (a modified Gesell assessment, at regular well-baby clinic visits)[37]; 3) motor domain of Bayley Scales of Infant Development (BSID III)[38]; 4) anxiety level of parents (Spielberger State-Trait Anxiety Inventory, Dutch version)[39]; 5) parental concerns about the child's future, possible teasing and uncertainty about the child's appearance (5-point Likert scale); 6) quality of life (Infant Toddler Quality of Life Questionnaire (ITQOL-SF47)[40]) and 7) parental satisfaction with treatment..

Compliance

The questionnaire at T12 assessed whether parents were compliant with the therapy to which their child was assigned. Also recorded, was whether parents switched groups, and if they did, the age this happened and the reason for it. The helmet providers also collected start and end dates of helmet therapy given to infants in the RCT. Furthermore, helmets in the RCT of the HEADS study are equipped with a logging device (LoD). The LoD measures the number of hours a helmet is worn per week (therapy compliance) and will be used to determine a dose-response relationship. The LoD was attached to the helmet and data were sent to the researcher after the invention period.

In both groups, parents were asked at T12 whether they provided extra care to treat the skull deformation of their child, such as the use of positioning devices, performing exercises with their child or applying various additional therapies.

Determination of costs

Cost data were collected alongside the effectiveness study. Both medical costs and indirect costs incurred by parents because of diagnostic work-up and treatment were recorded. Indirect costs were collected with the help of a diary completed by parents during the intervention period. Costs are being determined for both the RCT and the nRCT.

Sample size

The required sample size for the HEADS RCT, based on a significance level of 5%, power of 90% and a difference in mean improvement of at least 4 ODDI-points (SD 6 ODDI-points) was calculated as 72 infants (36 in each arm). Assuming a maximum estimated loss-to-follow up of 25%, we needed to include 96 children in the RCT.

In 2008, a preliminary study was performed into the feasibility of an RCT on helmet therapy for skull deformation. Of the parents of 61 children with a skull deformation, 39% agreed to participate in a study as described in the patient information and verbally clarified. In the light of this information, the size of the current study region was chosen and the inclusion period was estimated.

Statistical analyses

Data analyses will be performed using SPSS 18.0. A statistical significance level of 0.05 will be used and missing values will be imputed with multiple imputation.[41]

Cohort study

Data analysis will start with descriptive statistics of baseline demographic and clinical characteristics of the total population at T0. At T5, this will be repeated for the clinical characteristics.

Randomised controlled trial (RCT)

At T5, characteristics of the RCT population will be described. In a subsequent analysis, the intervention and control group will be compared with respect to prognostic factors using the independent samples *t*-test or the chi square test. The representativeness of the RCT population will be determined by comparing baseline demographic and clinical characteristics of the RCT population with those of the total eligible population at T5. Both the change score (continuous variable) and the success of recovery (dichotomous variable) will be compared between groups on an intention-to-treat basis. After analysis of covariance (ANCOVA), both multiple regression analyses (change score) and logistic regression analyses (success of recovery) will be carried out with predictor variables to control for confounders. Finally, a per-protocol analysis will be performed.

Non-randomised controlled trial (nRCT)

Baseline characteristics and applied therapies will be described for participants in the nRCT and compared between children treated with a helmet and children whose parents chose not to start helmet therapy. Similarly to the RCT, both the continuous and the dichotomous variables will be compared between groups on an intention-to-treat basis. After univariate analyses, both multivariate and logistic regression analyses will be carried out adding predictor variables.

Comparison between the randomized and the non-randomised controlled trials

Baseline characteristics will be compared between the RCT and the nRCT. To study differences in the continuous as well as the dichotomous variable between the RCT and the nRCT, both a multiple linear regression analysis and a logistic regression analysis will be carried out, with the interaction factor of study (RCT or nRCT) □ group (helmet or no helmet).

DISCUSSION

The HEADS trial is the first study to present an RCT on the long-term effects of helmet therapy compared to no helmet therapy in infants with moderate to severe skull deformation. The HEADS study started as a cohort study for infants aged two to four months, and continued as an RCT after the first follow-up assessment at the age of five months. In parallel with the RCT, a non-randomised controlled trial (nRCT) was carried out. This extensive cohort study will provide excellent opportunities to study the determinants of skull deformation. Outcomes of the RCT and the nRCT will provide objective information about treatment options for the parents of affected children. With this information, an informed decision can be made whether to start helmet therapy or not. Additionally, outcomes from the cost-effectiveness study are expected to influence future treatment and reimbursement policies.

Recruitment in RCTs is often a challenge and it is common that trials fail to reach their target sample size.[42] In the RCT of the HEADS study, enrolment also proved more difficult than expected. During the recruitment period, it gradually became clear that only 21% of the parents of eligible infants gave consent for the RCT (Figure 1). This is half of the 39% enrolment rate predicted in the preliminary study, and questions the validity of a preliminary study. A much longer recruitment period is needed to recruit the calculated sample size of 96, necessary in case of a maximal loss to follow-up of 25%.

However, most parents refusing participation in the RCT are willing to enrol in the nRCT. Figure 1 shows that only 21 participants who were eligible for participation in the RCT or nRCT were not recruited, implying that almost the complete group of eligible patients at T5 (n = 331) from the original cohort was followed in the HEADS study. This emphasizes the advantage of the nested RCT design; due to their participation in the cohort study, participants are already committed to the study once the RCT and nRCT recruitment starts.

Another methodological advantage of the present study design is its ability to better evaluate the representativeness of the RCT study population. Usually, RCTs have homogeneous yet very selective populations to maximize the likelihood of detecting significant differences. The cohort study of the HEADS study represents a broad population. Due to the nested study design, it is possible to determine the external validity of the RCT, by testing whether the RCT population is representative of the broad, eligible population at T5. The same can be determined for the nRCT population. Furthermore, we can study whether participants in the RCT are comparable to the nRCT participants by comparing the study outcomes and baseline characteristics in both studies.

Finally, as the decision for helmet therapy in the nRCT group was made by parents themselves, this will allow us to investigate the relationship between real-world decisions and treatment outcomes. This provides more information on the usefulness of data from non-randomised compared to randomised studies, which is relevant in comparative effectiveness research. Furthermore simultaneous analysis of data from an RCT and nRCT can strongly contribute to the generalizability of the study outcomes and the development of clinical practice guidelines as compared to single RCTs.[43]

Final results of the HEADS study are expected in 2013.

REFERENCES

1. Boere-Boonekamp MM, van der Linden-Kuiper LT. Positional preference: prevalence in infants and follow-up after two years. *Pediatrics.* 2001;107(2):339-343.

2. Mulliken JB, Vander Woude DL, Hansen M, LaBrie RA, Scott RM. Analysis of posterior plagiocephaly: deformational versus synostotic. *Plast. Reconstr. Surg.* 1999;103(2):371-380.

3. Argenta L, David L, Thompson J. Clinical classification of positional plagiocephaly. *J. Craniofac. Surg.* 2004;15(3):368-372.

4. Clarren SK. Plagiocephaly and torticollis: etiology, natural history, and helmet treatment. *J. Pediatr.* 1981;98(1):92-95.

5. Collett B, Breiger D, King D, Cunningham M, Speltz M. Neurodevelopmental implications of "deformational" plagiocephaly. *J. Dev. Behav. Pediatr.* 2005;26(5):379-389.

6. Balan P, Kushnerenko E, Sahlin P, Huotilainen M, Naatanen R, Hukki J. Auditory ERPs reveal brain dysfunction in infants with plagiocephaly. *J. Craniofac. Surg.* 2002;13(4):520-525; discussion 526.

7. Miller RI, Clarren SK. Long-term developmental outcomes in patients with deformational plagiocephaly. *Pediatrics.* 2000;105(2):E26.

8. Hutchison BL, Hutchison LA, Thompson JM, Mitchell EA. Plagiocephaly and brachycephaly in the first two years of life: a prospective cohort study. *Pediatrics.* 2004;114(4):970-980.

9. Hutchison BL, Stewart AW, Mitchell EA. Deformational plagiocephaly: a follow-up of head shape, parental concern and neurodevelopment at ages 3 and 4 years. *Arch. Dis. Child.* 2010;96(1):85-90.

10. van Vlimmeren LA, van der Graaf Y, Boere-Boonekamp MM, L'Hoir MP, Helders PJ, Engelbert RH. Effect of pediatric physical therapy on deformational plagiocephaly in children with positional preference: a randomized controlled trial. *Arch. Pediatr. Adolesc. Med.* 2008; 162(8):712-718.

11. Bialocerkowski AE, Vladusic SL, Wei Ng C. Prevalence, risk factors, and natural history of positional plagiocephaly: a systematic review. *Dev. Med. Child Neurol.* 2008;50(8):577-586.

12. Hutchison BL, Stewart AW, Mitchell EA. Characteristics, head shape measurements and developmental delay in 287 consecutive infants attending a plagiocephaly clinic. *Acta Paediatr.* 2009;98(9):1494-1499.

13. Hutchison BL, Thompson JM, Mitchell EA. Determinants of nonsynostotic plagiocephaly: a case-control study. *Pediatrics.* 2003;112(4):e316.

14. van Vlimmeren LA, van der Graaf Y, Boere-Boonekamp MM, L'Hoir MP, Helders PJ, Engelbert RH. Risk factors for deformational plagiocephaly at birth and at 7 weeks of age: a prospective cohort study. *Pediatrics.* 2007;119(2):e408-418.

15. McKinney CM, Cunningham ML, Holt VL, Leroux B, Starr JR. A case-control study of infant, maternal and perinatal characteristics associated with deformational plagiocephaly. *Paediatr. Perinat. Epidemiol.* 2009;23(4):332-345.

16. Michels AC, Van den Elzen ME, Vles JS, Van der Hulst RR. Positional plagiocephaly and excessive folic acid intake during pregnancy. *Cleft Palate. Craniofac. J.* 2012;49(1):1-4.

17. Weernink MGM, van Wijk RM, Groothuis-Oudshoorn CGM, Van Vlimmeren LA, Lanting CI, Boere-Boonekamp MM. De relatie tussen vitamine-D-inname en schedeldeformatie bij zuigelingen [abstract]. *Tijdschrift voor Jeugdgezondheidszorg.* 2011;4:1.

18. Hutchison BL, Stewart AW, De Chalain TB, Mitchell EA. A randomized controlled trial of positioning treatments in infants with positional head shape deformities. *Acta Paediatr.* 2010;99(10):1556-1560.

19. Pollack IF, Losken HW, Fasick P. Diagnosis and Management of Posterior Plagiocephaly. *Pediatrics.* 1997;99(2):180-185.

20. Lipira AB, Gordon S, Darvann TA, et al. Helmet versus active repositioning for plagiocephaly: a three-dimensional analysis. *Pediatrics.* 2010;126(4):e936-945.

21. Littlefield TR. Cranial remodeling devices: treatment of deformational plagiocephaly and postsurgical applications. *Semin. Pediatr. Neurol.* 2004;11(4):268-277.

22. Loveday BP, de Chalain TB. Active counterpositioning or orthotic device to treat positional plagiocephaly? *J. Craniofac. Surg.* 2001;12(4):308-313.

23. Vles JS, Colla C, Weber JW, Beuls E, Wilmink J, Kingma H. Helmet versus nonhelmet treatment in nonsynostotic positional posterior plagiocephaly. *J. Craniofac. Surg.* 2000;11(6):572-574.

24. Lee A, Van Pelt AE, Kane AA, et al. Comparison of perceptions and treatment practices between neurosurgeons and plastic surgeons for infants with deformational plagiocephaly. *Journal of Neurosurgery: Pediatrics.* 2010;5(4):368-374.

25. Thorpe KE, Zwarenstein M, Oxman AD, et al. A pragmatic-explanatory continuum indicator summary (PRECIS): a tool to help trial designers. *J. Clin. Epidemiol.* 2009;62(5):464-475.

26. Macpherson H. Pragmatic clinical trials. *Complement. Ther. Med.* 2004;12(2-3):136-140.

27. Schwartz D, Lellouch J. Explanatory and pragmatic attitudes in therapeutical trials. *J. Chronic Dis.* 1967;20(8):637-648.

28. Fransen GAJ, van Marrewijk CJ, Mujakovic S, et al. Pragmatic trials in primary care. Methodological challenges and solutions demonstrated by the DIAMOND-study. *BMC Med. Res. Methodol.* 2007;7(1):16.

29. Tunis SR, Stryer DB, Clancy CM. Practical clinical trials: increasing the value of clinical research for decision making in clinical and health policy. *JAMA.* 2003;290(12):1624-1632.

30. Relton C, Torgerson D, O'Cathain A, Nicholl J. Rethinking pragmatic randomised controlled trials: introducing the "cohort multiple randomised controlled trial" design. *BMJ.* 2010;340:c1066-c1066.

31. Donovan J, Mills N, Smith M, et al. Quality improvement report: Improving design and conduct of randomised trials by embedding them in qualitative research: ProtecT (prostate testing for cancer and treatment) study. Commentary: presenting unbiased information to patients can be difficult. *BMJ.* 2002;325(7367):766-770.

32. Ross S, Grant A, Counsell C, Gillespie W, Russell I, Prescott R. Barriers to participation in randomised controlled trials: a systematic review. *J. Clin. Epidemiol.* 1999;52(12):1143-1156.

33. Bartlett C, Doyal L, Ebrahim S, et al. The causes and effects of socio-demographic exclusions from clinical trials. *Health Technol. Assess.* 2005;9(38):iii-iv, ix-x, 1-152.

34. Bonell C, Oakley A, Hargreaves J, Strange V, Rees R. Assessment of generalisability in trials of health interventions: suggested framework and systematic review. *BMJ.* 2006;333(7563):346-349.

35. van Adrichem LNA, van Vlimmeren LA, Cadanova D, et al. Validation of a simple method for measuring cranial deformities (Plagiocephalometry). *J. Craniofac. Surg.* Jan 2008;19(1):15-21.

36. van Vlimmeren LA, Takken T, van Adrichem LN, van der Graaf Y, Helders PJ, Engelbert RH. Plagiocephalometry: a non-invasive method to quantify asymmetry of the skull; a reliability study. *Eur. J. Pediatr.* 2006;165(3):149-157.

37. Laurent de Angulo MS, Brouwers-de Jong EA, Bijlsma-Schlösser JFM, et al. *Ontwikkelingsonderzoek in de jeugdgezondheidszorg. Het Van Wiechenonderzoek – De Baecke-Fassaert Motoriektest*. Assen: Van Gorcum; 2005.

38. Bayley N. *Manual for the Bayley Scales of Infant and Toddler Development* 3rd ed. San Antonio, TX: Psychological Corp; 2006.

39. van der Ploeg HM, Defares PB, Spielberger CD. *Handleiding bij de Zelf-Beoordelings Vragenlijst, ZBV: Een Nederlandstalige bewerking van de Spielberger State-Trait Anxiety Inventory*. Lisse: Swets & Zeitlinger; 1980.

40. Raat H, Landgraf JM, Oostenbrink R, Moll HA, Essink-Bot M-L. Reliability and validity of the Infant and Toddler Quality of Life Questionnaire (ITQOL) in a general population and respiratory disease sample. *Qual. Life Res.* 2006;16(3):445-460.

41. Van Buuren S, Groothuis-Oudshoorn CGM. mice: Multivariate Imputation by Chained Equations in R. *Journal of Statistical Software.* 2011;45(3):1-67.

42. Haidich AB, Ioannidis JPA. Patterns of patient enrollment in randomized controlled trials. *J. Clin. Epidemiol.* 2001;54(9):877-883.

43. Petticrew M, Roberts H. Evidence, hierarchies, and typologies: horses for courses. *J. Epidemiol. Community Health.* 2003;57(7):527-529.

CHAPTER 3

Response to pediatric physical therapy in infants with positional preference and skull deformation

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ABSTRACT

Background – Pediatric physical therapy seems to reduce skull deformation in infants with positional preference. However, not all infants show improvement.

Objective – The purpose of this study was to determine which infant and parent characteristics were related to response to pediatric physical therapy in 2-4 month-old infants with positional preference and/or skull deformation.

Design – A prospective cohort study.

Methods – Infants 2-4 months old with positional preference and/or skull deformation were recruited by pediatric physical therapists at the start of pediatric physical therapy. Primary outcome was good or poor response (moderate/severe skull deformation) at 4.5 to 6.5 months of age. Potential predictors for response to pediatric physical therapy were assessed at baseline using questionnaires, plagiocephalometry, and the Alberta Infant Motor Scale. Univariate and multiple logistic regression analyses using a stepwise backward elimination method were performed.

Results – 657 infants participated in the study. At follow-up 364 infants (55.4%) showed good response and 293 infants (44.6%) poor response to therapy. Multiple logistic regression analysis resulted in the identification of four significant predictors at baseline for poor response to pediatric physical therapy: starting therapy after 3 months of age (adjusted odds ratio [aOR]: 1.50, 95% CI 1.04 to 2.17), skull deformation (plagiocephaly (aOR: 2.64, 1.67 to 4.17), brachycephaly (aOR: 3.07, 2.09 to 4.52)) and a low parental satisfaction score with the infant's head (aOR: 2.64, 1.67 to 4.17).

Limitations – Information about pediatric physical therapy was collected retrospectively and concerned general therapy characteristics. Subsequently no adjustment for therapy for the individual participants could be made.

Conclusions – Several predictors for response to pediatric physical therapy in infants of 2-4 months of age with positional preference and/or skull deformation were identified. Health professionals can use these predictors in daily practice to provide infants with more individualized therapy, resulting in better chances of a good outcome.

INTRODUCTION AND PURPOSE

Skull deformation in infants is a diverse condition with variations in clinical presentation and treatment policy. The 2 most common types of deformities are deformational plagiocephaly (unilateral occipital flattening of the skull) [1-3] and deformational brachycephaly (symmetrical occipital flattening).[3] Skull deformation seems to be most prevalent between 2 (16% to 22%) and 4 (20%) months of age.[4, 5] An important risk factor is positional preference.[5-7] Positional preference affects up to 18% of Dutch infants younger than 4 months and is defined as "the condition in which the infant, in supine position, shows head rotation to either the right or the left side for approximately three quarters of the time of observation. Active rotation of the head over a range of 180 degrees cannot be accomplished."[6] In a recently published guideline (2012), the Netherlands Centre of Preventive Child Health Care advised pediatric physical therapy for infants with positional preference and/or skull deformation starting at 2 months of age.[8] A standardized pediatric physical therapy program was proven more effective than usual care in infants with positional preference, in preventing or diminishing skull deformation at 6 months of age.[9] Despite the evidence supporting pediatric physical therapy, still a considerable percentage (30% [10 of 33]) of infants who received therapy presented with skull deformation at 6 months.[9]

Skull deformation is generally considered to be a cosmetic disorder that improves in time for most infants.[4, 6, 10, 11] However, because parents worry that skull deformation might influence their child's attractiveness with increased risk of teasing or having poor self-perception, they seek treatment.[12] Treatment modalities are conservative and include parental counselling on handling and repositioning their infants. In the Netherland most infants (95%) are monitored by preventive child health care professionals during well-baby visits. When parental counselling at well-baby clinics does not result in improvement of skull deformation, infants are referred for pediatric physical therapy at a young age (2-4 months).[8, 9] Because skull deformation might serve as a marker for developmental delays in infants[13-15], both positional preference and skull deformation are medical grounds for starting pediatric physical therapy.

Because most infants show symmetry in posture at 5-6 months of age[6, 9], no effects of continued pediatric physical therapy can be expected. Infants with persistent moderate or severe skull deformation at this age may then be treated with an orthotic helmet or headbands.[16-18] This type of treatment has not yet been proven effective and can be a burden for both infants and their parents because of costs, improper fit of the helmet, pressure sores, and problems with acceptance.[19, 20]

If more infants could benefit from pediatric physical therapy, fewer infants would need to be treated with helmet therapy. We believe that current pediatric physical therapist practice leaves room for improvement based on the high prevalence of positional preference and skull

deformation, malleability of the young infants' skull and the potential benefits of pediatric physical therapy started at 2 months of age. So that therapists can provide more targeted, individualized therapy, it is important to know the characteristics of infants who respond poorly to pediatric physical therapy and those of their parents. In the present study, a poor response to pediatric physical therapy was defined on the basis of the criterion used in The Netherlands to prescribe helmet therapy: moderate or severe skull deformation at 4.5 to 6.5 months.

As yet, no studies of predictors for responses to pediatric physical therapy in infants at risk of skull deformation have been performed. The outcomes of studies on risk factors for skull deformation have suggested several infant factors that may serve as predictors for poor response to pediatric physical therapy: male sex, low activity levels, bottle feeding, and tummy time when awake fewer than 3 times per day.[4-6, 21] Parental level of education, level of anxiety and expectations of therapy are known to influence therapy adherence and outcome.[22, 23] Additionally, we expect that parents' prior experiences with the condition also will influence responses to therapy. Finally, clinical factors such as severity of the condition and age at baseline are likely to be related to therapy outcome.[24]

The objective of the present study was to determine which early (measured at baseline) infant and parent characteristics were related to a poor response to pediatric physical therapy in infants with positional preference, skull deformation, or both.

METHODS

Design and setting

The present study of predictors for responses to pediatric physical therapy marks the first part of the comprehensive HEADS study (HElmet therapy Assessment in infants with Deformed Skulls). The HEADS study is a prospective cohort study with a nested randomized controlled trial on helmet therapy in infants who are 4.5 to 6.5 months old.[25] In this first part of the HEADS study infants at risk of skull deformation (positional preference), or with existing deformation were monitored from 2 to 4 months of age (baseline) until 4.5 to 6.5 months of age. Table 1 shows the means and standard deviations for the characteristics of the participants.

Infants were included from April 2009 to November 2011. In the eastern part of the Netherlands, 70 pediatric physical therapists working in primary care or in general hospitals recruited participants for the present study. All therapists had experience with the outcome measurement instrument used in the present study (plagiocephalometry). Additionally, they received 3 instruction sessions; theory lessons on positional preference and skull deformation, a refresher course in plagiocephalometry[26, 27] and instructions on how to recruit patients for research (conducted by RMW, MMB, LAV).

Between the baseline and follow-up assessments, all infants received pediatric physical therapy. Responses to therapy were determined from the outcome of the follow-up assessment at 4.5 to 6.5 months of age. Therapy and therapist characteristics were collected retrospectively in a questionnaire for pediatric physical therapists. This separate data collection took place after inclusion for the cohort had ended (from November 2011 until February 2012).

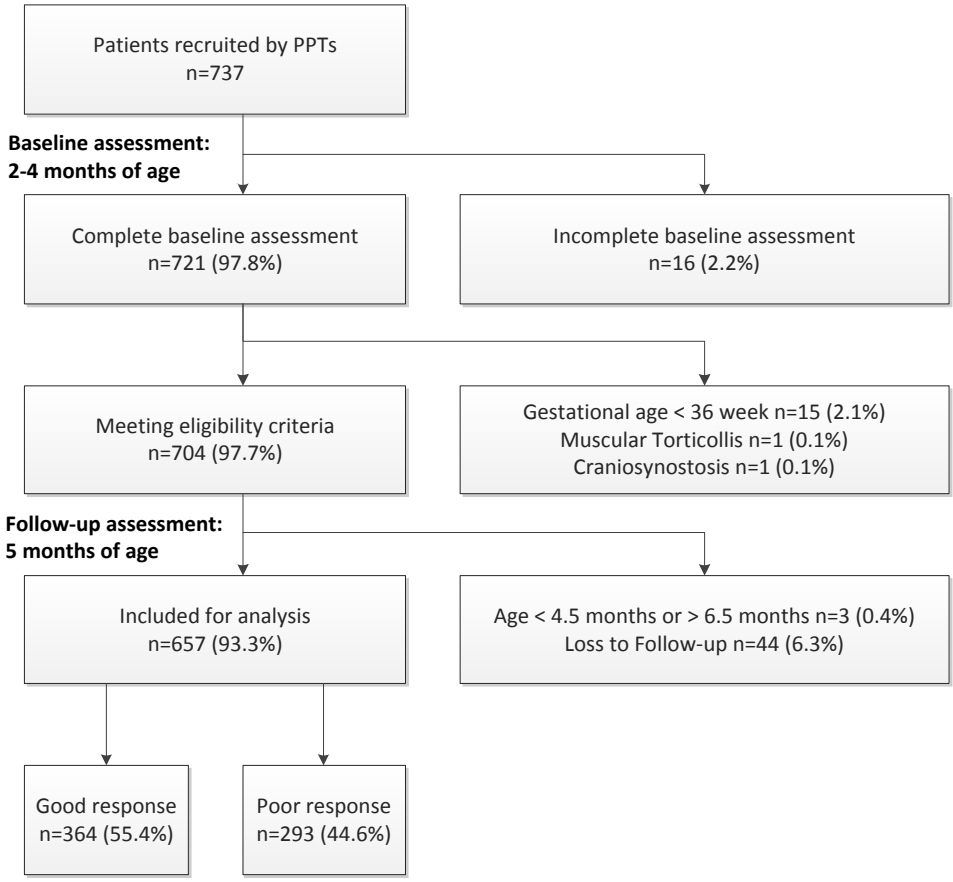
Participants

Infants who were 2-4 months, who had positional preference, skull deformation, or both, and who were presenting for pediatric physical therapy were included in the cohort study. Positional preference was determined as defined by Boere-Boonekamp and Van der Linden-Kuiper.[6] Skull deformation was determined by clinical diagnosis by the pediatric physical therapist. Infants were excluded from participation if their gestational age was less than 36 weeks or if they had congenital muscular torticollis, craniosynostosis, dysmorphic features, or a combination of these. Such infants need individualized diagnostics and treatment. All parents provided written informed consent before participation of their infants in the study.

A total of 704 infants were recruited for the study (Figure 1). At follow-up 3 infants did not meet the age criteria (between 4.5 and 6.5 months of age) and were therefore excluded. For 44 infants (6.3%), no follow-up information was available because of loss to follow-up, withdrawal or loss of data during transport to the researcher. This dropout group differed from the study cohort in the following way: the parents had lower levels of state anxiety and, more often, no experience with positional preference, and the infants had more severe skull deformation and were less often bottle-fed. The remaining 657 participants were included in the present study.

Data collection

The baseline assessment at 2 to 4 months of age consisted of a parental questionnaire and a clinical assessment by the pediatric physical therapist; the clinical assessment included an anthropometric assessment of the shape of the skull.. The pediatric physical therapists collected all of the data and sent the gathered assessment data to the researcher (RMW). All infants and their parents were invited by their pediatric physical therapists for follow-up assessments; if these follow-up assessments were performed when the infants were between 4.5 and 5.6 months of age, they were eligible for inclusion the present study. Baseline and follow-up assessments were performed by the same pediatric physical therapist. Because they were involved in the treatment of the infants, the therapists were not unaware of infant and parent characteristics. Details about the therapy were collected in a questionnaire for pediatric physical therapists.



Figuur 1. Flowchart of participants

Baseline assessment

The parental questionnaire included both infant and parent characteristics. Infant characteristics were sex, gestational age, birth rank, and health problems (eg, problems with sight or hearing, reflux, hip abnormalities or congenital defects). Furthermore, the method of feeding and positioning of the infant while awake were assessed. Additionally, the age at the start of therapy was measured in months; early start and late start of pediatric physical therapy were defined as a start before or after the age of 3 months, respectively.

Parent characteristics were maternal age; level of education of 1 parent (the parent who had the highest level of education, according to the Dutch equivalent of the *International Standard Classification of Education*[28]); experience with positional preference, skull deformation, or both in older children; satisfaction with their infant's head shape; concern for the infant's future; expectations of the outcome of pediatric physical therapy; and level of anxiety.

Parental satisfaction with their infant's head shape was assessed with a 5-point Likert scale ranging from 1 ("not satisfied at all") to 5 ("very satisfied"). A score below 4 represented a low parental satisfaction. Parental concern for the infant's future was also measured with a 5-point Likert scale, ranging from 1 ("very concerned") to 5 ("hardly concerned"). A score below four represented 'Parental concern'. The level of parental anxiety was measured with the Dutch version of the Spielberger State Trait Anxiety Inventory (STAI).[29] In the present study, general anxiety disposition was assessed (trait anxiety; 20 items). Scores ranged from 20 to 80; a higher score represented a higher level of anxiety. The STAI Trait Scale has an internal consistency by a Cronbach alpha of greater than .80.[29]

For the clinical assessment, the pediatric physical therapist assessed the presence of positional preference according to the definition of Boere- Boonekamp and van der Linden-Kuiper.[6] Next, the pediatric physical therapist measured skull deformation using plagiocephalometry. Plagiocephalometry is a noninvasive, valid (in agreement with measurements from 3-dimensional computed tomographic scanning[26]), and reliable (intraclass correlation coefficients of interrater and intrarater reliability for all indexes were >0,90[27]) method for measuring 2-dimensional skull shape at the widest transverse head circumference with a thermoplastic measuring ring (Figure 2).[26, 27] The oblique diameter difference index (ODDI) is an indicator of plagiocephaly, and the craniproportional index (CPI) is an indicator for brachycephaly. The ODDI was calculated by dividing the longest oblique diameter by shortest oblique diameter and multiplying by 100%. A value of 100% represented a purely symmetric head shape; the higher the score above 100%, the more severe the deformation. The CPI was calculated by dividing the width of the skull by the length of the skull and multiplying by 100%. A score of 80% represented an average head shape in Western countries[30]; a higher value represented a larger width-to-length ratio.

The presence of skull deformation as a predictor at baseline was determined using the plagiocephalometry cutoff values for visible skull deformation. Skull deformation was considered to be clearly visible and clinically meaningful when the ODDI was greater than or equal to 104% or the CPI was greater than or equal to 90% (Figure 2).[9]

Additionally, the pediatric physical therapist assessed the qualitative gross motor movement repertoire using the Alberta Infant Motor Scale (AIMS), a valid, norm-referenced measurement. The AIMS raw scores were converted into standardized *z* scores (ie, [individual score – the average score]/standard deviation).[31] A score of less than – 1 SD was considered to indicate moderately delayed motor development. High interrater and intrarater reliability values have been reported for the AIMS; intraclass correlation coefficients for both were .98 to .99.[32, 33]. Concurrent validity testing of the AIMS with both the Bailey Scales of Infant development II and the Peabody Developmental Motor Scales also generated high values ($r \geq .90$).[33]

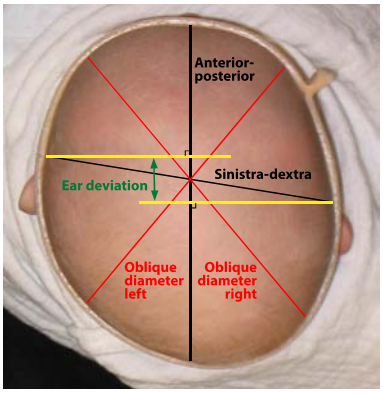
Pediatric physical therapists and therapy

The pediatric physical therapy program[9] consisted of positioning and handling in the direction opposite the observed positional preference and activities or exercises that facilitated positions or movements opposite the positional preference. Parents were taught how to incorporate the program into daily activities such as playing, nursing, changing, dressing, feeding, and sleeping. The aims of therapy included achieving full active cervical range of motion and symmetrical motor development. Parents were advised to apply tummy time as early, as long, and as frequently as possible but with strict supervision.[5, 8, 34, 35]

Pediatric physical therapists involved in the present study were asked to fill out a questionnaire in January 2012; topics of this questionnaire included sex, age and professional experience of the therapist, and the characteristics of therapy generally used for infants with positional preference, skull deformation, or both.

Outcome measurement

The outcome measurement was the response to therapy, measured when infants were 4.5 to 6.5 months old. A poor response was defined as skull deformation to such a degree that helmet therapy could be prescribed (moderate or severe skull deformation) (Figure 2). Again, the skull was measured by the pediatric physical therapists using plagiocephalometry. A poor response was reported as an ODDI of greater than or equal to 108% (plagiocephaly), a CPI greater than or equal to 95% (brachycephaly) or an ODDI greater than or equal to 106% and a CPI greater than or equal to 92% (mixed form).[25, 36] These cut-off point are used in practice in the Netherlands and therefore useful for clinical decision making.



	ODDI (%)		CPI (%)
Normal shape	<104	and	<90
Mild deformation	104 - 107	or	90 - 94
Moderate deformation	108 - 111	or	95 - 99
Severe deformation	≥ 112	or	≥ 100

Figure 2. Plagiocephalometry and cutoff points for severity of skull deformation
Illustration shows left occipital flattening of skull and thermoplastic measuring ring with digitally drawn lines used in plagiocephalometry. Indices were calculated by the following formulas: craniproportional index (CPI), sinistra-dextra/anterior-posterior×100%; oblique diameter difference index (ODDI), longest oblique diameter/shortest oblique diameter×100%; and ear deviation index, ear deviation/anterior-posterior×100%

Data analysis

The baseline characteristics of the study sample were described for the total sample and for the outcome groups separately (good and poor responses to therapy). Groups were compared using the student *t* test or chi-square test. The associations between responses to therapy and infant and parent characteristics were analyzed with univariate logistic regression analysis. Next, all variables were tested simultaneously in a multiple logistic regression analysis with stepwise backward elimination. Before multiple regression, we ruled out irrelevant correlations of any of the predictors with each other ($\alpha<.01$ and Pearson's $r>.80$). The likelihood ratio statistic was used for variable removal, and criteria for entry or removal of a variable in the model were set at respectively .20 and .05, respectively. The exclusion of 10% of participants with missing data in the multivariate analysis was allowed. Adjusted odds ratios (aORs) and 95% confidence intervals were used as estimates of association. We also examined the variance explained by the multiple logistic regression model with the pseudo (Nagelkerke) R^2 statistic. The level of significance was set at the 5% level (2-tailed). Statistical analyses were carried out with IBM SPSS Statistics for Windows version 21.0 (IBM Corp, Armonk, New York).

Role of the funding source

The HEADS study was funded by ZonMw, the Netherlands Organization for Health Research and Development (grant number 170.992.501). Besides the initial review process before funding and amendments, ZonMw did not have any involvement in the design and management of the study and publications.

RESULTS

Participants

Participants were split into 2 groups based on the basis of the outcome of the follow-up assessment: 364 infants (55.4%) responded well to therapy, 293 infants (44.6%) responded poorly. Table 1 shows the baseline characteristics of the total sample and of the outcome groups separately.

Male infants, (64,5% of the sample) were more likely to respond poorly to therapy than female participants. Additionally, infants with a poor response were more likely to have parents with a lower level of education and parents with a non-Dutch background.

Both groups had a mean age of 5.1 months (SD = 0.3 months) at follow-up. The mean time between baseline and follow-up measurements was 2.3 months (SD = 0.6 months); this time was similar for the 2 groups.

Table 1. Demographic characteristics of participants*

	Total Sample (n=657)	Infants with a good response to therapy (n=364)	Infants with a poor response to therapy (n=293)
No. (%) of male participants^	424 (64.5%)	222 (61.0%)	202 (68.9%)
Mean (SD) baseline age (mo)	2.8 (0.6)	2.8 (0.5)	2.9 (0.6)
Mean (SD) follow-up age (mo)	5.1 (0.3)	5.1 (0.3)	5.1 (0.3)
Mean (SD) pediatric phys. ther. duration (mo)	2.3 (0.6)	2.3 (0.6)	2.2 (0.6)
No. (%) of participants who were first born†	341 (52.4%)	195 (54.0%)	146 (50.3%)
No. (%) of participants with health problems‡	58 (8.8%)	33 (9.1%)	25 (8.5%)
Mean (SD) maternal age	30.4 (4.5)	31.8 (4.5)	31.1 (4.2)
Parental level of education, no. (%) of participants^†§			
Low	108 (16.5%)	51 (14.1%)	57 (19.5%)
Medium	242 (37.0%)	131 (36.2%)	111 (38.0%)
High	304 (46.3%)	180 (49.7%)	124 (42.5%)
Ethnic minority, no. (%) of participants ^†¥	31 (5.0%)	9 (2.6%)	22 (8.0%)

*groups were compared with the student *t*-test or chi-square test.
^p<0.05
†Numbers do not add up to the total population because of missing data.
‡Health problems: Problems with sight, hearing, esophageal reflux, developmental dysplasia of the hip, congenital heart disease, or inguinal hernia).
§Level of education: low education level=lower technical and vocational education and lower general secondary education; Medium education level=intermediate vocational education and advanced secondary education; and High educational level=higher vocational education and university.
¥Ethnic minority: at least one parent non-Dutch.

Predictors for response

The baseline characteristics male sex (odds ratio [OR] = 1.42; 95% confidence interval [95% CI] = 1.03 to 1.97), starting therapy after 3 months of age (OR = 1.49, 95% CI = 1.08 to 2.05), skull deformation (plagiocephaly [OR = 2.14, 95% CI = 1.41 to 3.26], brachycephaly [OR = 3.42, 95% CI = 2.46 to 4.76]), being bottle-fed (OR =1.81, 95% CI = 1.24 to 2.62), and a low parental satisfaction with their infant's head shape (OR = 3.26, 95% CI = 2.15 to 4.93) were significantly associated with poor response to therapy (Table 2).
Delayed motor development did not appear to be associated with poor response to therapy.

Table 2. Univariate and multivariate analysis of possible predictors at baseline for response to therapy*

	Missing	Good response	Poor response	Univariate Analysis		Multivariate Analysis^	
	N	(n=364)	(n=293)	OR (95% CI)	*P*	aOR (95% CI)	*P*
Infant characteristics							
Male participants	0	222 (61.0%)	202 (68.9%)	1.42 (1.03 to 1.97)	<.05	1.42 (0.98 to 2.06)	.07
≥3 months of age	0	118 (32.4%)	122 (41.6%)	1.49 (1.08 to 2.05)	<.05	1.50 (1.04 to 2.17)	<.05
Skull deformation	0						
Plagiocephaly (ODDI ≥ 104%)		278 (76.4%)	256 (87.4%)	2.14 (1.41 to 3.26)	<.01	2.64 (1.67 to 4.17)	<.01
Brachycephaly (CPI ≥ 90%)		90 (24.7%)	155 (52.9%)	3.42 (2.46 to 4.76)	<.01	3.07 (2.09 to 4.52)	<.01
Positional Preference	7	259 (72.1%)	207 (71.1%)	0.95 (0.68 to 1.34)	.78		
Motor development (AIMS *z* score < -1 SD)	5	98 (26.9%)	93 (32.3%)	1.30 (0.92 to 1.82)	.14	1.30 (0.88 to 1.93)	.19
Method of feeding (only bottle-fed)	8	254 (70.8%)	236 (81.4%)	1.81 (1.24 to 2.62)	<.01	1.48 (0.97 to 2.26)	.07
<3 times/d tummy time before therapy	4	232 (64.3%)	205 (70.2%)	1.31 (0.94 to 1.82)	.11	1.43 (0.98 to 2.09)	.06
Parent characteristics							
Level of education†	3				.09		
Low		51 (14.1%)	57 (19.5%)	1.62 (1.04 to 2.52)	<.05		
Medium		131 (36.2%)	111 (38.0%)	1.23 (0.88 to 1.73)	.23		
High		180 (49.7%)	124 (42.5%)				
Experience with positional preference	10	51 (14.3%)	56 (19.4%)	0.91 (0.61 to 1.37)	.65		
Low level of parental satisfaction	6	247 (68.4%)	254 (87.6%)	3.26 (2.15 to 4.93)	<.01	2.64 (1.67 to 4.17)	<.01
Parental concern	3	67 (18.5%)	70 (24.1%)	1.40 (0.96 to 2.04)	.08		
Low expectations of outcome of pediatric physical therapy	12	51 (14.1%)	56 (19.4%)	1.45 (0.96 to 2.20)	.08	1.37 (0.86 to 2.20)	.19
Trait anxiety	9	29 (25-35)	30 (25-30)	1.01 (0.99 to 1.03)	.25		

*Data are presented as number (percentage) of participants unless otherwise indicated. OR=odds ratio, 95% CI=95% confidence interval, ODDI=oblique diameter difference index, CPI=cranial proportional index, AIMS z score=standardized score on the Alberta Infant Motor Scale.
^Pseudo (Nagelkerke) R^2 =0.201, Predicted Percentage Correct=67.3%, 61 cases with missing data removed (9.3%)
†Level of education: low education level=lower technical and vocational education and lower general secondary education; Medium education level=intermediate vocational education and advanced secondary education; and High educational level=higher vocational education and university.
‡Total score on the Trait Scale of the Dutch version of the Spielberger State-Trait Anxiety Inventory; values are reported as median (interquartile range)

Table 2 shows the results of the multiple logistic regression analysis with stepwise backward elimination. Sixty-one participants (9.3%) were excluded from further analysis because of missing values of 1 of the variables included in the model. No strong correlations were found between the various characteristics (the Pearson *r* value for all variables was ≤.30).

The significant independent predictors for a poor response to therapy were starting therapy after 3 months of age (adjusted odds ratio [aOR] = 1.50, 95% CI = 1.04 to 2.17), skull deformation (plagiocephaly [aOR = 2.64, 95% CI = 1.67 to 4.17], brachycephaly [aOR = 3.07, 95% CI = 2.09 to 4.52]) and a low parental satisfaction score (aOR = 2.64, 95% CI = 1.67 to 4.17). Sex, method of feeding and frequency of tummy time at baseline had *P* values just above the level of significance in the stepwise backward multivariate model (*P*=.07, *P*=.07, and *P*=.06, respectively).

Pediatric physical therapists and therapy

Of the 70 pediatric physical therapists, 67 (96%) returned the questionnaire concerning therapist and therapy details. One therapist reported a lack of time to fill out the questionnaire because of a heavy workload, and 2 others did not return the questionnaire. Most of the pediatric physical therapists were women (96%) and their ages ranged from 20 to more than 60 years; 28 therapist were younger than 40 years old (42%), 39 therapists were 40 years old or older (58%). Ninety-four percent of the therapists had at least 3 years of clinical experience.

Almost all (96%) of the infants received between 3 and 8 sessions of pediatric physical therapy within a mean time frame of 2.3 months (SD = 0.6 month). Most therapists (67%) provided 2 or 3 sessions per month. The majority (61%) of therapy sessions lasted 31 to 45 minutes, and a minority (37%) lasted 16 to 30 minutes; one therapist reported "other". Almost all (98%) of the pediatric physical therapists, advised tummy time for at least 3 times per day from the age of 2 months on. About half (52%) of the de therapists provided a sheet or leaflet with information about the condition, exercises, or both.

DISCUSSION

In this article we reported infant and parent characteristics related to responses to pediatric physical therapy in infants with positional preference, skull deformation, or both. Independent predictors for a poor response to pediatric physical therapy were starting therapy after 3 months of age, skull deformation (ODDI ≥ 104% or CPI ≥ 90%) at the start of therapy, and a low parental satisfaction score regarding their infant's head shape. It can be expected that infants presenting with skull deformation at baseline (based on either anthropometric measurement or parental satisfaction) and infants who start therapy at an older age will be more likely to respond poorly

to pediatric physical therapy.[24] An older age at the start of therapy allows less time for pediatric physical therapy to improve the infant's skull deformation.

The *P* values for male sex, infants who were not used to frequent tummy time, and infants who were bottle-fed as predictors for therapy outcomes were just above the level of significance. Male sex is a known risk factor for the development of skull deformation,[6, 34, 37] and was identified as a predictor for a poor outcome in the univariate analysis in the present study. Since male infants tend to have larger heads than female infants, head control is expected to be more difficult and the weight of the larger head continues to function as an external molding force.[7, 37, 38] It also has been suggested that male infants have poorer motor developmental outcomes than to female infants.[39, 40] However, this association was not found in the present study. We expected that infants who had a lower frequency of tummy time and were bottle-fed might be less responsive to the therapy advice and exercises because they were not used to many variations in posture and position. This notion is in line with findings in literature on risk factors for developing deformational plagiocephaly. [5, 6] Infants who are bottle-fed are often approached from 1 side and are more at risk to developing a positional preference.[5] Because infants are fed frequently, this positioning factor can play an important role in the infant's development.

Comparison to other studies

It has frequently been suggested that developmental delays exist in infants with skull deformation [13, 15, 21, 40, 41], but no association of motor development with skull deformation at age 4.5 to 6.5 months was established in the present study. We did find a median AIMS *z* score of -0.50 at baseline, this *z* score was comparable to the *z* score found in the randomized controlled trial of Van Vlimmeren et al[9] but slightly lower than expected in an average population. However, the reference values are based on a Canadian population and were established 20 years ago.[31] Therefore, they may be inappropriate for Dutch infants, who appear to have lower scores.[42, 43]
The effectiveness of a standardized pediatric physical therapy program was studied in a randomized controlled trial by Van Vlimmeren et al (n=65).[9] The number of participants in that trial was sufficient for an effectiveness study but not for identifying predictors for response to pediatric physical therapy in daily practice – which is what we set out to do in the present study (n=657) . This number of participants is needed to explore relationships between various characteristics and pediatric physical therapy outcomes. However, to enable us to draw conclusions about predictors in the present cohort, it was also important to report details about the pediatric physical therapy program. Details about the therapy in the present study matched the description of the therapy under study in the randomized controlled trial of Van Vlimmeren et al.[9] Additionally, therapists gave advice to parents about frequency of tummy time, in line with the recommendations of the recently published Dutch guideline on positional preference and skull deformation (≥3 times per day).[8]

The responses to therapy in the present study could not be compared with the results found by Van Vlimmeren et al, because different outcome cutoff points were used, at the ages at follow-up were different, and the participants of the 2 studies were not comparable in terms of severity of skull deformation at baseline. The difference could be explained by use of different study designs: The inclusion criteria of the present study included positional preference skull deformation, or both and all of the infants were either referred for pediatric physical therapy or self-referred, whereas the sample in the randomized controlled trial of Van Vlimmeren et al was nested in a birth cohort and infants were screened for positional preference for inclusion.[9]

Strengths and limitations

A strength of this study was the large number of included infants; this large cohort was necessary to explore relationships between various characteristics and outcomes. In addition, the fact that the study was conducted in a geographically wide-spread area, in both primary care and general hospitals improved external validity. Together with the large number of participating pediatric physical therapists, these characteristics made selection bias by therapists unlikely.

Loss to follow-up is problematic in most cohort studies and often leads to bias.[44] However, only 6.3% of potential data were lost in this way in the present study.[45] Even though the data lost to follow-up are "missing not at random", we do not believe that this small selective loss to follow-up had a marked impact on the generalizability of the results.

The present study also had some limitations. First, the explained variance was 20% (Pseudo [Nagelkerke] R^2 =.2). We were able to identify predictors for outcome, but other factors remain unknown.

We collected general information about therapy per therapist and not per infant and collected this information retrospectively. We expect that therapy characteristics, collected per patient in a prospective manner might explain a large part of the remaining variance in outcome.

Furthermore, the fact that pediatric physical therapists who had taken a course on plagiocephalometry were invited to participate in the HEADS study might have generated a selective group of therapists more interested in and knowledgeable about positional preference or skull deformation than pediatric physical therapists in general. They might have provided a more targeted approach than pediatric physical therapist in general would have.

In conclusion, the factors found to be related to responses to pediatric physical therapy in the present study can be used in daily practice by health care professionals working with infants with positional preference or skull deformation. Health care professionals working in preventive child health care ideally should refer infants with persistent positional preference or skull deformation to a pediatric physical therapist before the infants are 3 months old. When pediatric physical therapy is started at this age, infants may be more likely to respond well to therapy

Additionally, pediatric physical therapists should be alert to infants matching the predictors found in this study. Infants who begin receiving pediatric physical therapy when they are older than 3 months old, have skull deformation, or have parents with a low satisfaction score regarding their infant's head shape appear to be less responsive to pediatric physical therapy and are at risk for poor response to therapy.

To determine the prognostic strength of the characteristics discussed here, future research should involve a prospective approach in which individual therapy characteristics are taken into account. Finally, whether infants at risk will profit from a more targeted pediatric physical therapy approach has yet to be determined.

REFERENCES

1. Clarren SK. Plagiocephaly and torticollis: etiology, natural history, and helmet treatment. *J. Pediatr.* 1981;98(1):92-95.

2. Mulliken JB, Vander Woude DL, Hansen M, LaBrie RA, Scott RM. Analysis of posterior plagiocephaly: deformational versus synostotic. *Plast. Reconstr. Surg.* 1999;103(2):371-380.

3. Argenta L, David L, Thompson J. Clinical classification of positional plagiocephaly. *J. Craniofac. Surg.* 2004;15(3):368-372.

4. Hutchison BL, Hutchison LA, Thompson JM, Mitchell EA. Plagiocephaly and brachycephaly in the first two years of life: a prospective cohort study. *Pediatrics.* 2004;114(4):970-980.

5. van Vlimmeren LA, van der Graaf Y, Boere-Boonekamp MM, L'Hoir MP, Helders PJ, Engelbert RH. Risk factors for deformational plagiocephaly at birth and at 7 weeks of age: a prospective cohort study. *Pediatrics.* 2007;119(2):e408-418.

6. Boere-Boonekamp MM, van der Linden-Kuiper LT. Positional preference: prevalence in infants and follow-up after two years. *Pediatrics.* 2001;107(2):339-343.

7. Oh AK, Hoy EA, Rogers GF. Predictors of severity in deformational plagiocephaly. *J. Craniofac. Surg.* 2009;20 Suppl 1:685-689.

8. Nederlands Centrum Jeugdgezondheid. *JGZ-richtlijn Preventie, signalering en aanpak van voorkeurshouding en schedelvervorming.* Utrecht: TNO innovation for life;2012.

9. van Vlimmeren LA, van der Graaf Y, Boere-Boonekamp MM, L'Hoir MP, Helders PJ, Engelbert RH. Effect of pediatric physical therapy on deformational plagiocephaly in children with positional preference: a randomized controlled trial. *Arch. Pediatr. Adolesc. Med.* 2008; 162(8):712-718.

10. Hutchison BL, Stewart AW, Mitchell EA. Deformational plagiocephaly: a follow-up of head shape, parental concern and neurodevelopment at ages 3 and 4 years. *Arch. Dis. Child.* 2011; 96(1):85-90.

11. Van Vlimmeren LA, Helders PJM. Het afgeplatte babyhoofd: meten van de afplatting en volgen van het beloop. *Praktische Pediatrie.* 2009;2:129-133.

12. Collett B, Breiger D, King D, Cunningham M, Speltz M. Neurodevelopmental implications of "deformational" plagiocephaly. *J. Dev. Behav. Pediatr.* 2005;26(5):379-389.

13. Collett BR, Gray KE, Starr JR, Heike CL, Cunningham ML, Speltz ML. Development at age 36 months in children with deformational plagiocephaly. *Pediatrics.* 2013;131(1):e109-115.

14. Hutchison BL, Stewart AW, Mitchell EA. Characteristics, head shape measurements and developmental delay in 287 consecutive infants attending a plagiocephaly clinic. *Acta Paediatr.* 2009;98(9):1494-1499.

15. Kennedy E, Majnemer A, Farmer JP, Barr RG, Platt RW. Motor development of infants with positional plagiocephaly. *Phys Occup Ther Pediatr.* 2009;29(3):222-235.

16. Bialocerkowski AE, Vladusic SL, Howell SM. Conservative interventions for positional plagiocephaly: a systematic review. *Dev. Med. Child Neurol.* 2005;47(8):563-570.

17. Flannery AB, Looman WS, Kemper K. Evidence-based care of the child with deformational plagiocephaly, part II: management. *J. Pediatr. Health Care.* 2012;26(5):320-331.

18. Xia JJ, Kennedy KA, Teichgraeber JF, Wu KQ, Baumgartner JB, Gateno J. Nonsurgical treatment of deformational plagiocephaly: a systematic review. *Arch. Pediatr. Adolesc. Med.* 2008;162(8):719-727.

19. Loveday BP, de Chalain TB. Active counterpositioning or orthotic device to treat positional plagiocephaly? *J. Craniofac. Surg.* 2001;12(4):308-313.

20. Wilbrand JF, Wilbrand M, Malik CY, et al. Complications in helmet therapy. *J. Craniomaxillofac. Surg.* 2012;40(4):341-346.

21. Bialocerkowski AE, Vladusic SL, Wei Ng C. Prevalence, risk factors, and natural history of positional plagiocephaly: a systematic review. *Dev. Med. Child Neurol.* 2008;50(8):577-586.

22. Hill JC, Lewis M, Sim J, Hay EM, Dziedzic K. Predictors of poor outcome in patients with neck pain treated by physical therapy. *Clin. J. Pain.* 2007;23(8):683-690.

23. Atalay NS, Akkaya N, Konukcu S, Balci CS, Sahin F. Psychic predictors of outcomes of physical therapy. *J. Back Musculoskelet. Rehabil.* 2013;26(1):71-77.

24. Cabrera-Martos I, Valenza MC, Benitez-Feliponi A, Robles-Vizcaino C, Ruiz-Extremera A, Valenza-Demet G. Clinical profile and evolution of infants with deformational plagiocephaly included in a conservative treatment program. *Childs Nerv. Syst.* 2013;29(10):1893-1898.

25. van Wijk RM, Boere-Boonekamp MM, Groothuis-Oudshoorn CG, van Vlimmeren LA, IJzerman MJ. HElmet therapy Assessment in infants with Deformed Skulls (HEADS): protocol for a randomised controlled trial. *Trials.* 2012;13:108.

26. van Adrichem LNA, van Vlimmeren LA, Cadanova D, et al. Validation of a simple method for measuring cranial deformities (Plagiocephalometry). *J. Craniofac. Surg.* 2008;19(1):15-21.

27. van Vlimmeren LA, Takken T, van Adrichem LN, van der Graaf Y, Helders PJ, Engelbert RH. Plagiocephalometry: a non-invasive method to quantify asymmetry of the skull; a reliability study. *Eur. J. Pediatr.* 2006;165(3):149-157.

28. Unesco Institute for Statistics. *International Standard Classification of Education.* Montreal, Canada2012.

29. van der Ploeg HM, Defares PB, Spielberger CD. *Handleiding bij de Zelf-Beoordelings Vragenlijst, ZBV: Een Nederlandstalige bewerking van de Spielberger State-Trait Anxiety Inventory*. Lisse: Swets & Zeitlinger; 1980.

30. Graham JM, Jr., Kreutzman J, Earl D, Halberg A, Samayoa C, Guo X. Deformational brachycephaly in supine-sleeping infants. *J. Pediatr.* 2005;146(2):253-257.

31. Piper MC, Pinnell LE, Darrah J, Maguire T, Byrne PJ. Construction and validation of the Alberta Infant Motor Scale (AIMS). *Can. J. Public Health.* 1992;83 Suppl 2:S46-50.

32. Blanchard Y, Neilan E, Busanich J, Garavuso L, Klimas D. Interrater reliability of early intervention providers scoring the alberta infant motor scale. *Pediatr Phys Ther.* Spring 2004;16(1):13-18.

33. Piper MC, Darrah J. *Motor Assessment of the Developing Infant.* . Pennsylvania, PA, USA: Saunders Company; 1994.

34. Hutchison BL, Thompson JM, Mitchell EA. Determinants of nonsynostotic plagiocephaly: a case-control study. *Pediatrics.* 2003;112(4):e316.

35. Persing J, James H, Swanson J, Kattwinkel J, Comm Practice Ambulatory M. Prevention and management of Positional skull deformities in infants. *Pediatrics.* 2003;112(1):199-202.

36. Fleming PJ, Gilbert R, Azaz Y, et al. Interaction between bedding and sleeping position in the sudden infant death syndrome: a population based case-control study. *BMJ.* 14 1990;301(6743):85-89.

37. Joganic JL, Lynch JM, Littlefield TR, Verrelli BC. Risk factors associated with deformational plagiocephaly. *Pediatrics.* 2009;124(6):e1126-1133.

38. Graham JM, Jr., Gomez M, Halberg A, et al. Management of deformational plagiocephaly: repositioning versus orthotic therapy. *J. Pediatr.* 2005;146(2):258-262.

39. Knight SJ, Anderson VA, Meara JG, Da Costa AC. Early neurodevelopment in infants with deformational plagiocephaly. *J. Craniofac. Surg.* 2013;24(4):1225-1228.

40. Kordestani RK, Panchal J. Neurodevelopment delays in children with deformational plagiocephaly. *Plast. Reconstr. Surg.* 2006;118(3):808-809; author reply 809-810.

41. Hutchison BL, Stewart AW, Mitchell EA. Deformational plagiocephaly: a follow-up of head shape, parental concern and neurodevelopment at ages 3 and 4 years. *Arch. Dis. Child.* 2010;96(1):85-90.

42. Mortenson P, Steinbok P, Smith D. Deformational plagiocephaly and orthotic treatment: indications and limitations. *Childs Nerv. Syst.* 2012;28(9):1407-1412.

43. Fleuren KM, Smit LS, Stijnen T, Hartman A. New reference values for the Alberta Infant Motor Scale need to be established. *Acta Paediatr.* 2007;96(3):424-427.

44. Kristman V, Manno M, Cote P. Loss to follow-up in cohort studies: how much is too much? *Eur. J. Epidemiol.* 2004;19(8):751-760.

45. Altman DG. Statistics in medical journals: some recent trends. *Stat. Med.* 2000;19(23):3275-3289.

CHAPTER 4

Parents' decision for helmet therapy in infants with skull deformation

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ABSTRACT

Purpose – Helmet therapy is regularly prescribed in infants with positional skull deformation. Evidence on the effectiveness is lacking, which complicates decision making. This study aims to assess the relation between parents' decision for treatment of skull deformation in their infant and their level of anxiety, decisional conflict, expectations of treatment effect, perceived severity of deformation and perceived side effects.

Methods – Parents of 5-month-old infants with skull deformation were invited to participate in a survey. Data collection included background characteristics, anthropometric assessment, parent-reported outcomes, decision for treatment (helmet therapy or awaiting natural course), Decisional Conflict Scale and questions about perceived (side) effects of helmet therapy. Factors significantly correlated with treatment decision ($p<.10$) were tested in a multiple logistic regression analysis.

Results – The results of 186 respondents were included in the analysis. Parental satisfaction with their infant's head shape (adjusted odds ratio (aOR) 0.2; 95 % confidence interval (CI) 0.1 to 0.4), expected effect of helmet therapy compared to natural course (aOR 13.4; 95 % CI 5.0 to 36.1) and decision uncertainty (aOR 1.0; 95 % CI 0.9 to 1.0; $p=.03$) were related to the decision for helmet therapy in infants with skull deformation.

Conclusion – With the outcomes of this study, we can better understand parental decision making for elective 'normalizing' treatments in children, such as helmet therapy in infants with skull deformation. Health care professionals should address the parents' perception of the severity of skull deformation and their expectations of helmet therapy. Furthermore they can support parents in decision making by balancing medical information with parents' expectations, values and beliefs.

INTRODUCTION

Since patients are increasingly involved in medical decision making through shared or even informed decision making[1], there is a growing need for theoretically valid ways to support patients in this process. To assist patients in making rational decisions in health care, it is important to understand what drives patients decisions, to match their information needs. Where in most clinical fields, it is the patient and his/her values and assumptions drive decision making, decision making in pediatrics can be more complicated due to proxy decision making by parents.[2, 3]. Parents have to use their value system to judge the desirability of an intervention for their child, while taking into account short and long term harms and benefits. An example of preference sensitive decision in pediatrics is the treatment of skull deformation in infants. Skull deformation is a cosmetic condition, which affects 10-20% of infants in the first months of life.[4, 5] The infant's head is malleable and growing rapidly, hence susceptible to deformation when the infant develops a preference for a specific head position (positional preference).[6] Depending on the preference, the subsequent skull deformation can result in a more asymmetrical shape (plagiocephaly) or a more symmetrical flattening of the head (brachycephaly).

In the Netherlands, the vast majority (95%) of infants is monitored by preventive youth health care professionals during well-baby visits. When parental counselling on handling and (re) positioning of the infants does not result in improvement of the skull deformational, infants are referred for pediatric physical therapy at a young age (2 to 4 months).[5, 7] As the majority of infants show symmetry in posture at 5-6 months of age[5, 6], no effects of continued PPT can be expected. Also, when infants grow older, become more mobile and spend less time lying on their back, most cases of skull deformation improve without further treatment.[4, 6, 8, 9] However some cases still present with substantial skull deformation at 6 months of age.[5] In these infants helmet therapy can be started.[10, 11] A helmet is a cranial orthosis made up of a rigid plastic shell with a foam lining. The helmet is meant to redirect skull growth. It is recommended that the helmet is worn 23 hours a day for a duration of 6 months, starting at 5 to 6 months of age.[12] Although the known complications of helmet therapy are mild, the treatment itself is seen as a burden to both parents and their child.[13] Nevertheless, prescription rates of helmet therapy are increasing and at the time of this study about 3000-4000 6-month-old infants with skull deformation are treated with a helmet in the Netherlands each year (176.000 newborns in 2012[7]).

As yet, no randomized controlled trials (RCTs) have been performed to study the effectiveness of helmet therapy compared to awaiting natural course.[14-16] The few prospective comparative studies tend to show positive results in favor of helmet therapy, but have several limitations.[13, 14, 17-19] Long-term outcomes and assessment of side effects are missing in most studies and the clinical relevance of the reported effects is questioned.[10, 11, 20, 21]

Health professionals themselves are divided about the necessity to treat skull deformation.[22] Due to the lack of evidence supporting helmet therapy[23, 24], a recently published national guideline for the management of skull deformation advised health professionals to be conservative in prescribing helmet therapy.[25] Although health care professionals are consulted in the process

leading up to the decision[26], the decision to start helmet therapy is made by parents.
Given the lack of evidence on benefits and harms in the current situation, it is not possible to weight the additional effect of the helmet against the perceived severity of and probability of side effects.[27] Non-clinical factors, such as knowledge, availability, social norm and costs may be equally or even more influential as clinical factors in decision making by patients.[2, 28] Parents of infants with skull deformation often have concerns about their child's appearance, possible bullying and consequences of physical appearance and psychological development.[8, 29] It has also been suggested that parents feel an increasing need to act on skull deformation.[30] Parental concern may drive treatment trends and possibly the preference for helmet therapy.[29] Professionals need to understand the reasons for parents of an infant with skull deformation for choosing either helmet treatment or natural recovery to be able to accurately inform and support them in decision making.[31, 32] A recent retrospective chart review identified two factors significantly influencing treatment decision, namely parents' perception of severity of the skull deformation and time off work for follow-up appointments, but did not include factors like parental concern, anxiety and expectations.[30]

The aim of this study is to assess the relation between parents' decision for treatment of their infant's skull deformation and their level of anxiety, decision uncertainty, satisfaction with their infant's skull shape, concern for their infant's future, severity of the deformation, expected additional effect of helmet therapy and perception of side effects. It was hypothesized that parents of infants with a more severe skull deformation or who are not satisfied with their infant's skull shape, who have high expectations of the effects of the helmet, concern for their infant's future, low perception of side effects, high anxiety levels and low levels of uncertainty about their decision, are more likely to choose the an active intervention, i.e. helmet therapy.

METHODS

Study design

The current study was performed as a survey within the HEADS Study (Helmet therapy Assessment in Deformed Skulls.[33] The HEADS study is a large cohort study with a nested RCT on the effects of helmet therapy on skull's shape compared to the effects of awaiting natural course in infants with skull deformation (Figure 1). Parallel to the RCT a cohort was included, in which parents made the decision for helmet therapy or awaiting natural course themselves. How this decision was made by parent in the cohort was determined in the current study.
The HEADS study was performed in the east of the Netherlands (in the provinces of Drenthe, Overijssel and parts of Gelderland). Ethics approval was given on the 8th January 2009 (ref: NL24352.044.08) by the Medical Ethics Committee of Medisch Spectrum Twente, hospital of Enschede, The Netherlands.

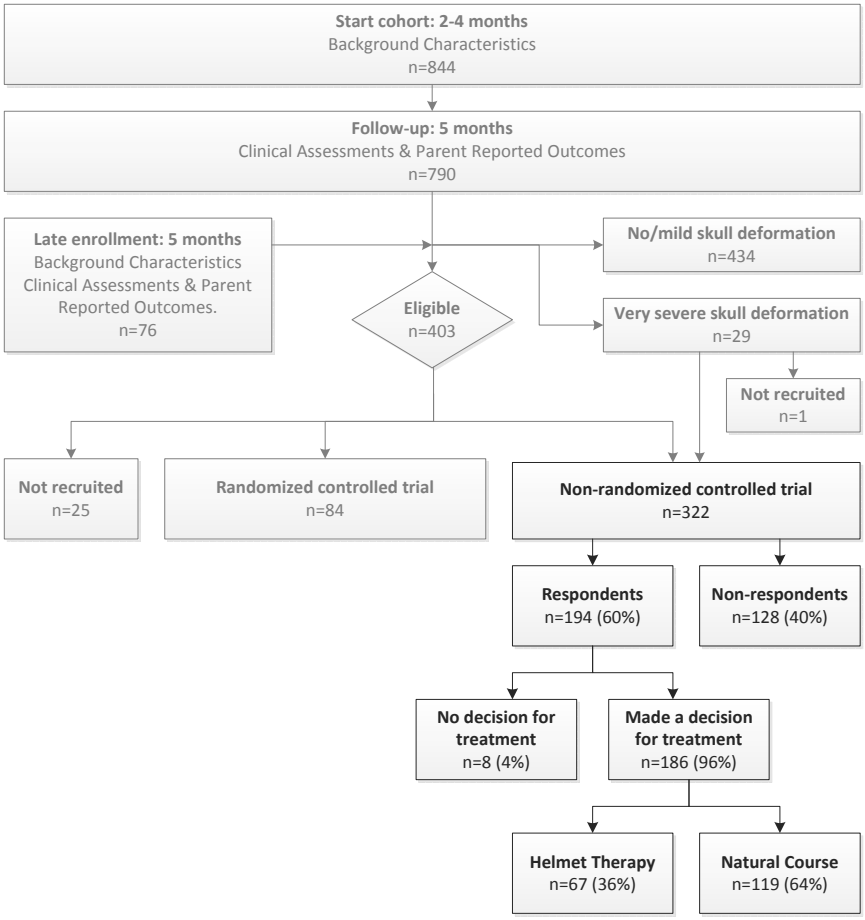

Figure 1. Flowchart of the HElmet therapy Assessment in Deformed Skulls study

Respondent sample

Criteria for eligibility for parents in this study were having a child of 4.5 to 6.5 months of age with moderate to very severe skull deformation, who was born after 36 weeks gestation, and who had no congenital muscular torticollis, craniosynostosis and/or dysmorphic features.[33] The severity of skull deformation was determined by pediatric physical therapists using plagiocephalometry; a reliable, valid, non-invasive method to measure the shape of the skull.[34, 35]

Plagiocephalometry assessed the degree of deformational plagiocephaly (asymmetrical deformation) using the Oblique Diameter Difference Index (ODDI) and the degree of deformational brachycephaly (symmetrical deformation) using the Cranio Proportional Index (CPI). ODDI is the ratio between the longest oblique diameter and the shortest oblique diameter multiplied by 100%. CPI is the ratio between the width and the length of the skull multiplied by 100%. Infants with ODDI ≥ 108.0% or CPI ≥ 95.0% or a mix of ODDI >106% and CPI > 92% were

considered to have moderate to very severe skull deformation.[33]
Parents of eligible infants in the non-randomized controlled trial (nRCT) of the study were sent a questionnaire about the process leading up to the decision on the treatment of skull deformation of their infant.

Data collection

Baseline characteristics, clinical outcomes and parent reported outcomes were collected as part of the HEADS study at the start of the study. After follow-up assessment, the Decision Making survey was distributed among parents if they consented to participate in the nRCT. A phone-call reminder to parents about filling out and returning the questionnaire was scheduled two weeks after sending out the questionnaires.

Background characteristics

Background characteristics included gender of the infant, birth rank, age of the parents, educational level of the parents and level of anxiety.

Anthropometric assessment

Objective measurement of skull shape was obtained by pediatric physical therapists using plagiocephalometry. [34, 35] Both deformational plagiocephaly using the ODDI and the degree of deformational brachycephaly using the CPI were assessed. An ODDI of 100% represents a purely symmetrical shape of the skull; the higher the score, the more severe the deformation. A CPI score of 80% represents an average head shape in Western countries; a higher value represents a larger width to length ratio.

Parent reported outcomes

Parental level of anxiety was measured using the Spielberger State Trait Anxiety Inventory (STAI), Dutch Version.[36, 37] 'Trait anxiety' (20 items) is a general anxiety disposition, 'state anxiety' (20 items) concerns the state of anxiety of parents when infants were 5 months of age. Both assessment scores range from 20 to 80; a higher score represents a higher anxiety.
Parental satisfaction with their infant's head shape was assessed using a 5-point Likert scale ranging from '1—not satisfied at all' to '5—very satisfied'. Parental concern for the infant's future was also rated on a 5-point Likert scale, ranging from '1—hardly concerned' to '5—very concerned'.

Decision making survey

First, parents were asked to indicate their decision (revealed preference) for the treatment of the skull deformation in their infant; 'helmet therapy', 'natural course' or 'not decided yet'.
Parents rated the expected effect of both helmet therapy and natural course on a 5-point Likert scale, ranging from '1—no recovery expected' to '5—complete recovery expected. To calculate

the 'expected additional effect of helmet therapy', the expected natural recovery of the skull shape was deducted from expected recovery in skull shape due to helmet therapy.

Perception of side effects of helmet therapy ('perception of side effects') was measured using six items derived from previous interviews with parents: the extent to which parents expected negative remarks from others (two items) and the extent to which parents expected less cuddling with their child, pressure spots, acceptation problems and skin irritation or eczema. The items were scored on a 5-point Likert scale ranging from '1—strongly disagree' to '5—strongly agree'. The average score on the six items, converted to a score ranging from 0 to 100, with a higher score indicating a higher perception of side effects of helmet therapy.

The DCS measures the level of decisional conflict of a person while making health care decisions, and consists of three subscales.[38] The DCS has been translated into Dutch and was previously validated.[39] The subscale 'uncertainty' is based on three items and measures the level of perceived uncertainty while making a healthcare decision ('difficult decision', 'not sure what to decide', 'unclear what's best for my child'). The subscale 'factors contributing' measures the degree to which various factors, including 'feels informed', 'clarity about personal values' and 'feels supported in decision making' contributed to decision uncertainty. This subscale originally consisted of nine items, but in this study three items were added to obtain more information about both management strategies and also we assessed whether both parents agreed on the decision. 'effective decision making' is the final subscale and uses four items to assess how effective people perceive their decision was ('informed decision', 'consistent with personal values', 'expect to stick to decision' and 'satisfied with decision'). Each subscale was converted to a score ranging from 0 to 100, with a higher score indicating higher decision uncertainty.

Statistical analyses

Background characteristics were described for the total sample, and separately for respondents who chose for either helmet therapy or awaiting natural course. Background characteristics have been compared between both groups, using univariate logistic regression.

The reliability of the three subscales of the DCS and the scale 'perception of side effects' was tested using Cronbach's α for internal consistency. [40] For comparing groups, α values ≥ 0.70 are adequate. [41] Subsequently, clinical outcomes as well as parent reported outcomes were presented. For all variables, the association with the parents' decision has been estimated using univariate logistic regression.

Those variables related to treatment decision ($p<0.1$) were entered in a multiple logistic regression model. Prior to multiple regression, it was ruled out if any of the predictors relevantly correlated with each other ($\alpha<.01$ and Pearson's $r\geq0.80$). Adjusted odds ratios (aORs), along with 95% confidence intervals were used as estimates of association. Besides, we examined the explained variance of the multiple logistic regression model using pseudo (Nagelkerke) R^2 statistic. The level of significance was set at 5% (2-tailed). Bootstrapping was performed and used as a robust

test to confirm the stability of the outcomes of the multiple logistic regression analysis. Statistical analyses were carried out using SPSS 21.0 for Windows.

RESULTS

At the 5-month measurement point 432 infants met inclusion criteria for the cohort study; 26 parents refused to participate, 84 were included in the RCT of the HEADS study and 322 infants were included for follow-up in the nRCT (Figure 2). Parents of 194 of the 323 infants (60%) responded to the decision making questionnaire. Participants of the survey did not differ from non-participants on the tested background variables, expect for age of the mother. However the mean difference was 1.4 year and therefore not considered relevant in the decision making context.

Table 1. Background characteristics of the study population, presented ad mean (SD) or n (%)

	Total Sample (n=186)	Helmet Therapy (n=67)	Natural Course (n=119)
Gender (n=186)			
Male	125 (67)	47 (70)	78 (65)
Female	61 (33)	20 (29)	41 (35)
Firstborn (n=184)			
No	90 (49)	38 (56)	53 (45)
Yes	94 (51)	29 (44)	65 (55)
Parental level of education* (n=186)			
Low	30 (16)	11 (16)	19 (16)
Middle	76 (41)	24 (36)	52 (44)
High	80 (43)	32 (48)	48 (40)
Age mother (n=186)	31.3 (4.3)	31.8 (4.5)	31.1 (4.2)
Age father (n=184)	34.0 (4.9)	34.8 (5.3)	33.5 (4.7)
Trait Anxiety (STAI-DY) (n=181)	31.0 (7.4)	31.8 (6.9)	30.6 (7.7)

No differences (α<0.05) were found between the groups 'Helmet Therapy' and 'Natural Course'.
*Low education level: lower technical and vocational training and lower general secondary education; Medium education level: intermediate vocational training and advanced secondary education; High educational level: higher vocational education and university.
STAI-DY: Dutch version of the Spielberger State-Trait Anxiety Inventory. Scores range from 20 to 80; a higher score represents a higher state anxiety

186 parents had decided for the management option of their infant's skull deformation (either helmet therapy of awaiting natural course) at the time of the survey and were included for analysis. 67 parents chose to start helmet therapy (36%), while 119 parents chose to await natural course (64%).

Two-third of the infants were male (67%) and half of the population was firstborn (51%). In the helmet therapy group 44% of the infants were firstborn compared to 55% in the natural course group. Parents in the helmet therapy group had a slightly higher level of education compared to the parents who chose natural course. However, none of these differences were statistically significant (Table 1).

The internal consistency coefficient of the three subscales of the DCS and 'perception of side effects', expressed by Cronbach's α, was adequate (α ranging from 0.70 to 0.81).
On average, parents who chose to start helmet therapy had infants with more severe plagiocephaly than parents who chose awaiting natural course (mean difference 1.7, 95 % confidence interval (CI) 0.7 to 2.8), but no statistically significant differences were found for brachycephaly. Parents who chose helmet therapy also had higher expectations of the effectiveness of helmet therapy compared to the natural course of the skull deformation (1.9, 95 % CI 1.6 to 2.1) and were less satisfied with the shape of their infant's head (-1.2, 95 % CI -1.5 to -0.9). Furthermore, parents who decided for helmet therapy had a statistically significant higher state anxiety (3.3, 95% CI 0.9 to 5.7) and were more concerned for their infant's future (0.4, 95% CI 0.2 to 0.7) . Finally, parents who chose helmet therapy were more certain about their decision compared to parents who awaited natural course (-7.7, 95% CI -14.8 to -0.5) (Table 2).

Severity of asymmetric skull deformation, state anxiety, expected additional effect of helmet therapy, parental satisfaction, parental concern and decision uncertainty were included in a multiple logistic regression analysis (Table 2).

The analysis showed that parental satisfaction (aOR 0.2; 95% CI 0.1 to 0.4; p<.01), expected additional effect of helmet therapy (aOR 13.4; 95% CI 5.0 to 36.1; p<.01), and decision uncertainty aOR 1.0; 95% CI 0.9 to 1.0; p=.03) were related to the decision to start helmet therapy in infants with skull deformation. The multivariate model predicted 91.3% of cases in this study correctly; additional analysis using bootstrapping confirmed these results.

Table 2. Univariate and multivariate analysis of the relationship between clinical and parent reported outcomes and parents' decision. Data are expressed as mean (SD)

		Helmet Therapy	Natural Course	Univariate Analysis		Multivariate Analysis*	
	N	(n=67)	(n=119)	OR (95% CI)	*p*	aOR (95% CI)	*p*
Plagiocephaly (ODDI)	186	109.7 (4.1)	108.0 (3.2)	1.2 (1.1 to 1.3)	<.01	1.0 (0.8 to 1.1)	.60
Brachycephaly (CPI)	186	92.0 (7.4)	90.9 (6.9)	1.0 (1.0 to 1.1)	.32		
Parental satisfaction	183	2.2 (0.9)	3.4 (0.9)	0.3 (0.2 to 0.4)	<.01	0.2 (0.1 to 0.4)	<.01
Parental concern	180	1.9 (1.0)	1.5 (0.7)	1.7 (1.2 to 2.5)	<.01	0.6 (0.3 to 1.5)	.33
Expected additional effect helmet therapy	173	2.0 (1.2)	0.1 (0.6)	14.1 (6.5 to 30.7)	<.01	13.4 (5.0 to 36.1)	<.01
Perception of side effects	182	38.9 (21.5)	40.8 (24.1)	1.0 (1.0 to 1.0)	.59		
State anxiety (STAI-DY)	177	32.1 (8.8)	28.8 (7.0)	1.1 (1.0 to 1.1)	<.01	1.0 (0.9 to 1.1)	.78
DCS – Uncertainty	185	25.6 (22.3)	33.3 (24.4)	1.0 (1.0 to 1.0)	.04	1.0 (0.9 to 1.0)	.03
DCS – Factors contributing	184	19.2 (13.6)	19.5 (11.8)	1.0 (1.0 to 1.0)	.86		
DCS – Effective decision making	184	8.2 (11.4)	8.5 (12.2)	1.0 (1.0 to 1.0)	.85		

* Pseudo (Nagelkerke) R^2 =0.783, Predicted Percentage Correct=91.3%

ODDI: Oblique Diameter Difference Index. A value of 100% represents a purely symmetric head shape. A value above 100 represents asymmetric skull deformation; the higher the score, the more severe the deformation. **CPI:** Cranial Proportional Index. A score of 80% represents an average head shape in Western countries. A higher value represents a larger width to length ratio. **STAI-DY:** Dutch version of the Spielberger State-Trait Anxiety Inventory. Scores range from 20 to 80; a higher score represents a higher state anxiety. **DCS:** Decisional Conflict Scale. A higher score represents more decision uncertainty.

DISCUSSION

The results of this study indicate that parents' decision to choose helmet therapy for their infant in a real life situation is mostly influenced by their expectation of the additional effect of helmet therapy and (dis)satisfaction with their infant's appearance. Anxiety, decision uncertainty and the parents' perception of side effects ultimately did not influence decision making.

In rational decision making in the treatment of skull deformation, parents are expected to trade off the additional expected effects of the helmet and the perceived severity of and probability of side effects [27], while taking into account the severity of their child's skull deformation. Despite the lack of clinical evidence on the effects and side-effects for both options and variation in clinical practice, it seems that parents behave quite 'rational' in taking into account both perceived effectiveness and severity of the condition. In contrast to our expectations, the perception of side-effects of helmet therapy did not influence the parents' preference for treatment of skull deformation . This could be explained by the fact that the adverse events of helmet therapy are mild and are therefore not perceived as risks by parents. Higher expectations of helmet therapy compared to awaiting natural course increased the likelihood of a decision for helmet therapy.
Both actual severity as well as parental satisfaction with the infant's appearance influenced preference for treatment of skull deformation. However, when tested in the multiple logistic regression analysis, actual severity of the skull deformation dropped out as a significant predictor for decision making. We found that parental satisfaction accounted for some, but not all, of the relationship between actual severity of skull deformation and treatment decision. Other studies indeed confirm that subjective outcomes not always represent the same results as objective outcomes in skull deformation [42, 43], however parental satisfaction has been suggested to be a very important factor in decision making. [30]
In the univariate analysis parental concern, state anxiety and decision uncertainty were also related to a preference for helmet therapy. Emotions and values and beliefs are known to influence parental decision making [2]. In accordance to our beliefs, parents with a preference for helmet therapy did have higher levels of state anxiety compared to parents choosing for awaiting natural course. People with high anxiety levels search for ways to reduce their feelings of uncertainty: they strive for control of the situation .[44] It could be expected that in skull deformation, the helmet offers the sense of control in an uncertain situation; parents will do everything that is within their power to neutralize the unpleasant feeling of "anxiety". When adjusting for all variables related to treatment decision in the multivariate analysis, only 'decision uncertainty' showed a significant association with treatment decision. However this factor had no relevant influence on the decision.
It remains unknown whether the parents' perception of the condition and expectations of treatment are realistic, or whether these parents have extreme or irrational thoughts and emotions (wishful thinking). The latter could be supported by the fact that we found higher state

anxiety levels in parents choosing for helmet therapy as well as lower satisfaction scores and higher expectations of treatment effect. However, despite the type of treatment, various studies suggest that most parents are satisfied with the long term outcomes, while only the minority of parent remain concerned. [8, 9, 30, 45]

To determine whether the parents' expectations about the additional treatment effect of helmet therapy are realistic, results from a RCT comparing helmet therapy to awaiting natural course are needed. [33] Until scientific evidence of treatment effect, the preference for helmet therapy based on low satisfaction with the appearance of an infant and high expectations of helmet therapy seems sensible.

With regard to the methodology, the internal validity of the present model was confirmed by a high number of predicted cases and a large Nagelkerke R^2. However, since the number of cases (parents of 67 infants choosing helmet therapy) is small for estimating a model with six factors, this might have contributed to the high R^2 value. External validity of the model should be checked in future studies.

Throughout the study duration, helmet therapy was being reimbursed by Dutch insurance companies, so no financial trade-offs had to be made by participants. Costs of a helmet are on average €1,100 in The Netherlands, excluding costs of accompanying visits to the medical specialist. While it could be expected that insurance coverage would impact preferences in the treatment of skull deformation and decision for helmet treatment, this was not found by Naidoo et al. [30]

With the outcomes of this study we can better understand parental decision making for elective 'normalizing' treatments in children, such as helmet therapy in infants with skull deformation. Health care professionals should address the parents' perception of the severity of skull deformation and their expectations of helmet therapy. Furthermore they can assist parents in more rational decision making by balancing medical information with parents' expectations, values and beliefs. [9] Since 1-2% of infants present with persisting skull deformation at 5 to 6 months of age, a broad group of health care professionals can be confronted with parental decision making for helmet therapy. Therefore, the results of this study can be relevant for pediatricians, general practitioners, youth health care professionals, pediatric physical therapists, orthotists, pediatric neurosurgeons and craniofacial plastic surgeons. Since health professionals' recommendations are known to influence decision making [2, 46], future research could investigate the advice that professionals provide to parents of infants with skull deformation and the effect on parents' treatment preference. Also the effect of the parents' preference on treatment outcome could be investigated.

REFERENCES

1. Stiggelbout AM, Van der Weijden T, De Wit MP, et al. Shared decision making: really putting patients at the centre of healthcare. *BMJ.* 2012;344:e256.

2. Lipstein EA, Brinkman WB, Britto MT. What is known about parents' treatment decisions? A narrative review of pediatric decision making. *Med Decis Making.* 2012;32(2):246-258.

3. Nelson PA, Caress AL, Glenny AM, Kirk SA. 'Doing the "right" thing': how parents experience and manage decision-making for children's 'normalising' surgeries. *Soc Sci Med.* 2012;74(5):796-804.

4. Hutchison BL, Hutchison LA, Thompson JM, Mitchell EA. Plagiocephaly and brachycephaly in the first two years of life: a prospective cohort study. *Pediatrics.* 2004;114(4):970-980.

5. van Vlimmeren LA, van der Graaf Y, Boere-Boonekamp MM, L'Hoir MP, Helders PJ, Engelbert RH. Effect of pediatric physical therapy on deformational plagiocephaly in children with positional preference: a randomized controlled trial. *Arch. Pediatr. Adolesc. Med.* 2008;162(8):712-718.

6. Boere-Boonekamp MM, van der Linden-Kuiper LT. Positional preference: prevalence in infants and follow-up after two years. *Pediatrics.* 2001;107(2):339-343.

7. Nederlands Centrum Jeugdgezondheid. *JGZ-richtlijn Preventie, signalering en aanpak van voorkeurshouding en schedelvervorming.* Utrecht: TNO innovation for life;2012.

8. Hutchison BL, Stewart AW, Mitchell EA. Deformational plagiocephaly: a follow-up of head shape, parental concern and neurodevelopment at ages 3 and 4 years. *Arch. Dis. Child.* 2011;96(1):85-90.

9. Steinbok P, Lam D, Singh S, Mortenson PA, Singhal A. Long-term outcome of infants with positional occipital plagiocephaly. *Childs Nerv. Syst.* 2007;23(11):1275-1283.

10. Flannery AB, Looman WS, Kemper K. Evidence-based care of the child with deformational plagiocephaly, part II: management. *J. Pediatr. Health Care.* 2012;26(5):320-331.

11. Xia JJ, Kennedy KA, Teichgraeber JF, Wu KQ, Baumgartner JB, Gateno J. Nonsurgical treatment of deformational plagiocephaly: a systematic review. *Arch. Pediatr. Adolesc. Med.* 2008;162(8):719-727.

12. Mortenson P, Steinbok P, Smith D. Deformational plagiocephaly and orthotic treatment: indications and limitations. *Childs Nerv. Syst.* 2012;28(9):1407-1412.

13. Loveday BP, de Chalain TB. Active counterpositioning or orthotic device to treat positional plagiocephaly? *J. Craniofac. Surg.* 2001;12(4):308-313.

14. Lipira AB, Gordon S, Darvann TA, et al. Helmet versus active repositioning for plagiocephaly: a three-dimensional analysis. *Pediatrics.* 2010;126(4):e936-945.

15. Littlefield TR. Cranial remodeling devices: treatment of deformational plagiocephaly and postsurgical applications. *Semin. Pediatr. Neurol.* 2004;11(4):268-277.

16. Bialocerkowski AE, Vladusic SL, Howell SM. Conservative interventions for positional plagiocephaly: a systematic review. *Dev. Med. Child Neurol.* 2005;47(8):563-570.

17. Kluba S, Kraut W, Calgeer B, Reinert S, Krimmel M. Treatment of positional plagiocephaly - Helmet or no helmet? *J. Craniomaxillofac. Surg*.

18. Vles JS, Colla C, Weber JW, Beuls E, Wilmink J, Kingma H. Helmet versus nonhelmet treatment in nonsynostotic positional posterior plagiocephaly. *J. Craniofac. Surg.* 2000;11(6):572-574.

19. Mulliken JB, Vander Woude DL, Hansen M, LaBrie RA, Scott RM. Analysis of posterior plagiocephaly: deformational versus synostotic. *Plast. Reconstr. Surg.* 1999;103(2):371-380.

20. Goh JL, Bauer DF, Durham SR, Stotland MA. Orthotic (helmet) therapy in the treatment of plagiocephaly. *Neurosurg. Focus.* 2013;35(4):E2.

21. Robinson S, Proctor M. Diagnosis and management of deformational plagiocephaly. *J. Neurosurg. Pediatr.* 2009;3(4):284-295.

22. Lee A, Van Pelt AE, Kane AA, et al. Comparison of perceptions and treatment practices between neurosurgeons and plastic surgeons for infants with deformational plagiocephaly. *Journal of Neurosurgery: Pediatrics.* 2010;5(4):368-374.

23. Bialocerkowski AE, Vladusic SL, Wei Ng C. Prevalence, risk factors, and natural history of positional plagiocephaly: a systematic review. *Dev. Med. Child Neurol.* 2008;50(8):577-586.

24. Robinson S. Deformational plagiocephaly delays motor skill development in 6-month-old infants. *J. Pediatr.* 2010;157(3):514-515.

25. Nederlands Centrum Jeugdgezondheid. *JGZ-richtlijn Preventie, signalering en aanpak van voorkeurshouding en schedelvervorming.* Utrecht: Nederlands Centrum Jeugdgezondheid;2012.

26. Pogliani L, Mameli C, Fabiano V, Zuccotti GV. Positional plagiocephaly: what the pediatrician needs to know. A review. *Childs Nerv. Syst.* 2011;27(11):1867-1876.

27. Silveira MJ, Rhodes L, Feudtner C. Deciding how to decide: what processes do patients use when making medical decisions? *J Clin Ethics.* 2004;15(3):269-281.

28. Suarez-Almazor ME, Conner-Spady B, Kendall CJ, Russell AS, Skeith K. Lack of congruence in the ratings of patients' health status by patients and their physicians. *Med. Decis. Making.* 2001; 21(2):113-121.

29. Collett B, Breiger D, King D, Cunningham M, Speltz M. Neurodevelopmental implications of "deformational" plagiocephaly. *J. Dev. Behav. Pediatr.* 2005;26(5):379-389.

30. Naidoo SD, Cheng AL. Long-term satisfaction and parental decision making about treatment of deformational plagiocephaly. *J. Craniofac. Surg.* 2014;25(1):160-165.

31. Guerriere DN, McKeever P, Llewellyn-Thomas H, Berall G. Mothers' decisions about gastrostomy tube insertion in children: factors contributing to uncertainty. *Dev Med Child Neurol.* 2003;45(7):470-476.

32. Hyde M, Punch R, Komesaroff L. Coming to a decision about cochlear implantation: parents making choices for their deaf children. *J Deaf Stud Deaf Educ.* 2010;15(2):162-178.

33. van Wijk RM, Boere-Boonekamp MM, Groothuis-Oudshoorn CG, van Vlimmeren LA, IJzerman MJ. HElmet therapy Assessment in infants with Deformed Skulls (HEADS): protocol for a randomised controlled trial. *Trials.* 2012;13:108.

34. van Adrichem LNA, van Vlimmeren LA, Cadanova D, et al. Validation of a simple method for measuring cranial deformities (Plagiocephalometry). *J. Craniofac. Surg.* 2008;19(1):15-21.

35. van Vlimmeren LA, Takken T, van Adrichem LN, van der Graaf Y, Helders PJ, Engelbert RH. Plagiocephalometry: a non-invasive method to quantify asymmetry of the skull; a reliability study. *Eur. J. Pediatr.* 2006;165(3):149-157.

36. van der Ploeg HM, Defares PB, Spielberger CD. *Handleiding bij de Zelf-Beoordelings Vragenlijst, ZBV: Een Nederlandstalige bewerking van de Spielberger State-Trait Anxiety Inventory*. Lisse: Swets & Zeitlinger; 1980.

37. Van der Ploeg HM. De ontwikkeling en validatie van een Nederlandstalige vragenlijst voor het meten van angst. *Tijdschrift voor Psychiatrie.* 1982;24:46-50.

38. O'Connor AM. Validation of a decisional conflict scale. *Med Decis Making.* 1995;15(1):25-30.
39. Koedoot N, Molenaar S, Oosterveld P, et al. The decisional conflict scale: further validation in two samples of Dutch oncology patients. *Patient Educ Couns.* 2001;45(3):187-193.
40. Cronbach LJ. *Essentials of Psychology Testing*. New York: Harper Collins; 1990.
41. Nunnally JC, Bernstein IH. *Psychometric Theory*. New York: McGraw-Hill; 1994.
42. Feijen M, Schuckman M, Habets E, van der Hulst R. Positional plagiocephaly and brachycephaly: is there a correlation between subjective and objective assessment of cranial shape? *J. Craniofac. Surg.* 2012;23(4):998-1001.
43. Katzel EB, Koltz PF, Sbitany H, Girotto JA. Treatment of plagiocephaly with helmet molding therapy: do actual results mimic perception? *Cleft Palate. Craniofac. J.* 2011;48(2):205-209.
44. American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5™)*2013.
45. Govaert B, Michels A, Colla C, van der Hulst R. Molding therapy of positional plagiocephaly: subjective outcome and quality of life. *J. Craniofac. Surg.* 2008;19(1):56-58.
46. Gurmankin AD, Baron J, Hershey JC, Ubel PA. The role of physicians' recommendations in medical treatment decisions. *Med Decis Making.* 2002;22(3):262-271.

CHAPTER 5

Helmet therapy in infants with positional skull deformation: randomised controlled trial

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ABSTRACT

Objectives – To determine the effectiveness of helmet therapy for positional skull deformation compared with the natural course of the condition in infants aged 5 to 6 months.
Design Pragmatic, single blinded, randomised controlled trial (HEADS, HElmet therapy Assessment in Deformed Skulls) nested in a prospective cohort study.

Setting – 29 Paediatric physiotherapy practices; helmet therapy was administered at four specialised centres.

Participants – 84 infants aged 5 to 6 months with moderate to severe skull deformation, who were born after 36 weeks of gestation, and had no muscular torticollis, craniosynostosis, or dysmorphic features. Participants were randomly assigned to helmet therapy (n=42) or to natural course of the condition (n=42) according to a randomisation plan with blocks of eight.

Interventions – Six months of helmet therapy compared with the natural course of skull deformation. In both trial arms parents were asked to avoid any (additional) treatment for the skull deformation.

Main outcome measures – The primary outcome was change in skull shape from baseline to 24 months of age assessed using plagiocephalometry (anthropometric measurement instrument). Change scores for plagiocephaly (oblique diameter difference index) and brachycephaly (cranioproportional index) were each included in an analysis of covariance, using baseline values as the covariate. Secondary outcomes were ear deviation, facial asymmetry, occipital lift, and motor development in the infant, quality of life (infant and parent measures), and parental satisfaction and anxiety. Baseline measurements were performed in infants aged between 5 and 6 months, with follow-up measurements at 8, 12, and 24 months. Primary outcome assessment at 24 months was blinded.

Results – The change score for both plagiocephaly and brachycephaly was equal between the helmet therapy and natural course groups, with a mean difference of −0.2 (95% confidence interval −1.6 to 1.2, P=0.80) and 0.2 (−1.7 to 2.2, P=0.81), respectively. Full recovery was achieved in 10 of 39 (26%) participants in the helmet therapy group and 9 of 40 (23%) participants in the natural course group (odds ratio 1.2, 95% confidence interval 0.4 to 3.3, P=0.74). All parents reported one or more side effects.

Conclusions – Based on the equal effectiveness of helmet therapy and skull deformation following its natural course, high prevalence of side effects, and high costs associated with helmet therapy, we discourage the use of a helmet as a standard treatment for healthy infants with moderate to severe skull deformation.

INTRODUCTION

Positional skull deformation is a condition in which the shape of an infant's skull deforms as a result of prolonged external forces. The infant's head is malleable and growing rapidly, hence it is susceptible to deformation, especially when infants develop a positional preference of the head when lying in the supine position.[1] Two typical components of skull deformation are unilateral occipital flattening of the skull (plagiocephaly) and symmetrical occipital flattening (brachycephaly).[2] A strong plagiocephalic flattening is often presented with ipsilateral frontal bossing of the forehead and anterior shift of the ipsilateral ear (ear deviation) and cheek.[3-5] Brachycephaly can be accompanied by temporal bossing or an occipital lift.[3]

Skull deformation is generally considered a cosmetic condition. Developmental delays are regularly associated with skull deformation,[6-9] but the deformation is increasingly seen as a marker for delays, instead of causing delays.[6-8] Parents fear the negative physical and psychosocial effects of skull deformation on their child.[10, 11]

The prevalence of skull deformation increased substantially after it was recommended that infants should be placed in a supine sleep position to prevent sudden infant death syndrome.[12-18] Nowadays skull deformation seems most prevalent between two (16% to 22%) and four months (20%) after birth.[19, 20] The prevalence drops when infants become older.[1, 19-21]

The preferred treatment is usually conservative. In a recently published guideline (2012), the Netherlands Centre of Preventive Child Health Care advised to start counselling parents during well baby visits on the handling and repositioning infants with an observed positional preference or skull deformation. When no improvement is seen at follow-up visits, infants are referred for paediatric physiotherapy.[22, 23] Infants younger than 4 months may benefit from active repositioning, yet not all cases show improvement.[22, 24, 25] As most infants show symmetry in posture at 5 or 6 months of age,[1, 22] no effects of continued pediatric physical therapy can be expected. In infants with persistent skull deformation at 6 months of age, orthotic helmets or headbands are frequently prescribed.[26-28] A helmet is a cranial orthosis made up of a rigid plastic shell with a foam lining. The helmet is expected to redirect skull growth by fitting closely to the infant's head but leaving room for the skull to grow at the flattened area. The helmet is recommended to be worn for 23 hours a day from 6 months until 12 months of age. In the Netherlands 1-2% of all infants (176,000 newborns in 2012[29]) received helmet therapy for skull deformation.

Since conclusive evidence from randomized trials is lacking, the clinical benefit of helmet therapy compared with the natural course of skull deformation remains unknown. The few prospective comparative studies to date tend to show positive results in favour of helmet therapy, but have several limitations.[5, 30-33] Long term outcomes and assessment of side effects are missing in most studies and the clinical relevance of the reported effects is questionable.[26, 28, 34, 35]

The HElmet therapy Assessment in Deformed Skulls (HEADS) study is a randomized controlled trial designed to compare helmet therapy for six months with the natural course of skull deformation in infants aged 6 months. Although helmet therapy is expected to give slightly better results on the short term, we hypothesized that the natural course would catch up with the effects of helmet therapy over time and that no clinically meaningful differences would be present between the two groups at 2 years of age.

METHODS

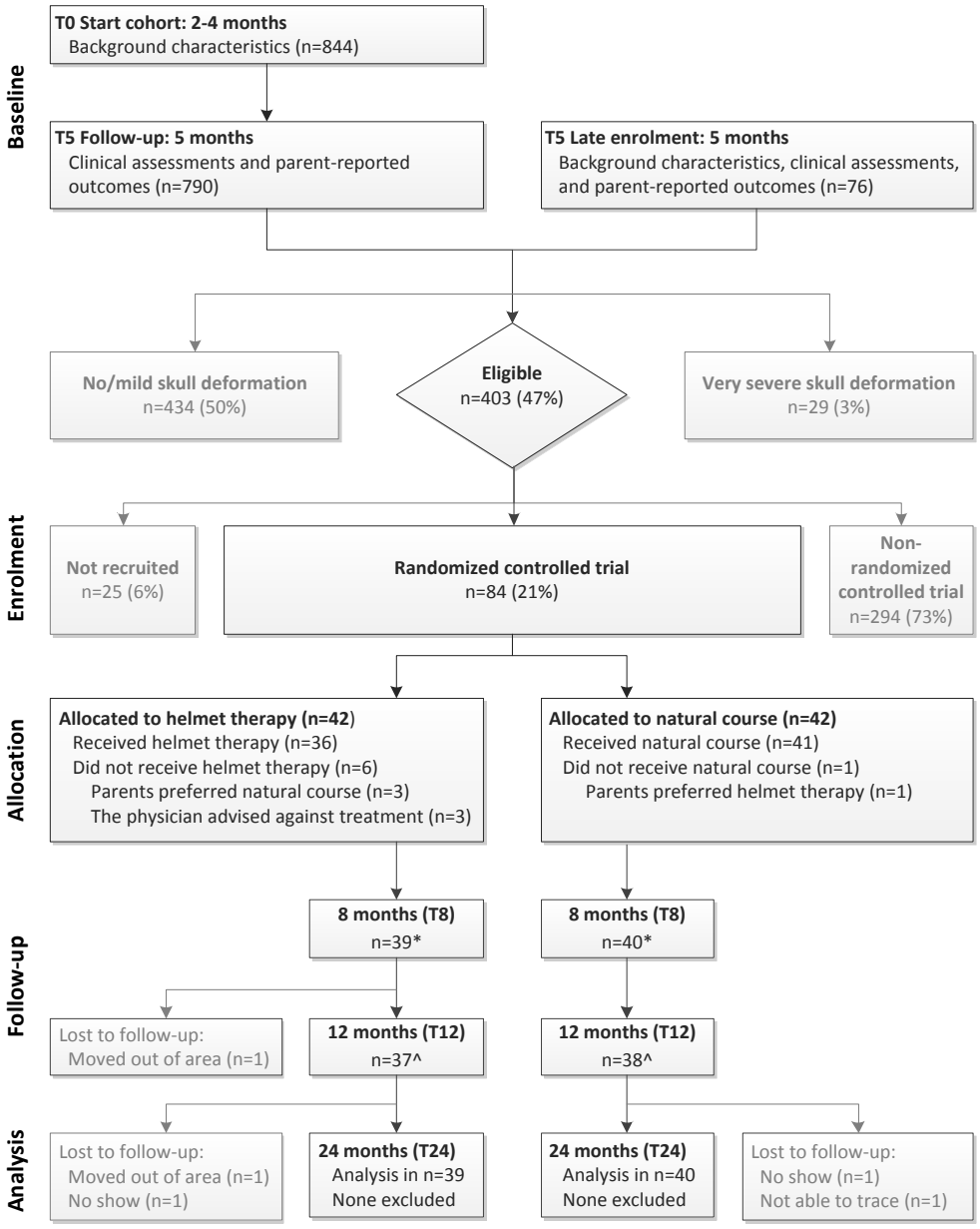
Study design

The HEADS study is a two armed pragmatic randomized controlled trial nested in a prospective cohort study (Figure 1). The follow-up study was designed to catch all infants eligible for helmet therapy after a period of peadiatric physical therapy or a single consultation. We invited the parents of eligible infants with moderate to severe skull deformation to include their infants in the study at 5 months of age. Participants were randomized 1:1 to either the helmet therapy arm, or the natural course arm. Follow-up assessments were performed at 8, 12 and 24 months of age (Figure 1). The primary outcome was anthropometric measurement of the skull. A more detailed description of the HEADS study is published elsewhere.[36]

Setting and participants

Recruitment for the randomised controlled trial was conducted in 29 paediatric physiotherapy practices in the east of the Netherlands between July 2009 and July 2011 by 29 specially trained paediatric physiotherapists. We considered infants to be eligible for the study if they had moderate to severe skull deformation, were aged 5 to 6 months, were born after 36 weeks of gestation, and had no muscular torticollis, craniosynostosis, or dysmorphic features. The course for participating paediatric physiotherapists included detailed information on differentiating between synostotic and non-synostotic skull deformation and between positional and congenital muscular torticollis.

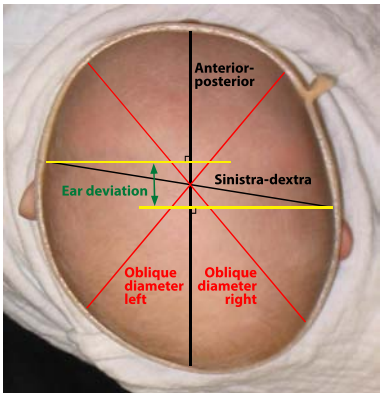
We determined the severity of skull deformation in the transversal plane using the oblique diameter difference index and the craniproportional index of plagiocephalometry (Figure 2).[37, 38] The oblique diameter difference index provides the degree of the plagiocephalic component of skull deformation and is the ratio between the longest cranial diagonal and the shortest cranial diagonal (Figure 2) multiplied by 100%, with both located at 40° from the anterior-posterior line. In addition, we determined the brachycephalic component using the craniproportional index, which is the ratio between the width and the length of the skull (Figure 2).



* 5 infants were missing at T8; 2 infants were assessed at T12, 3 infants were assessed at T24.
^ 8 infants were missing at T12, but were assessed up at T24.

Figure 1. Flowchart of HElmet therapy Assessment in Deformed Skulls study

We included infants in the study if the oblique diameter difference index was 108% or more or if the craniproportional index was 95% or more, or in the case of a mixed form if the oblique diameter difference index was 106% or more and the craniproportional index was 92% or more. Infants with very severe skull deformation were excluded (oblique diameter difference index >113% or craniproportional index >104%). A value of 100% on the oblique diameter difference index represents a symmetrical head shape. A value of more than 100% represents asymmetrical skull deformation; the higher the score, the more severe the deformation. A score of 80% on the craniproportional index represents an average head shape in Western countries. A higher value represents a larger head width compared with length.



	ODDI (%)		CPI (%)
Normal shape	<104	and	<90
Mild deformation	104 - 107	or	90 - 94
Moderate deformation	108 - 111	or	95 - 99
Severe deformation	≥ 112	or	≥ 100

Figure 2. Plagiocephalometry and cutoff points for severity of skull deformation
Illustration shows left occipital flattening of skull and thermoplastic measuring ring with digitally drawn lines used in plagiocephalometry. Indices were calculated by the following formulas: craniproportional index (CPI), sinistra-dextra/anterior-posterior×100%; oblique diameter difference index (ODDI), longest oblique diameter/shortest oblique diameter×100%; and ear deviation index, ear deviation/anterior-posterior×100%

Randomization and blinding

At age 5 months, the paediatric physiotherapists selected infants meeting the inclusion criteria for the trial and requested informed consent from the parents. The parents could consult an independent doctor for questions related to trial participation. After inclusion, infants were allocated to their trial arm by computer generated randomisation in blocks of eight. An independent researcher managed the randomisation plan. The research team and parents were blinded for group allocation until the parents had signed the informed consent form and confirmed participation. A researcher (RMW) called the parents and informed them about the randomisation allocation. It was not possible to blind parents during the treatment period. The infant's paediatric physiotherapist, general practitioner, and youth healthcare professional were informed about group allocation after randomisation. Blinded outcome assessments were, however, performed at the 24 month follow-up.

Intervention and control group

Parents of infants allocated to the helmet therapy group were asked to make an appointment at one of the four collaborating institutes to obtain a custom-made helmet. Between the institutes two brands of helmets were provided; both helmets used the same mechanism to redirect skull growth. The aim was to start helmet therapy in the infants no later than 6.5 months of age. Parents were instructed to ensure that the helmet was worn for 23 hours a day until their infant was 12 months of age or until satisfactory outcomes were obtained according to both parents and professionals. Parents received additional information on starting the helmet therapy, how the helmet should be worn, cleaning the helmet, and general care. An orthotist regularly monitored the infants for signs of pressure spots, and the helmet was modified or replaced to accommodate skull growth as necessary. The treatment was always supervised by a (paediatric) doctor. During the intervention period, Dutch health insurance companies reimbursed the costs of helmet therapy.
The control group did not receive helmet therapy and natural skull growth was monitored.

Outcome measures

The paediatric physiotherapists performed measurements at baseline and at age 5, 8, and 12 months. Six of the paediatric physiotherapists who were involved in the study were selected to perform the blinded assessments at 24 months in all infants. These measurements were carried out from February 2011 until March 2013. Every assessment included anthropometric measurement of the skull's shape, a clinical assessment of skull deformation, a motor assessment, and a parental questionnaire. The questionnaire was used to gather information on background characteristics (sex, age, birth rank, health problems, ethnicity, and educational level of the parents) at baseline and parent reported outcomes during all assessments.

Therapy compliance

The questionnaire administered at 12 months was used to determine whether parents were compliant with the regimen to which their infant was assigned. The questionnaire assessed the age of infants when treatment was discontinued and the reasons for discontinuation. Parents were also asked whether they used additional therapies. Furthermore, the questionnaires at 8 and 12 months also included questions about the fit of the helmet.
Originally the protocol specified that compliance would be determined using data from an electronic device built into the helmet to measure compliance with wear. Despite a pilot study, data from the measuring devices proved to be unreliable and we therefore omitted them from further analysis.

Primary outcome

Skull shape

The primary outcome was the anthropometric measurement of the skull's shape at 24 months using the oblique diameter difference index and craniproportional index.[37, 38] We considered a difference in change score from age 5 to 24 months of 4 oblique diameter difference index points or 5 craniproportional index points to be relevant between the groups, consistent with one level of severity in skull deformation according to plagiocephalometry criteria (Figure 2). Additionally, we report the number of infants who fully recovered, with full recovery defined as an oblique diameter difference index of less than 104% and a craniproportional index of less than 90% (Figure 2).

Secondary outcomes

Ear deviation

Severity of ear deviation was expressed by the ear deviation index using plagiocephalometry. The ear deviation index is the ratio between the ear deviation and the length of the skull (Figure 2).

Facial asymmetry and occipital lift

During the clinical assessment the paediatric physiotherapists reported the presence of any facial asymmetry and occipital lift.

Parental satisfaction

Parental satisfaction with their infant's head shape was assessed in the parental questionnaire using a five point Likert scale, ranging from 1 (not satisfied at all) to 5 (very satisfied).

Motor development

At baseline, a paediatric physiotherapist assessed the repertoire of gross motor movement using the Alberta infant motor scale, a valid, norm-referenced measurement. We converted raw scores on the scale into standardised Z scores, using the formula: (individual score–average score)/ standard deviation.[39]

To assess motor development at 24 months we used the Bayley scales of infant and toddler development, third edition.[40] Specially trained physiotherapists administered the test. We converted raw scores to standardised motor composite scores (mean 100 (SD 15)) and scaled scores for fine and gross motor development separately (mean 10 (SD=3)).

Anxiety

We measured the level of parental state anxiety using the Spielberger state trait anxiety inventory, Dutch version.[41] The state anxiety scale (20 items) concerns the state of anxiety of parents at a specific moment, and scores range from 20 to 80; a higher score represents a higher state of anxiety.

Quality of life

The infant toddler quality of life questionnaire—short form 47 is a parent reported measure that provides information about the health status and health related quality of life in children aged between 2 months and 5 years.[42] Since the questionnaire is a "proxy" measure and parental concern might influence outcomes, parent specific scales are included. The questionnaire consists of eight multi-item scales and two single items: the child scales include physical abilities (six items), growth and development (five), bodily pain (two), temperament and moods (six), behaviour (12), general health (six), and change in health (one); the parent scales include parental-impact emotional (four items), parental-impact time (four), and family cohesion (one). Scores for all scales range from 0 to 100, with a higher score indicating better health.

Side effects

The questionnaires at 8 and 12 months contained questions about side effects associated with helmet therapy. In consultation with health professionals we defined side effects as skin irritation, pain, sweating, odour of the helmet, problems with accepting the helmet, and feeling hindered in cuddling because of the helmet. Furthermore, in both groups at 8 months parents were asked about the number of hours their baby cried a day and whether their baby had sleep problems. Criteria to define sleep problems in infants are not used consistently in the literature[43]; in this study we defined sleep problems as taking more than 20 minutes to fall asleep (daily), or waking more than once every night.

Statistical analyses

The sample size of the randomised controlled trial of the HEADS study was calculated at 72 (36 in each arm), based on a significance level of 5%, a power of 90%, and a difference in mean improvement of at least 4 (SD 6) oblique diameter difference index points.

We described background and baseline clinical characteristics of the sample for the total group as well as for the intervention and control groups separately; continuous variables with means and standard deviation, and discrete variables with counts and percentages. In a subsequent analysis, we compared the baseline characteristics of the intervention and control groups by means of the independent *t* test or $\chi 2$ test.

We determined the representativeness of the randomised controlled trial population by comparing background characteristics and baseline clinical characteristics of the population with eligible non-participants at age 5 months using the independent *t* test or $\chi 2$ test.
For analysis we used two continuous outcome variables (plagiocephaly change score: oblique diameter difference index at age 5 months minus 24 months; and brachycephaly change score: cranioproportional index at age 5 months minus 24 months) and the dichotomous outcome variable (full recovery). Treatment effect was presented as change score in the helmet therapy group minus change score in the natural course group. To test differences in the change scores between the groups, we used analysis of covariance with baseline value (age 5 months) as covariate. Thereafter we carried out multiple regression analyses with baseline values (age 5 months), sex, and parental level of education as covariates. We compared secondary outcomes between groups by means of the independent *t* test or $\chi 2$ test. To analyse the 10 subscales of the infant toddler quality of life questionnaire we performed a multivariate analysis of variance.
We compared the groups on an intention to treat basis. Additionally, we carried out a per protocol analysis. Data analysis was performed using SPSS (version 21.0), and we set the level of significance at 0.05.

RESULTS

Study population

At the start of this study, the paediatric physiotherapists identified 403 eligible infants (47% of 866 assessed infants, Figure 1). The parents of 84 infants (21%) agreed to participate in the trial and those infants were assigned to two groups (42 infants in each group). The main baseline personal and clinical characteristics (sex, age, birth rank, health problems, ethnicity, severity of skull deformation, motor development, and parental satisfaction) did not differ significantly between those who agreed to participate and the infants who were not enrolled, except for the educational level of the parents, which was lower among the participants. The background characteristics of the two trial arms were comparable (Table 1).

A total of 79 infants (94%) were followed up at the final assessment at 24 months (Figure 1). The parents of two infants did not show up for final assessments despite repeated attempts to contact them, two families moved out of the study area, and the parents of one infant could not be contacted.

Table 1. Characteristics of study population of infants with skull deformation. Values are numbers (percentages) unless stated otherwise*

	Total Population (n=84)	Helmet Therapy (n=42)	Natural Course (n=42)
Boys	61/84 (73)	32/42 (76)	29/42 (69)
Mean (SD) age at baseline (months)	5.1 (0.4)	5.1 (0.4)	5.1 (0.3)
Mean (SD) age at follow-up (months)	24.8 (4.4)	25.0 (3.5)	24.6 (5.1)
Birth rank (first born)	39/79 (49)	20/40 (50)	19/39 (49)
Health problems†	6/84 (7)	4/42 (10)	2/40 (5)
Ethnicity (ethnic minority)‡	5/77 (7)	4/41 (10)	1/36 (3)
Education level of parents§			
Low	24/81 (30)	15/42 (36)	9/39 (23)
Medium	34/81 (42)	15/42 (36)	19/39 (49)
High	23/81 (28)	12/42 (29)	11/39 (28)

Numbers may not add up to group totals because of missing data.
*Groups compared using *t* test or χ^2 test.
†Problems with sight, hearing, oesophageal reflux, developmental dysplasia of hip, congenital heart disease, or inguinal hernia.
‡At least one parent born outside of the Netherlands.
§Low education level: lower technical and vocational education and lower general secondary education; medium education level: intermediate vocational education and advanced secondary education; and high education level: higher vocational education and university. Percentages may not total 100%, due to rounding off.

Table 2. Baseline clinical characteristics of the study population at age 5 months. Values are means (standard deviation) unless stated otherwise*

	Helmet Therapy (n=42)	Natural Course (n=42)
Plagiocephaly (ODDI) †	107.2 (3.9)	109.2 (2.9)
Brachycephaly (CPI) †	93.4 (6.9)	90.3 (6.2)
Ear Deviation Index (EDI)	4.7 (3.5)	5.5 (3.0)
No (%) with facial asymmetry	7/42 (17)	13/42 (31)
No (%) with occipital lift	18/42 (43)	10/42 (24)
Motor development (AIMS Z-score)	-0.7 (1.0)	-0.7 (1.0)
Parental satisfaction	2.8 (0.8)	3.0 (1.0)
State anxiety (STAI-DY)	30.8 (7.1)	32.2 (8.6)

ODDI=oblique diameter difference index (value of 100% represents purely symmetrical head shape, value >100 represents asymmetrical skull deformation; the higher the score, the more severe the deformation); CPI=cranioproportional index (score of 80% represents an average head shape in Western countries, higher value represents a larger head width compared with length); EDI=ear deviation index (value of 0 represents no ear deviation; the higher the score above 0, the more severe the ear deviation). AIMS=Alberta infant motor scale standardised Z scores (individual score minus average score divided by standard deviation); STAI-DY=Dutch version of Spielberger state-trait anxiety inventory (scores range from 20 to 80; a higher score represents a higher state anxiety).
*Groups compared using *t* test or χ^2 test.
†P<0.05.

All infants met the inclusion criteria for either the plagiocephalic component of skull deformation (oblique diameter difference index ≥108%) or the brachycephalic component (cranioproportional index ≥95%), or both. The baseline assessments showed statistically significant differences in the shape of the infants' skulls between the two groups (Table 2). Infants in the natural course group presented with more severe plagiocephaly and more often presented with facial asymmetry, whereas infants in the helmet therapy group showed higher brachycephaly scores and more often showed the accompanying occipital lift (Table 2).

Therapy allocation and compliance

After randomisation, seven infants did not start the assigned treatment. Six infants who were allocated to helmet therapy did not start this treatment: in three cases the parents preferred to allow the skull deformity to follow its natural course; in three other cases the doctor advised against helmet therapy. Additionally, parents of one infant allocated to the natural course arm preferred helmet therapy.

In infants who started in the helmet therapy group, helmet therapy was discontinued at a mean age of 10.0 months (SD 2.0 months, n=30). Ten of 30 infants received helmet therapy until 12 months of age. The main reasons for parents discontinuing the helmet therapy before 12 months (n=20) was satisfaction with results (n=8), side effects (n=10), dissatisfaction with the results (n=1), and "other" (n=1). Problems with fitting the helmet were reported for 22 of 30 infants (73%); the helmet rotated or shifted a few times a week to several times a day. Parents of one infant reported that the helmet came off spontaneously.

Two infants in the natural course group received helmet therapy after the 8 month assessment; the parents were not satisfied with the skull shape.

Three infants in the helmet therapy group and two in the natural course group received additional therapy during the intervention period: manual therapy, osteopathy, or chiropractic.

Primary outcome

The plagiocephaly change score from age 5 months to 24 months was almost equal for both groups (Table 3): the difference in oblique diameter difference index, calculated as change score in the helmet therapy group minus change score in the natural course group, was −0.2 (95% confidence interval −1.6 to 1.2, P=0.80). The brachycephaly change score from age 5 months to 24 months was also almost equal for both groups, with a difference in cranioproportional index of 0.2 (−1.7 to 2.2, P=0.81). Additionally, the numbers of infants showing full recovery were comparable in both groups (odds ratio 1.2, 95% confidence interval 0.4 to 3.3).

When adjusting for baseline values, change scores between groups did not differ significantly (adjusted difference in mean plagiocephaly change score 0.9, 95% confidence interval −0.3 to 2.0 and in mean brachycephaly change score −1.0, −2.5 to 0.5). Adjusting for sex and parental level of education did not alter the treatment effect (plagiocephaly change score: β=1.0 (−0.3 to 2.3),

P=0.12; brachycephaly change score: β=−1.1 (−2.8 to 0.5), P=0.17).
A per protocol analysis of covariance (helmet therapy n=34, natural course n=45) provided outcomes comparable to the intention to treat analysis (plagiocephaly change score −0.4, −1.8 to 1.1, P=0.31; brachycephaly change score 0.5, −1.5 to 2.4, P=0.11).

Table 3. Primary outcomes, measured at 24 months. Values are means (standard deviations) unless stated otherwise

	Helmet Therapy (n=39)	Natural Course (n=40)	*p**	ANCOVA; adjusted means (95% CI)† Helmet Therapy	Natural Course	*p*
Plagiocephaly change score	2.9 (2.9)	3.1 (3.3)	.80	3.4 (2.6 to 4.2)	2.6 (1.8 to 3.4)	.13
Brachycephaly change score	7.0 (4.1)	6.8 (4.4)	.81	6.4 (5.3 to 7.5)	7.4 (6.4 to 8.5)	.20
No (%) with full recovery	10/39 (26)	9/40 (23)	.74	**	**	**

ANCOVA=analysis of covariance.
*Groups compared using *t* test or χ^2 test.
†ANCOVA model with baseline measurement at age 5 months as covariate.
‡Oblique diameter difference index at age 5 months minus at age 24 months.
§Craniproportional index at age 5 months minus at age 24 months.
¶Oblique diameter difference index <104% and craniproportional index <90%.
** Not analysed because of low number of cases

Secondary outcomes

No significant differences were found for the additional clinical outcomes, parent reported outcomes, and motor development. Parents in both arms showed high scores for satisfaction with their infants' skull shape at 24 months (Table 4).
Finally, a multivariate analysis of variance revealed no significant differences between groups for subscales on the infant toddler quality of life questionnaire: Wilks' λ=.826, $F_{10,63}$=1.3, P=0.24.

Side effects

The helmet therapy group had fewer sleep problems (helmet therapy 5/35, 14%; natural course 10/41, 24%) and spent fewer hours crying than the natural course group (helmet therapy mean 1.4 (SD 1.2); natural course mean 1.2 (SD 0.9)), although these differences were not significant. In the intervention group all parents (35/35) reported one or more side effects related to helmet therapy: problems with acceptance of the helmet (8/33, 24%), skin irritation (32/34, 96%), augmented sweating (24/34, 71%), unpleasant odour of the helmet (25/33, 76%), pain associated with the helmet (9/27, 33%), and feeling hindered from cuddling their child (24/31, 77%).

Table 4. Secondary outcomes, measured at age 24 months. Values are means (standard deviations) unless stated otherwise

	Helmet Therapy (n=39)	Natural Course (n=40)	*p**	Helmet Therapy – Natural Course
Ear deviation change score (n=79) †	2.0 (4.0)	1.9 (3.6)	.86	0.2 (-1.5 to 1.8)
Facial asymmetry	5/38 (13%)	10/39 (26%)	.17	0.4 (0.1 to 1.4)‡
Occipital lift	4/38 (11%)	2/40 (5%)	.36	2.2 (0.4 to 13.0) ‡
Parental satisfaction (n=77)	4.6 (0.5)	4.4 (0,6)	.06	0.2 (-0.1 to 0.5)
State anxiety (STAI-DY) (n=76)	27.4 (6.5)	31.3 (9.2)	.04	-3.9 (-7.5 to -0.2)
BSID-III composite score (n=77)	97.2 (9.4)	99.0 (11.6)	.17	-1.8 (-6.6 to 3.0)
BSID-III fine scale (n=78)	10.0 (1.9)	10.8 (2.2)	.21	-0.7 (-1.7 to 0.2)
BSID-III gross scale (n=78)	9.1 (1.8)	8.8 (2.4)	.58	0.2 (-0.7 to 1.2)

STAI-DY=Dutch version of Spielberger state-trait anxiety inventory (scores range from 20 to 80; a higher score represents a higher state anxiety); BSID III=Bayley scales of infant and toddler development, third edition (standardised motor composite scores mean 100 (SD 15), scaled scores for fine and gross motor development mean 10 (SD 3).
*Groups compared using *t* test or χ^2 test.
†Ear deviation index measurement at age 5 months minus at age 24 months.
‡Odds ratio (95% confidence interval).

DISCUSSION

This pragmatic randomised controlled trial found no evidence of a significant or clinically meaningful difference in improvement of skull shape at 2 years of age between infants who were treated with helmet therapy and those in whom the natural course of skull deformation was awaited. Despite improvement in skull shape in both groups, only a quarter of the participants showed full recovery. Overall, parents were satisfied to very satisfied with the recovery of their infants' skull deformation at 2 years old. However, the parents of infants who were treated with a helmet showed slightly higher satisfaction scores and a slightly lower state of anxiety when their infants were 2 years of age.
Helmet therapy did not influence the infants' motor development, quality of life, sleeping, or crying. Side effects of helmet therapy were reported by all parents.

Strengths and limitations of the study

Strengths of this study include the randomised allocation of treatment, nested design, high follow-up rates, use of various long term outcomes measures, and both plagiocephaly and brachycephaly being studied.
The HEADS trial is the first study to provide evidence from a randomised controlled trial on the long term effectiveness of helmet therapy for skull deformation. The nested design enables us

to determine the generalizability of study outcomes. As well as having anthropometric outcome measures, this study presented parent reported outcomes (for example, subjective assessments and quality of life assessment) and side effects. A high follow-up rate of 94% ensures the power of the study and indicates that the follow-up was not selective.
The use of two outcome measures (oblique diameter difference index and analysis of covariance) could be disputed. However, positional skull deformation usually presents with components of both brachycephaly and plagiocephaly and not just as one type or the other.[2] Moreover, helmets are prescribed for all variations of moderate to severe positional skull deformation, so we therefore included both components of skull deformation.

Limitations of this study include the difference of severity of skull deformation at baseline between both arms of the trial, a low participation rate, limited generalisability of study results to specific subgroups of infants, and no assessment of daily wearing time of the helmet.
Despite between group differences in the baseline clinical characteristics at randomization, this was tackled using the planned analysis of covariance for the comparison of mean differences. The improvement assessed by anthropometric measurements showed no differences at 24 months, yet the parents of infants in the helmet therapy group showed slightly higher satisfaction scores and lower anxiety levels. This might be explained by the fact that simply offering treatment may reassure parents.
The parents of 21% of eligible infants agreed to participate in the trial. Participating parents had a lower level of education than non-participating parents. It has been described before that parents with a higher level of education might have stronger preferences for treatment and are thereby less likely to agree with randomisation.[44, 45]
Another limitation of the study is that the results concern infants with moderate to severe skull deformation and therefore are not generalisable to cases of very severe skull deformation. We decided to exclude very severe cases, since we expected selection bias on the basis of severity of the deformation and selective loss to follow-up in infants with very severe skull deformation who would have been allocated to the natural course. Eventually, only 29/432 (7%) of infants who were eligible for helmet therapy at age 5 months were excluded on the basis the severity of skull deformation. Results are also not generalisable to infants with an underlying congenital condition or muscular torticolllis, or infants who were born preterm. Inclusion of infants born preterm would have complicated the treatment protocol and the interpretation of outcomes. The prevalence of positional skull deformation in infants born preterm is high, but the natural course seems favourable.[46] Additionally, in infants born preterm the corrected age has to be used for the start of treatment and outcome measurements, which would have complicated interpretation and the generalisability of study outcomes.
A final limitation is that we were not able to study the exact wear time of the helmet. However, in this pragmatic study we wanted to study the effect of helmet therapy in routine everyday practice, including parent instructions and regular check-ups to monitor treatment and assess improvements in skull shape.

Strengths and weaknesses in relation to other studies

The various literature reviews suggest that helmet therapy may be more effective in correcting skull deformation in infants aged 6 months than other conservative treatments, but urge the need for evidence from randomised controlled trials.[26, 28, 34, 35, 47] Contrary to the present study, a recent study advocated the use of a helmet for moderate to severe skull deformation. Both this and our study had an equal intervention period: therapy started at 6 months of age and ended at 10 months on average. However, the recent study was a non-randomised study with no blinded assessors, using different time intervals of follow-up and a non-validated outcome measure.[30]

Previous studies often did not comprise long term outcomes and systematic assessment of side effects. One retrospective study described how 22.4% of infants experienced side effects of helmet therapy. This is in contrast with our study, in which side effects were reported in all infants, probably because we used a broader definition of side effects and side effects were self reported by the parents.[48] Additionally, the clinical meaning of the effects of helmet therapy presented in previous studies can be disputed.[34] In the present study we defined a clinically meaningful difference as 4 oblique diameter difference index points or 5 craniproportional index points, consistent with one level of severity in skull deformation according to plagiocephalometry criteria (Figure 2). We chose this cut-off point based on expert opinion, and it should represent a difference that is clinically visible. Both our randomised study design and its focus on clinically meaningful differences, rather than just significant differences, are strengths of this study compared with previous studies.

In both arms of this study, brachycephaly showed a more favourable course of recovery than plagiocephaly. A cohort study of 129 infants with skull deformation at age 6 months showed comparable results at age 4 years when the natural course was awaited: the improvement in plagiocephaly (oblique cranial length ratio at age 6 months: 108.6 (SD 3.3); age 4 years: 105.4 (SD 2.6)) is almost equal to the mean change score at age 5 months to 24 months of the natural course group (oblique diameter difference index 3.1 (SD 3.3)) in the present study. The improvement of brachycephaly (cephalic index at age 6 months: 92.6 (SD 6.6); age 4 years: 87.0 (SD 4.7)) is also in line with findings in the natural course group in the present study (change score on craniproportional index from 5 months to 24 months 6.8 (SD 4.4)).[21]
Finally, interpreting parent reported outcomes can be difficult. As in other studies, the objective outcomes in this study did not match the subjective assessments.[27, 49, 50] Non-clinical factors may be as important as clinical factors in assessement of satisfaction.[51]

Practice implications

This study indicates that helmet therapy has no added value in the treatment of moderate to severe skull deformation in healthy infants. A cost study performed in both arms of the present study, parallel to the HEADS effectiveness study, showed that the total costs per infant treated with a helmet were substantially higher (n=20, €1401; £1157; $1935) than for infants in whom the natural course of skull deformation was awaited (n=14, €157).[52] Based on the equal effectiveness of helmet therapy compared with the natural course, the high prevalence of side effects and the high costs of treatment, we discourage the use of helmet therapy as a standard treatment for healthy infants with moderate to severe skull deformation. Outcomes are expected to hold for all types of custom-made helmets comprising a rigid plastic shell with a foam lining that are designed to fit snugly over the infant's head and leaving room for skull growth at the flattened area.

This conclusion is therefore likely to affect decisions of parents, policymakers, insurance companies, and a wide range of clinicians such as paediatricians, general practitioners, youth healthcare professionals, paediatric physiotherapists, orthotists, paediatric neurosurgeons, and craniofacial surgeons internationally.

Our study also indicated that 75% of infants continued to have some degree of skull deformation at 2 years of age, mainly the plagiocephalic component. Skull deformation does not completely resolve in all cases by natural course, and helmet therapy does not seem to have an added value for recovery. Therefore we emphasise the importance of prevention, early detection and early treatment with paediatric physiotherapy of skull deformation.[22, 35, 47] Additionally, our cutoff points for normal head shape might be rigid in comparison with others.[2, 53] Therefore, the 75% of infants with persisting skull deformation in the present study could be an overestimation of the prevalence of the condition at an older age. It remains arguable what an acceptable head shape is in young infants and at an older age when the head is covered with hair.

Unanswered questions and future research

This is the first randomised controlled trial on helmet therapy in infants with positional skull deformation. Although we conclude no significant difference, this study was not powered for equivalence. Ideally, the study should be repeated with an adequate sample size to confirm the non-inferiority of helmet therapy. However, we question whether aiming for another randomised controlled trial will be realistic since helmet therapy is not reimbursed in most countries. Results from the HEADS non-randomised controlled trial will be presented in the near future and might provide additional evidence to set next to the results of the present randomised controlled trial. Future research should determine the effects of helmet therapy in very severe skull deformation.

REFERENCES

1. Boere-Boonekamp MM, van der Linden-Kuiper LT. Positional preference: prevalence in infants and follow-up after two years. *Pediatrics.* 2001;107(2):339-343.

2. Meyer-Marcotty P, Bohm H, Linz C, et al. Spectrum of positional deformities - Is there a real difference between plagiocephaly and brachycephaly? *J. Craniomaxillofac. Surg.* 2014.

3. Argenta L, David L, Thompson J. Clinical classification of positional plagiocephaly. *J. Craniofac. Surg.* 2004;15(3):368-372.

4. Clarren SK. Plagiocephaly and torticollis: etiology, natural history, and helmet treatment. *J. Pediatr.* 1981;98(1):92-95.

5. Mulliken JB, Vander Woude DL, Hansen M, LaBrie RA, Scott RM. Analysis of posterior plagiocephaly: deformational versus synostotic. *Plast. Reconstr. Surg.* 1999;103(2):371-380.

6. Collett BR, Gray KE, Starr JR, Heike CL, Cunningham ML, Speltz ML. Development at age 36 months in children with deformational plagiocephaly. *Pediatrics.* 2013;131(1):e109-115.

7. Hutchison BL, Stewart AW, Mitchell EA. Characteristics, head shape measurements and developmental delay in 287 consecutive infants attending a plagiocephaly clinic. *Acta Paediatr.* 2009;98(9):1494-1499.

8. Kennedy E, Majnemer A, Farmer JP, Barr RG, Platt RW. Motor development of infants with positional plagiocephaly. *Phys Occup Ther Pediatr.* 2009;29(3):222-235.

9. Kordestani RK, Panchal J. Neurodevelopment delays in children with deformational plagiocephaly. *Plast. Reconstr. Surg.* 2006;118(3):808-809; author reply 809-810.

10. Collett B, Breiger D, King D, Cunningham M, Speltz M. Neurodevelopmental implications of "deformational" plagiocephaly. *J. Dev. Behav. Pediatr.* 2005;26(5):379-389.

11. Steinbok P, Lam D, Singh S, Mortenson PA, Singhal A. Long-term outcome of infants with positional occipital plagiocephaly. *Childs Nerv. Syst.* 2007;23(11):1275-1283.

12. Argenta LC, David LR, Wilson JA, Bell WO. An increase in infant cranial deformity with supine sleeping position. *J. Craniofac. Surg.* 1996;7(1):5-11.

13. de Jonge GA, Engelberts AC, Koomen-Liefting AJ, Kostense PJ. Cot death and prone sleeping position in The Netherlands. *BMJ.* 1989;298(6675):722.

14. Dwyer T, Ponsonby AL, Blizzard L, Newman NM, Cochrane JA. The contribution of changes in the prevalence of prone sleeping position to the decline in sudden infant death syndrome in Tasmania. *JAMA.* 1995;273(10):783-789.

15. Fleming PJ, Gilbert R, Azaz Y, et al. Interaction between bedding and sleeping position in the sudden infant death syndrome: a population based case-control study. *BMJ.* 1990; 301(6743):85-89.

16. Kane AA, Mitchell LE, Craven KP, Marsh JL. Observations on a recent increase in plagiocephaly without synostosis. *Pediatrics.* 1996;97(6 Pt 1):877-885.

17. Turk AE, McCarthy JG, Thorne CH, Wisoff JH. The "back to sleep campaign" and deformational plagiocephaly: is there cause for concern? *J. Craniofac. Surg.* 1996;7(1):12-18.

18. American Academy of Pediatrics Task Force on Infant Sleep Positioning and SIDS. Positioning and SIDS. *Pediatrics.* 1992;89(6 Pt 1):1120-1126.

19. Hutchison BL, Hutchison LA, Thompson JM, Mitchell EA. Plagiocephaly and brachycephaly in the first two years of life: a prospective cohort study. *Pediatrics.* 2004;114(4):970-980.

20. van Vlimmeren LA, van der Graaf Y, Boere-Boonekamp MM, L'Hoir MP, Helders PJM, Engelbert RHH. Risk Factors for Deformational Plagiocephaly at Birth and at 7 Weeks of Age: A Prospective Cohort Study. *Pediatrics.* 2007;119(2):e408-e418.

21. Hutchison BL, Stewart AW, Mitchell EA. Deformational plagiocephaly: a follow-up of head shape, parental concern and neurodevelopment at ages 3 and 4 years. *Arch. Dis. Child.* 2010;96(1):85-90.

22. van Vlimmeren LA, van der Graaf Y, Boere-Boonekamp MM, L'Hoir MP, Helders PJ, Engelbert RH. Effect of pediatric physical therapy on deformational plagiocephaly in children with positional preference: a randomized controlled trial. *Arch. Pediatr. Adolesc. Med.* 2008;162(8):712-718.

23. Nederlands Centrum Jeugdgezondheid. *JGZ-richtlijn Preventie, signalering en aanpak van voorkeurshouding en schedelvervorming.* Utrecht: TNO innovation for life;2012.

24. Cabrera-Martos I, Valenza MC, Benitez-Feliponi A, Robles-Vizcaino C, Ruiz-Extremera A, Valenza-Demet G. Clinical profile and evolution of infants with deformational plagiocephaly included in a conservative treatment program. *Childs Nerv. Syst.* 2013;29(10):1893-1898.

25. Persing J, James H, Swanson J, Kattwinkel J, Comm Practice Ambulatory M. Prevention and management of Positional skull deformities in infants. *Pediatrics.* 2003;112(1):199-202.

26. Flannery AB, Looman WS, Kemper K. Evidence-based care of the child with deformational plagiocephaly, part II: management. *J. Pediatr. Health Care.* 2012;26(5):320-331.

27. Kluba S, Kraut W, Reinert S, Krimmel M. What is the optimal time to start helmet therapy in positional plagiocephaly? *Plast. Reconstr. Surg.* 2011;128(2):492-498.

28. Xia JJ, Kennedy KA, Teichgraeber JF, Wu KQ, Baumgartner JB, Gateno J. Nonsurgical treatment of deformational plagiocephaly: a systematic review. *Arch. Pediatr. Adolesc. Med.* 2008;162(8):719-727.

29. Statistics Netherlands. Population; sex, age, origin and generation, 1 January. 2013; http://statline.cbs.nl/StatWeb/publication/?VW=T&DM=SLEN&PA=37325eng&D1=0-2&D2=0&D3=0&D4=0&D5=0-1,3-4,139,145,210,225&D6=4,9,(l-1)-l&HD=090611-0858&LA=EN&HDR=G3,T&STB=G5,G1,G2,G4. Accessed 13-11-2013.

30. Kluba S, Kraut W, Calgeer B, Reinert S, Krimmel M. Treatment of positional plagiocephaly - Helmet or no helmet? *J. Craniomaxillofac. Surg.* 2014 (in press).

31. Lipira AB, Gordon S, Darvann TA, et al. Helmet versus active repositioning for plagiocephaly: a three-dimensional analysis. *Pediatrics.* 2010;126(4):e936-945.

32. Loveday BP, de Chalain TB. Active counterpositioning or orthotic device to treat positional plagiocephaly? *J. Craniofac. Surg.* 2001;12(4):308-313.

33. Vles JS, Colla C, Weber JW, Beuls E, Wilmink J, Kingma H. Helmet versus nonhelmet treatment in nonsynostotic positional posterior plagiocephaly. *J. Craniofac. Surg.* 2000;11(6):572-574.

34. Goh JL, Bauer DF, Durham SR, Stotland MA. Orthotic (helmet) therapy in the treatment of plagiocephaly. *Neurosurg. Focus.* 2013;35(4):E2.

35. Robinson S, Proctor M. Diagnosis and management of deformational plagiocephaly. *J. Neurosurg. Pediatr.* 2009;3(4):284-295.

36. van Wijk RM, Boere-Boonekamp MM, Groothuis-Oudshoorn CG, van Vlimmeren LA, IJzerman MJ. HElmet therapy Assessment in infants with Deformed Skulls (HEADS): protocol for a randomised controlled trial. *Trials.* 2012;13:108.

37. van Adrichem LNA, van Vlimmeren LA, Cadanova D, et al. Validation of a simple method for measuring cranial deformities (Plagiocephalometry). *J. Craniofac. Surg.* 2008;19(1):15-21.

38. van Vlimmeren LA, Takken T, van Adrichem LN, van der Graaf Y, Helders PJ, Engelbert RH. Plagiocephalometry: a non-invasive method to quantify asymmetry of the skull; a reliability study. *Eur. J. Pediatr.* 2006;165(3):149-157.

39. Piper MC, Pinnell LE, Darrah J, Maguire T, Byrne PJ. Construction and validation of the Alberta Infant Motor Scale (AIMS). *Can. J. Public Health.* 1992;83 Suppl 2:S46-50.

40. Bayley N. *Manual for the Bayley Scales of Infant and Toddler Development* 3rd ed. San Antonio, TX: Psychological Corp; 2006.

41. van der Ploeg HM, Defares PB, Spielberger CD. *Handleiding bij de Zelf-Beoordelings Vragenlijst, ZBV: Een Nederlandstalige bewerking van de Spielberger State-Trait Anxiety Inventory*. Lisse: Swets & Zeitlinger; 1980.

42. Landgraf JM, Vogel I, Oostenbrink R, van Baar ME, Raat H. Parent-reported health outcomes in infants/toddlers: measurement properties and clinical validity of the ITQOL-SF47. *Qual. Life Res.* 2013;22(3):635-646.

43. Mindell JA, Kuhn B, Lewin DS, Meltzer LJ, Sadeh A. Behavioral treatment of bedtime problems and night wakings in infants and young children. *Sleep.* 2006;29(10):1263-1276.

44. Harth SC, Thong YH. Sociodemographic and motivational characteristics of parents who volunteer their children for clinical research: a controlled study. *BMJ.* 1990;300(6736):1372-1375.

45. Rovers MM, Straatman H, Ingels K, van der Wilt GJ, van den Broek P, Zielhuis GA. Generalizability of trial results based on randomized versus nonrandomized allocation of OME infants to ventilation tubes or watchful waiting. *J. Clin. Epidemiol.* 2001;54(8):789-794.

46. Nuysink J, Eijsermans MJ, van Haastert IC, et al. Clinical course of asymmetric motor performance and deformational plagiocephaly in very preterm infants. *J. Pediatr.* 2013; 163(3):658-665 e651.

47. Bialocerkowski AE, Vladusic SL, Howell SM. Conservative interventions for positional plagiocephaly: a systematic review. *Dev. Med. Child Neurol.* 2005;47(8):563-570.

48. Wilbrand JF, Wilbrand M, Malik CY, et al. Complications in helmet therapy. *J. Craniomaxillofac. Surg.* 2012;40(4):341-346.

49. Feijen M, Schuckman M, Habets E, van der Hulst R. Positional plagiocephaly and brachycephaly: is there a correlation between subjective and objective assessment of cranial shape? *J. Craniofac. Surg.* 2012;23(4):998-1001.

50. Katzel EB, Koltz PF, Sbitany H, Emerson C, Girotto JA. Real versus perceived improvements of helmet molding therapy for the treatment of plagiocephaly. *Plast. Reconstr. Surg.* 2010;126(1): 19e-21e.

51. Suarez-Almazor ME, Conner-Spady B, Kendall CJ, Russell AS, Skeith K. Lack of congruence in the ratings of patients' health status by patients and their physicians. *Med. Decis. Making.* 2001;21(2):113-121.

52. van der Ploeg CBP, Van Wijk RM, van den Akker EM, Boere-Boonekamp MM. *Cost assessment of helmet treatment compared to natural course in infants with skull deformation.* Leiden: TNO;2013.

53. Hutchison BL, Hutchison LA, Thompson JM, Mitchell EA. Quantification of plagiocephaly and brachycephaly in infants using a digital photographic technique. *Cleft Palate. Craniofac. J.* 2005;42(5):539-547.

CHAPTER 6

Non-controlled study confirms previous findings of an RCT into helmet therapy in skull deformation

This chapter has been submitted as: van Wijk RM, Groothuis-Oudshoorn CG, van Vlimmeren LA, IJzerman MJ, Boere-Boonekamp MM. Non-controlled study confirms previous findings of an RCT into helmet therapy in skull deformation.

ABSTRACT

Introduction – A recent RCT concluded no benefit of helmet therapy to natural course in infants with positional skull deformation (plagiocephaly and/or brachycephaly). This study compares outcomes a parallel non-randomized controlled trial (nRCT) to the outcomes of the RCT. The objective is to draw conclusions about the effects of helmet therapy using data of both sources to improve external validity.

Methods – A prospective study in which a nested RCT (n=84, random allocation) and a parallel nRCT (n=294, treatment of preference) were incorporated, studying the effect of helmet therapy compared to natural course in healthy infants 5 to 6 months old with moderate or severe skull deformation. Treatment effects in the RCT and nRCT were compared separately at 12 and 24 months. The effects of helmet therapy were studied in a combined dataset with imputed data of both the RCT and nRCT using multiple linear regression analysis.

Results – Comparable outcomes were found in both studies. Helmet therapy was not significantly related to the change score in the combined dataset (plagiocephaly p=.18, brachycephaly p=.15). Baseline severity of deformation was the only significant predictor for change score (plagiocephaly B=0.54, 95%CI=0.44 to 0.63, p<.01; brachycephaly B=0.43, 95%CI=0.37 to 0.49, p<.01).

Conclusions – This real-world non-randomized controlled study confirms the findings of a previous RCT concluding helmet therapy not to produce clinically meaningful additional benefit. The use of helmet therapy in healthy infants with moderate or severe positional skull deformation is discouraged. The design chosen in HEADS may be recommended for future studies comparing RCT data with real-world data.

INTRODUCTION

Infants with positional skull deformation are frequently treated with an orthotic helmet.[1-5] Helmet therapy is a preference sensitive treatment since there is no medical argument for treatment: skull deformation is generally considered as a cosmetic condition in which the young infants' malleable skull deforms as a result of prolonged external forces. The cosmetic nature of the condition and free availability of treatment in the Netherlands made that subjective measures as 'parental (dis)satisfaction with the infant's appearance' and '(high) expectations of the helmet therapy' are the most important predictors for the decision for treatment.[6] The HEADS (HElmet therapy Assessment in Deformed Skulls) RCT concluded that helmet therapy has no added value compared to awaiting natural recovery in infants with positional skull deformation.[7]

Randomized controlled trials (RCTs) are widely accepted as the gold standard in comparative effectiveness research.[8, 9] The random allocation and concealment of treatments reduce bias, making the RCT the most reliable design to determine the exact treatment effects. By minimizing the possibility of bias, the internal validity of these studies is ensured. However, the generalizability of study outcomes may be limited.[10] Before outcomes from RCTs can be implemented, it is necessary to determine whether the results are valid in clinical practice and to whom the results apply.[11] In the debate about pros and cons of RCTs versus observational studies, it is advised to study non-participants parallel to an RCT, to compare outcomes and asses the generalizability of the RCT.[12-14] In addition, a medical decision taken after consulting parents for their preferences could possibly yield better therapy adherence and thereby a larger effect size than in an RCT. In order to address these issues, investigators have proposed alternative trial designs and other approaches using real-world data to estimate the effect once implemented in medical practice.[15-18] We expect better treatment compliance in a non-randomized controlled trial (nRCT), which could lead to better outcomes, however based on the results of the pragmatic RCT showing no effect of helmet therapy we hypothesize that treatments effect will be similar in both studies.

METHODS

Study design, setting and participants

The HEADS study is a two-armed pragmatic RCT nested in a prospective cohort study (Figure 1). In parallel to the RCT a non-randomized controlled trial (nRCT) was conducted. The study was designed to include all infants eligible for helmet therapy in pediatric physical therapy practices in the east of the Netherlands between July 2009 and July 2011. Seventy specially trained pediatric physical therapists (PPTs) recruited infants with moderate or severe skull deformation

(plagiocephaly—unilateral flattening, brachycephaly—symmetrical flattening, or both), who were 5 to 6 months old and born after 36 weeks gestation, and who had no congenital muscular torticollis, craniosynostosis and/or dysmorphic features, were eligible for the study. The severity of skull deformation in the transversal plane was determined using plagiocephalometry's Oblique Diameter Difference Index (ODDI) for plagiocephaly and Cranio Proportional Index (CPI) for brachycephaly (Figure 2) as described before.[19-21] Infants with moderate or severe skull deformation were included: ODDI was ≥ 108% or CPI was ≥ 95% mixed forms (ODDI ≥106% and CPI ≥ 92%). Infants with very severe skull deformation were excluded (ODDI >113% or CPI > 104%). A more detailed description of the study design of the HEADS study was published previously.[7, 21]

The Medical Ethics Committee of Medisch Spectrum Twente Hospital, Enschede, the Netherlands, granted ethical approval for this study on January 8, 2009 (ref: NL24352.044.08).

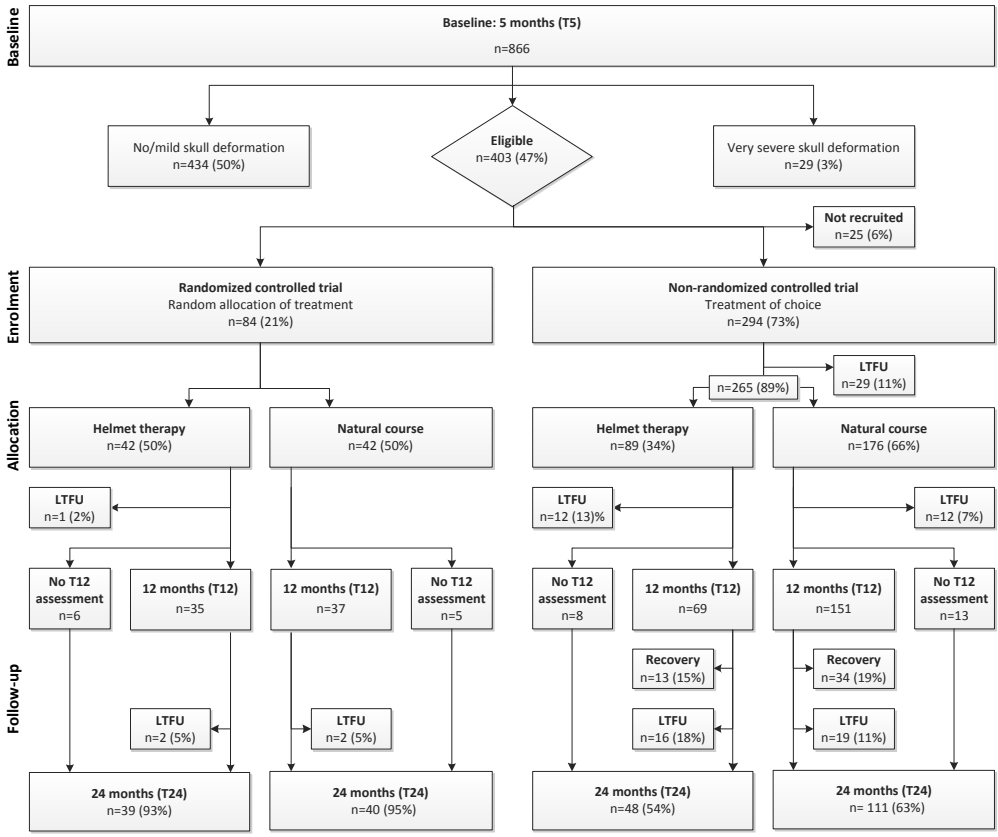


Figure 1. Flowchart of the HElmet therapy Assessment in Deformed Skulls study

Recruitment and follow-up

Parents of 84 eligible infants (21%) gave informed consent for the RCT and were randomly allocated to the helmet therapy arm (n=42) or the natural course arm (n=42). Subsequently, 294 eligible infants whose parents did not wish to enroll in the RCT were included in the nRCT (73%). After consent, 29 of 294 infants (10%) were lost to follow-up (LTFU) and consequently no treatment decision could be determined. The infants LTFU did not differ from the nRCT participants on baseline variables, except for health problems (nRCT: 36/259, 14%; non-participants 0/28, 0%; p=.04). Participants of the nRCT could start a preferred treatment, which is in practice limited to awaiting natural course (n=176, 66%) or helmet therapy (n=89, 34%).
Participants of the RCT and nRCT were followed-up at 12 and 24 months of age (Figure 1), and at 8 months parents filled out a questionnaire. Infants in the nRCT who presented with full recovery (no skull deformation, Figure 1) at T12 were discharged from further follow-up, since no deterioration of the skull shape was expected.

Treatment

Treatment modalities

In this study the effects of helmet therapy were compared to the effects of natural course in infants with positional skull deformation. In The Netherlands helmet therapy is typically started when infants are 5 to 6 months of age, helmets were supposed to be used for 23 hours/day until 12 months of age or until obtaining satisfying outcomes according to both parents and professionals. Orthotists regularly monitored the infants for signs of pressure spots, and the helmet was modified or replaced to accommodate skull growth as necessary. The treatment was always supervised by a (pediatric) doctor. During the time of this study, the cost of helmet therapy was reimbursed by Dutch health insurance companies.
The natural course group did not receive helmet therapy and natural skull growth was monitored. As healthy infants show symmetry in posture at 5-6 months of age[22, 23], no effects of (continued) pediatric physical therapy can be expected after this age.

Group allocation RCT

After inclusion for the RCT, infants were randomized by using a computer-generated randomization plan with blocks of eight.[7, 21] Parents of infants allocated to the helmet therapy group were asked to make an appointment at one of the four collaborating institutes to obtain a custom-made helmet. In our study only experienced orthotists provided helmet therapy. Two types of helmets were studied. One type is from the largest helmet manufacturer of the Netherlands with over 15 years of experience and a production of over 2000 helmets a year producing helmets formed as a solid whole, with several inner layers. The other type of a second manufacturer consists of two 'half-shells' connected by a 'hinge' and the fit can be adjusted by Velcro-strap fastening. Both

helmets work according the same mechanism: custom-made helmets, comprising a rigid plastic shell with foam lining that are designed to fit snugly over the infant's head and leaving room for skull growth at the flattened area.

Group allocation nRCT

In the nRCT, parents were free to start either option natural course or helmet therapy, at an institute of choice. Of the parents who chose for helmet therapy only three chose for another helmet manufacturer than the RCT companies.

Outcome measures

63 PPTs performed measurements at T5 and T12. Six of the PPTs performed the blinded assessments at T24 in all infants from February 2011 until March 2013. Assessments included anthropometric measurements of the shape of the skull, a motor assessment, and a parental questionnaire.

Baseline (T5)

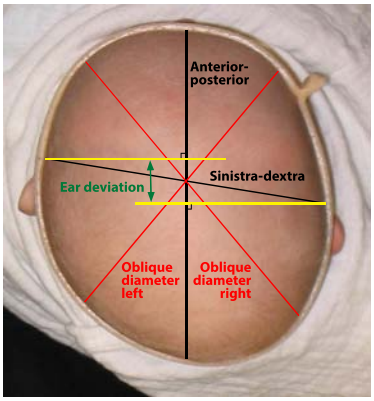
A parental questionnaire was used to gather information on background characteristics and parent-reported outcomes at baseline.
Furthermore the qualitative gross motor movement repertoire was assessed by a PPT using the Alberta Infant Motor Scale (AIMS), a valid, norm-referenced measurement.[24]

Therapy compliance

The T12 questionnaire was used to assess whether parents were compliant with the therapy to which their infant was allocated: the age of the infant when parents decided to discontinue therapy and additional therapies during the intervention period. Furthermore, parents were asked three questions whether the helmet rotated, shifted or came off spontaneously (frequency: several times a day – few times a day – few times a week – never). We scored 'fitting issues' when parents would cross anything else but 'never' on one of the three questions at either the 8-months or 12-months assessment.

Primary outcome (T24)

The primary outcome was the anthropometric measurement of the skull shape using the change score (T5 minus T24) of plagiocephalometry's ODDI for plagiocephaly and CPI for brachycephaly.[19, 20] A difference in change score of 4 ODDI points or 5 CPI points was considered a relevant difference between groups, consistent with one level of severity in skull deformation according to plagiocephalometry criteria (Figure 2). Additionally, the number of infants fully recovered (no skull deformation, Figure 2) was reported.[21]



	ODDI (%)		CPI (%)
Normal shape	<104	and	<90
Mild deformation	104 - 107	or	90 - 94
Moderate deformation	108 - 111	or	95 - 99
Severe deformation	≥ 112	or	≥ 100

Figure 2. Plagiocephalometry and cutoff points for severity of skull deformation
Illustration shows left occipital flattening of skull and thermoplastic measuring ring with digitally drawn lines used in plagiocephalometry. Indices were calculated by the following formulas: craniproportional index (CPI), sinistra-dextra/anterior-posterior×100%; oblique diameter difference index (ODDI), longest oblique diameter/shortest oblique diameter×100%; and ear deviation index, ear deviation/anterior-posterior×100%

Secondary outcome

Parental satisfaction was used as secondary outcome at T24. Parental satisfaction with their infant's head shape was assessed in the parental questionnaire using a five-point Likert scale ranging from '1 – not satisfied at all' to '5 – very satisfied'.

Side effects

The questionnaires at 8 and 12 months contained questions about side effects associated with helmet therapy. Furthermore, in both groups at 8 months parents were asked about the number of hours their baby cried a day and whether their baby had sleep problems (taking more than 20 minutes to fall asleep (daily), or waking more than once every night).

Statistical analyses

The sample size of the RCT of the HEADS study was calculated at 72 (36 in each arm), based on a significance level of 5%, a power of 90% and a difference in mean improvement of at least 4 ODDI points (SD 6 ODDI points).

We described and compared background and baseline clinical characteristics of the sample for three groups based on the decision of parents; 1) infants of parents who consented with randomization, 2) infants of parents who decided to start helmet therapy, and 3) infants of parents who chose to await natural recovery.

Change score in plagiocephaly (ODDI), change score in brachycephaly (CPI), parental satisfaction and achieving full recovery were used for outcome analysis at 12 months and 24 months, and compared between both treatment groups with analysis of covariance (ANCOVA) using baseline

values (T5) as the covariate, or using the chi-square test. The RCT groups were analyzed on an intention-to-treat basis.
Next, in infants who were measured at the T12 and the T24 assessment, or one of both, all variables with one or more missing values were imputed under fully conditional specification based on all relevant variables, resulting in 20 complete though different datasets.[25] Outcome analysis was repeated for each imputed dataset and combined using Rubin's rules at T24.
Finally, we tested the effect of helmet therapy compared to natural course in the imputed datasets of the RCT and nRCT together (combined dataset), controlling for baseline skull shape, gender, parental level of education, study design, the interaction of study design and treatment. Data analysis was performed using IBM SPSS Statistics for Windows version 21.0 (IBM Corp, Armonk, New York) and a level of significance of 0.05 was used.

RESULTS

In the RCT one of 84 infants (2%) was LTFU after inclusion, in the nRCT this were 25 of 294 infants (9%). At T24, 79 of 84 included infants in the RCT (94%) were followed up, compared to 206 (followed-up at T24: n=159; discharged at T12 because of full recovery: n=47) of 294 (70%) in the nRCT (Figure 1).

Study population

The only significant difference between the three groups of participants ($p<.05$) was the parental satisfaction with their infant's head shape. Parents who chose to start helmet therapy had the lowest level of satisfaction (2.2, SD 0.9), and parents who chose to await natural recovery the highest (3.4, SD 1.0). Parents who consented with randomization had a mean satisfaction score of 2.9 (0.9).

Outcomes per study design

The original data of the T12 (n=292) and T24 (n=238) assessment are presented and compared between groups within each study in Table 2. Although statistically significant differences were found in the original datasets, none of these represent clinically meaningful difference (e.g. a 4 point difference in ODDI or a 5 point difference in CPI between the two groups).

Comparable differences were determined in the imputed T24 data (n=324) (Table 3): a slightly higher adjusted parental satisfaction score in the helmet therapy group in the RCT compared to natural course (mean difference 0.3, 95% confidence interval [CI] 0.0 to 0.5), a higher adjusted plagiocephaly change score in the helmet therapy group in the nRCT compared to natural course (0.9, 95% CI 0.0 to 1.9), but a lower brachycephaly change score (-1.2, 95% CI -2.2 to -0.2).

Table 1. Demographic and baseline clinical characteristics. Values are means (standard deviation) unless stated otherwise*

	RCT	nRCT		
	(n=84)	Helmet therapy (n=89)	Natural Course (n=176)	*p*
No (%) boys	61/84 (73)	59/88 (67)	113/174 (65)	.47
Age at baseline (months)	5.1 (0.4)	5.1 (0.3)	5.1 (0.3)	.39
Age at follow-up (months)	24.8 (4.4)	25.1 (3.8)	25.4 (4.9)	.69
No (%) birth rank (first born)	39/79 (49)	37/86 (43)	96/173 (56)	.16
No (%) with health problems†	6/84 (7)	12/88 (14)	24/171 (14)	.26
No (%) ethnicity (ethnic minority)‡	5/77 (7)	4/81 (5)	16/160 (10)	.34
No (%) education level of parents§				.07
Low	24/81 (30)	14/87 (16)	31/174 (18)	
Medium	34/81 (42)	35/87 (40)	67/174 (39)	
High	23/81 (28)	38/87 (44)	76/174 (44)	
Plagiocephaly (ODDI)	108.2 (3.6)	108.2 (3.9)	107.5 (3.2)	.16
Brachycephaly (CPI)	91.8 (6.7)	93.2 (7.2)	91.3 (6.6)	.09
Motor development (AIMS Z-score), n=327	-0.6 (1.0)	-0.8 (0.9)	-0.8 (0.9)	.50
Parental satisfaction, n=343	2.9 (0.9)	2.2 (0.9)	3.4 (1.0)	<.001

*Groups were compared using the One way Independent ANOVA or chi-square test.
†Problems with sight, hearing, esophageal reflux, developmental dysplasia of the hip, congenital heart disease, or inguinal hernia.
‡At least one parent born outside of The Netherlands.
§Low education level: lower technical and vocational education and lower general secondary education; Medium education level: intermediate vocational education and advanced secondary eduction; and High educational level: higher vocational education and university.
ODDI = Oblique Diameter Difference Index. A value of 100% represents a purely symmetric head shape. A value above 100 represents asymmetric skull deformation; the higher the score, the more severe the deformation. CPI = Cranial Proportional Index. A score of 80% represents an average head shape in Western countries. A higher value represents a larger width of the head, compared to the length. AIMS= Alberta Infant Motor Scale standardized z-scores (individual score minus the average score divided by standard deviation).

Table 2. Outcomes measured at 12 and 24 months using original data. Values are adjusted means (95% CI) unless stated otherwise

	12 months (n=292)			24 months (n=238)		
	Helmet Therapy	Natural Course		Helmet Therapy	Natural Course	
RCT	n=35	n=37	*p*	n=39	n=40	*p*
Plagiocephaly Change score*	3.7 (2.9 to 4.5)	2.3 (1.5 to 3.1)	.02	3.4 (2.6 to 4.2)	2.6 (1.8 to 3.4)	.13
Brachycephaly Change score*	4.4 (3.1 to 5.6)	5.5 (4.3 to 6.7)	.22	6.4 (5.3 to 7.5)	7.4 (6.4 to 8.5)	.20
No (%) with full recovery †	9 (26)	7 (19)	.49	10 (26)	9 (23)	.74
Parental satisfaction‡	4.6 (4.4 to 4.8)	4.0 (3.8 to 4.2)	<.001	4.7 (4.5 to 4.8)	4.4 (4.2 to 4.6)	.03
nRCT	n=69	n=151	*p*	n=48	n=111	*p*
Plagiocephaly Change score*	3.0 (2.3 to 3.6)	2.3 (1.8 to 2.7)	.08	3.9 (3.1 to 4.6)	2.6 (2.1 to 3.1)	.01
Brachycephaly Change score*	3.8 (2.9 to 4.6)	4.5 (3.9 to 5.0)	.15	5.9 (5.0 to 6.8)	7.2 (6.6 to 7.8)	.02
No (%) with full recovery†	13 (19)	34 (23)	.54	12 (25)	35 (32)	.40
Parental satisfaction*	4.3 (4.1 to 4.5)	4.2 (4.1 to 4.4)	.49	4.4 (4.2 to 4.6)	4.2 (4.1 to 4.4)	.19

Plagiocephaly change score: oblique diameter difference index at T5 minus T12 and T5 minus T24.
Brachycephaly change score: cranial proportional index at T5 minus T12 and T5 minus T24.
Full recovery: oblique diameter difference index < 104% and cranial proportional index < 90%
* ANCOVA model with baseline measurement at T5 as covariate.
† Groups were compared using the chi-square test.
‡ Groups were compared using the *t*-test.

Combined study results: imputed data of RCT and nRCT together

Treatment was not significantly related to the change score in the combined, imputed dataset (n=323), for both plagiocephaly (ODDI) and brachycephaly (CPI (Table 4). The baseline values showed to be the only variables to be related to the skull shape change score. Each point higher on the baseline ODDI meant 0.5 point more improvement in change score; for CPI this was 0.4.

Table 3. Outcomes at T24 using imputed data (n=324). Values are adjusted means (95% CI) unless stated otherwise

	Helmet Therapy	Natural Course		Helmet therapy – Natural course
RCT	n=41	n=42	*p*	95% CI
Plagiocephaly Change score*	3.4 (2.6 to 4.2)	2.5 (1.7 to 3.3)	.14	0.9 (-0.3 to 2.0)
Brachycephaly Change score*	6.5 (5.4 to 7.5)	7.6 (6.5 to 8.6)	.16	-1.1 (-2.6 to 0.4)
No (%) with full recovery†	11 (27)	10 (24)	.74	1.2 (0.4 to 3.4)
Parental satisfaction*	4.6 (4.5 to 4.8)	4.4 (4.2 to 4.5)	.03	0.3 (0.0 to 0.5)
nRCT	n=77	n=164	*p*	
Plagiocephaly Change score*	3.7 (2.9 to 4.4)	2.7 (2.3 to 3.2)	.04	0.9 (0.0 to 1.9)
Brachycephaly Change score*	6.3 (5.4 to 7.1)	7.5 (6.9 to 8.1)	.02	-1.2 (-2.2 to -0.2)
No (%) with full recovery†	22 (29)	60 (37)	.33	0.7 (0.3 to 1.5)
Parental satisfaction*	4.4 (4.2 to 4.6)	4.2 (4.1 to 4.4)	.28	0.1 (-0.1 to 0.4)

Plagiocephaly change score: oblique diameter difference index at T5 minus T24.
Brachycephaly change score: cranial proportional index at T5 minus T24
Full recovery: oblique diameter difference index < 104% and cranial proportional index < 90%
* ANCOVA model with baseline measurement at T5 as covariate.
† Groups were compared using univariate logistic regression analysis. Difference presented as odds ratio (95% CI).

Side effects

In the RCT, no significant differences were determined for infant sleep problems (helmet therapy 5/35, 14%; natural course 10/41, 24%), however the nRCT showed differences (helmet therapy 14/54, 26%; natural course 12/104, 12%; p=.02). Both studies showed comparable hours spent crying between groups (RCT: helmet therapy mean 1.4 (SD 1.2); natural course 1.2 (0.9); nRCT helmet therapy 1.0 (0.7); natural course 1.0 (0.8)). Parent-reported side effects of helmet therapy were comparable in both studies (Table 5).

Table 4. Multivariate regression analysis of plagiocephaly (ODDI) and brachycephaly (CPI) change scores, using the combined dataset of the imputed RCT and nRCT data (n=323)

	Plagiocephaly (ODDI)*			**Brachycpehaly (CPI)^**		
	B (95% CI)	SE	P	B (95% CI)	SE	P
Constant	-55.11 (-65.78 to 44.44)	5.43	<.001	-30.94 (-36.49 to 25.38)	2..82	<.001
Treatment (helmet)	0.83 (-0.37 to 2.02)	0.61	.18	-1.06 (-2.49 to 0.38)	0.73	.15
Baseline	0.54 (0.44 to 0.63)	0.05	<.001	0.43 (0.37 to 0.49)	0.03	<.001
Gender (male)	-0.12 (0.85 to 0.61)	0.37	.75	-0.73 (-1.53 to 0.08)	0.41	.08
Level of education						
Low						
Middle	-0.20 (-1.21 to 0.81)	0.51	.69	0.04 (-1.04 to 1.13)	0.55	.08
High	-0.07 (-1.16 to 1.00)	0.55	.89	-0.14 (-1.29 to 1.02)	0.59	.82
Study design (nRCT)	0.46 (-0.48 to 1.40)	0.48	.34	-0.15 (-1.32 to 1.02)	0.60	.80
Study design * Treatment	0.12 (-1.36 to 1.60)	0.75	.87	-0.13 (-1.85 to 1.59)	0.88	.88

* Pseudo (Nagelkerke) R^2 =0.354
^ Pseudo (Nagelkerke) R^2 =0.461

Table 5. Helmet therapy compliance and side effect in the RCT and nRCT. Values are adjusted means (95% CI) unless stated otherwise

	RCT	**nRCT**
Helmet fitting issues	22/30 (73)	48/60 (80)
Mean (SD) satisfaction with fitting helmet (range 1-5)*	3.8 (1.0)	3.8 (1.3)
Mean (SD) age at discontinuation helmet therapy^	10.0 (2.0)	11.1 (1.3)
Side effects	35/35 (100)	79/79 (100)
Problems accepting the helmet	8/33 (24)	4/53 (8)
Skin irritation	32/34 (96)	77/79 (98)
Augmented sweating	34/34 (71)	58/70 (65)
Unpleasant odour of helmet	25/33 (76)	70/73 (96)
Pain associated with helmet	9/27 (33)	11/65 (24)
Feeling hindered from cuddling child	24/31 (77	53/65 (82)

* RCT n=30, nRCT n=67
^ RCT n=34, nRCT n=68

DISCUSSION

This non-randomized controlled study found similar outcomes compared to a parallel randomized controlled trial. The combined sample of imputed RCT and nRCT data showed neither significant, nor clinically meaningful, differences in treatment effects. These results suggest that, even an open label clinical trial where physicians and parents decide about helmet prescription showed no added value of helmet therapy compared to the natural course of skull deformation. The only variable that was significantly related to the improvement in skull deformation was the baseline deformity. More precisely, in infants with more severe skull deformation, more recovery could be expected regardless of the therapy provided. However, the majority of infant did not show full recovery. Still, parents of infants with helmet therapy compared to parents who awaited natural course were equally satisfied with the outcome.

This study was performed in order to generalize from an RCT to real-life where more variation in treatment and subsequent outcomes exists. This study was unique because of the nested design of the study with an nRCT in parallel to a RCT, the high recruitment rate and follow-up, and the assessment of a range of outcome measures.

The nested design enabled us to determine the generalizability of the study population and study outcomes of the RCT. Since the study populations of the RCT and nRCT were rather similar and no influence of study design on treatment outcomes was found, we can use the nRCT data as additional evidence next to the RCT. It also suggests that the pragmatic nature of our RCT ensured the generation of evidence that is relevant for real-world decision making.[26]

Of all eligible infants within the cohort, 94% were recruited for either the RCT or the nRCT. This is high compared to other studies.[14, 27] The HEADS study meets the criteria for a relevant trial for patients: broad recruitment, meaningful outcomes and comparison against best current evidence.[18] These aspects can improve recruitment and retention in trials. Within the RCT 94% of infants were followed-up at 24 months.

A reason to look at real-world data next to an RCT is to provide an estimation of what the therapy encompassed in daily practice, and the effects of it. In the nRCT, treatment decisions are made by physicians and parents together. It has been described that compliance and satisfaction to the treatment are important benefits of shared decision making.[28, 29] We were not able to demonstrate a difference in the parental satisfaction between both studies, but we learned that participants of the nRCT were indeed more compliant to therapy compared to participants of an RCT. Conversely, the follow-up rate was much lower in the nRCT (70%) compared to the RCT (94%). An explanation for the variation in follow-up rates could be that both assessors and researchers were keener to keep RCT participants empowered and committed to the study objectives. Also, the RCT participants might feel they were involved in an important scientific study explaining their commitment. Nevertheless, it can be concluded that the population and clinical outcomes in both studies were almost similar and thus the real-world data can be used to support the RCT in a general population.

From a health economic standpoint, this study was also very informative. As resource utilization in a controlled RCT may not be reflecting true consumption, we were able to estimate the direct and indirect costs of treatment using data from both the RCT and the nRCT. The helmet therapy cost €1401 in the RCT(n=14) and € 1577 in the nRCT (n=49), natural course brought along costs of €157 in the RCT (n=13) and € 177 in the nRCT (n=36).[30] Higher costs in the helmet therapy group of the nRCT can be explained by the higher rate of parents who started other, additional, treatments during the intervention period. Presumably, the lower satisfaction score at baseline of parents choosing for helmet therapy, led to "shopping" to find the proper treatment.
By reporting real-world evidence of the differences in costs, next to a range of other outcome measures, we provide a unique, very comprehensive overview of all aspects of helmet therapy compared to awaiting natural course, which can be used for decision-making.

It would be appealing to state that a real-world and non-controlled study draws the same conclusion as the RCT. However, there were some factors preventing firm conclusions. The follow-up protocol differed for both studies in the HEADS study. In the nRCT infants who presented with full recovery at T12 were discharged from follow-up at T24, since no deterioration of the skull shape was expected. We chose to impute data of all variables with missing data of infants of both the RCT and nRCT who had T12 data or T24 data, or both. Secondly, we aimed to study routine everyday practice intervention in our pragmatic RCT, but we determined a difference in treatment compliance between both studies. Except for treatment compliance, no other differences were determined neither in the contents of both treatment groups, nor in effects.

Conclusions

In this unique nested study design, we compared a range of outcomes measures from an RCT and a parallel non-randomized controlled trial. Even though loss-to-follow up in the nRCT was substantially lower, this real-world study confirms the findings of a previous RCT concluding helmet therapy not to produce additional benefit in infants with positional skull deformation. Baseline severity of deformation was the only significant predictor for change in skull shape.
The nRCT implemented a shared decision made by physicians and parents about starting helmet therapy, thereby increasing compliance with treatment compared to the RCT. However this did not increase the treatment effects. The RCT results can be generalized to the target population of healthy infants of 5 to 6 months old with moderate to severe skull deformation.
Our study excluded a few sub-groups; the effects of helmet therapy for positional skull deformation in these groups still needs to be studied.[7] Furthermore we did not assess a-priori treatment preferences of parents of RCT participants to determine the effects of preferences on outcomes in a randomized study. We recommend researchers of future RCTs studying usual care, to follow-up non-participants as well to compare RCT data with real-world data.

REFERENCES

1. Bialocerkowski AE, Vladusic SL, Howell SM. Conservative interventions for positional plagiocephaly: a systematic review. *Dev. Med. Child Neurol.* 2005;47(8):563-570.
2. Flannery AB, Looman WS, Kemper K. Evidence-based care of the child with deformational plagiocephaly, part II: management. *J. Pediatr. Health Care.* 2012;26(5):320-331.
3. Goh JL, Bauer DF, Durham SR, Stotland MA. Orthotic (helmet) therapy in the treatment of plagiocephaly. *Neurosurg. Focus.* 2013;35(4):E2.
4. Robinson S, Proctor M. Diagnosis and management of deformational plagiocephaly. *J. Neurosurg. Pediatr.* 2009;3(4):284-295.
5. Xia JJ, Kennedy KA, Teichgraeber JF, Wu KQ, Baumgartner JB, Gateno J. Nonsurgical treatment of deformational plagiocephaly: a systematic review. *Arch. Pediatr. Adolesc. Med.* 2008;162(8):719-727.
6. van Wijk RM, van Til JA, Groothuis-Oudshoorn CG, L'Hoir MP, Boere-Boonekamp MM, MJ IJ. Parents' decision for helmet therapy in infants with skull deformation. Childs Nerv Syst. 2014;30(7):1225-1232..
7. van Wijk RM, van Vlimmeren LA, Groothuis-Oudshoorn CG, Van der Ploeg CP, IJzerman MJ, Boere-Boonekamp MM. Helmet therapy in infants with positional skull deformation: randomised controlled trial. *BMJ.* 2014;348:g2741.
8. Abel U, Koch A. The role of randomization in clinical studies: myths and beliefs. *J. Clin. Epidemiol.* 1999;52(6):487-497.
9. Dreyfuss D. Is it better to consent to an RCT or to care? Muetadeltaepsilonnu alphagammaalphanu ("nothing in excess"). *Intensive Care Med.* 2005;31(3):345-355.
10. King M, Nazareth I, Lampe F, et al. Impact of participant and physician intervention preferences on randomized trials: a systematic review. *JAMA.* 2005;293(9):1089-1099.
11. Rothwell PM. External validity of randomised controlled trials: "To whom do the results of this trial apply?". *The Lancet.* 2005;365(9453):82-93.
12. Bower P, King M, Nazareth I, Lampe F, Sibbald B. Patient preferences in randomised controlled trials: conceptual framework and implications for research. *Soc. Sci. Med.* 2005;61(3):685-695.
13. Torgerson DJ, Klaber-Moffett J, Russell IT. Patient preferences in randomised trials: threat or opportunity? *J. Health Serv. Res. Policy.* 1996;1(4):194-197.
14. Rovers MM, Straatman H, Ingels K, van der Wilt GJ, van den Broek P, Zielhuis GA. Generalizability of trial results based on randomized versus nonrandomized allocation of OME infants to ventilation tubes or watchful waiting. *J. Clin. Epidemiol.* 2001;54(8):789-794.
15. Macpherson H. Pragmatic clinical trials. *Complement. Ther. Med.* 2004;12(2-3):136-140.
16. Schwartz D, Lellouch J. Explanatory and pragmatic attitudes in therapeutical trials. *J. Chronic Dis.* 1967;20(8):637-648.
17. Weinstein SL, Dolan LA, Wright JG, Dobbs MB. Design of the Bracing in Adolescent Idiopathic Scoliosis Trial (BrAIST). *Spine (Phila Pa 1976).* 2013;38(21):1832-1841.
18. Mullins CD, Vandigo J, Zheng Z, Wicks P. Patient-Centeredness in the Design of Clinical Trials. *Value Health.* 2014.
19. van Adrichem LNA, van Vlimmeren LA, Cadanova D, et al. Validation of a simple method for measuring cranial deformities (Plagiocephalometry). *J. Craniofac. Surg.* 2008;19(1):15-21.
20. van Vlimmeren LA, Takken T, van Adrichem LN, van der Graaf Y, Helders PJ, Engelbert RH. Plagiocephalometry: a non-invasive method to quantify asymmetry of the skull; a reliability study. *Eur. J. Pediatr.* 2006;165(3):149-157.

21. van Wijk RM, Boere-Boonekamp MM, Groothuis-Oudshoorn CG, van Vlimmeren LA, IJzerman MJ. HElmet therapy Assessment in infants with Deformed Skulls (HEADS): protocol for a randomised controlled trial. *Trials.* 2012;13:108.

22. van Vlimmeren LA, van der Graaf Y, Boere-Boonekamp MM, L'Hoir MP, Helders PJ, Engelbert RH. Effect of pediatric physical therapy on deformational plagiocephaly in children with positional preference: a randomized controlled trial. *Arch. Pediatr. Adolesc. Med.* 2008;162(8): 712-718.

23. Boere-Boonekamp MM, van der Linden-Kuiper LT. Positional preference: prevalence in infants and follow-up after two years. *Pediatrics.* 2001;107(2):339-343.

24. Piper MC, Pinnell LE, Darrah J, Maguire T, Byrne PJ. Construction and validation of the Alberta Infant Motor Scale (AIMS). *Can. J. Public Health.* 1992;83 Suppl 2:S46-50.

25. van Buuren S. *Flexible Imputation of Missing Data*. Boca Raton, FL. : Chapman & Hall/CRC Press; 2012.

26. Roland M, Torgerson DJ. Understanding controlled trials: What are pragmatic trials? *BMJ.* 1998; 316(7127):285.

27. Weinstein SL, Dolan LA, Wright JG, Dobbs MB. Effects of bracing in adolescents with idiopathic scoliosis. *N. Engl. J. Med.* 2013;369(16):1512-1521.

28. Merenstein D, Diener-West M, Krist A, Pinneger M, Cooper LA. An assessment of the shared-decision model in parents of children with acute otitis media. *Pediatrics.* 2005;116(6):1267-1275.

29. Stacey D, Legare F, Col NF, et al. Decision aids for people facing health treatment or screening decisions. *Cochrane Database Syst. Rev.* 2014;1:CD001431.

30. van der Ploeg CBP, Van Wijk RM, van den Akker EM, Boere-Boonekamp MM. *Cost assessment of helmet treatment compared to natural course in infants with skull deformation.* Leiden: TNO;2013.

CHAPTER 7

Why do treatment policies for positional skull deformation differ between the Netherlands and New Zealand?

This chapter has been submitted as: van Wijk RM, Hutchison BL, Boere-Boonekamp MM, Mitchell EA, van Til JA, IJzerman MJ. Why do treatment policies for positional skull deformation differ between the Netherlands and New Zealand?

ABSTRACT

Background – In the Netherlands, helmet therapy is regularly prescribed, while in New Zealand hardly any infants receive helmet therapy. The aim of this study was to increase understanding regarding the difference in treatment policy.

Methods – A self-completed survey in 387 healthcare professionals working with infants in the Netherlands (n=314) or New Zealand (n=73). The questionnaire concerned demographics, experience, beliefs, attitudes and expectations of healthcare professionals regarding natural course of positional skull deformation and helmet therapy.

Results – Consequences of positional skull deformation and helmet therapy in infants younger than 1 year old were perceived as more burdensome by healthcare professionals in New Zealand, compared to the Netherlands. According to healthcare professionals, New Zealand parents are more positive about the natural course than Dutch parents are.

Conclusions – Differences in treatment policy between the Netherlands and New Zealand can be associated with differences in beliefs and attitudes among healthcare professionals in both countries. We speculate that these observations might also relate to differences in the funding model of the health systems, dissimilarity in infants' health status and a contradictory evidence base.

INTRODUCTION

In the 1980s and 1990s, several epidemiological studies found prone sleeping was an important risk factor for Sudden Infant Death Syndrome (SIDS).[1-5] In 1987, the Netherlands was the first country where pediatricians recommended against the prone sleeping position,[6] followed by New Zealand in 1991,[7] with the United States of America and England following soon afterwards.[8] Subsequently, studies started to demonstrate a significant decrease in SIDS cases. This is believed to be directly related to the follow up of the changed sleeping position advice by parents.[9-13]
Now that infants were spending large amounts of time on their backs, many of them developed a skull deformation because of the high malleability and fast growth of the cranium.[14] The prevalence of positional skull deformation (deformational plagiocephaly and brachycephaly) after the 'Back to sleep' campaign increased up to 21.5 % of children younger than six months.[14-16]

Positional skull deformation is generally considered a cosmetic condition. Naturally, parents of young infants with a clearly visible skull deformation fear possible physical or psychological consequences of skull deformation in the short and long-term.[17, 18] The preferred strategy to prevent or treat positional skull deformation in infants younger than 5 months is conservative and consists of advice to parents regarding how to position and hold their infant (active repositioning) in order to reduce the amount of time spent resting the head on the flattened part.[19, 20] Consequently, the natural skull growth will improve head shape to some extent, i.e. natural recovery will occur.[14] Yet, a considerable number of infants who suffer from persistent skull deformation at 6 months of age are prescribed orthotic helmets or headbands.[21-23] Studies comparing these two strategies (helmet therapy versus awaiting natural course or active repositioning) in positional skull deformation do not provide conclusive evidence for the superiority of one of both options.[24-28] Hence, the decision of healthcare professionals to prescribe helmet therapy is based on perceived effectiveness and burden of treatment and preferences over these different outcomes of the alternatives, which can be related to their experiences in the past.[29-31]
Interestingly, we also see profound differences in prescription rates between countries, like New Zealand and the Netherlands. Infants with skull deformation undergo extensive treatment regimens in the Netherlands, including the use of helmet therapy, while New Zealand healthcare professionals hardly prescribe any helmets.

Comparison of the Netherlands and New Zealand

The reason for this difference in treatment policy for skull deformation is highly speculative. On many aspects related to skull deformation both countries are comparable. They have a comparable research history with respect to SIDS and adopted the recommendations to promote the supine sleeping position for infants. In both countries high prevalence of skull deformation

was found, namely 19.7% at age 4 months in New Zealand,[14] and 21.5% at age 7 weeks and 9.9% under 6 months in the Netherlands.[15, 16] Accordingly, skull deformation received a lot of attention in both countries; in research, in media and among parent and healthcare professionals. Also, in both countries the helmet is available as a treatment option.

However, there are also some profound differences between the two countries. Firstly, there are differences in the funding of health care between the countries. The Netherlands has implemented mandatory health insurance for all citizens and health insurance companies have to provide coverage for health services as defined by the government. Helmet therapy is part of the medical supplies budget which is strictly defined by the government. Health insurance companies reimbursed the costs of helmet therapy until 2013. In addition, pay for performance (by diagnosis-related group) was implemented for contracting hospitals. This has created a stimulating environment for the prescription of helmet treatment. In New Zealand, healthcare is mainly funded by taxes and the Government determines how much is allocated to the 21 district health boards (DHBs). The DHBs in turn determine what health services are funded for their population. In addition, some families have private health insurance. Therefore, depending on where you live and whether or not you have private health insurance, the cost of the helmet might or might not be reimbursed.

A second important difference between the Netherlands and New Zealand is the level of experience and the number of services available to provide helmet therapy. In contrast to the Netherlands, few New Zealand centers have the facilities or experience to construct infant helmets.

Thirdly, there might be differences in the evidence base underlying physicians' treatment decisions. An early retrospective case study conducted in New Zealand in 2001 showed no differences in effectiveness of helmet therapy (n=29) and active counter positioning (n=45). Soon afterwards a large prospective cohort study (n=200) supported the favorable course of natural recovery.[14, 26] At the same time, in 2000, a prospective cohort study in the Netherlands that compared helmet therapy (n=85) and head positioning (n=20) found significantly better results in the helmeted group.[28] Although all the studies were published in international journals, the studies might have influenced clinicians in the countries where the studies were carried out to a greater extent because of their familiarity with the setting in which the study took place.

Objective

Differences in health policy and reimbursement are likely to result in differences in the prescription rate of helmet treatment. However, expectations, beliefs and attitudes towards skull deformation and helmet therapy might also influence the perceived need for helmet therapy. Therefore, the objective of this study is to compare the beliefs, attitudes and expectations of health professionals involved in infant healthcare in the Netherlands with those in New Zealand.

METHODS

Study design

We conducted an explorative study. The survey participants were a convenience sample of healthcare professionals. Beliefs, expectations and attitudes of healthcare professionals were assessed using a self-completed questionnaire. In the Netherlands, the survey was part of an ancillary study of the HEADS study (Helmet therapy Assessment in Deformed Skull). The Medical Ethics Committees of the Medisch Spectrum Twente hospital in Enschede, the Netherlands, granted ethical approval of the HEADS study.[32] In New Zealand, ethics approval was obtained from The University of Auckland Human Participants Ethics Committee in Auckland. The following institutes were asked for consent to participate in the study and additionally granted ethical approval: Auckland District Health Board, Waitemata District Health Board, Counties Manukau District Health Board and the Plunket Society.

Participants

Healthcare professionals responsible for infant healthcare and referral of healthy infants with skull deformation for treatment were invited to participate in the study (Table 1).
In the Netherlands, preventive child health care physicians and pediatricians were invited to participate in the survey as part of the HEADS study. They were approached between April 2011 and August 2011 using membership lists of the Pediatric Association of the Netherlands and the association of Preventive Child Health Care Physicians Netherlands. In New Zealand, team leaders of the various groups of healthcare professionals within the Auckland District Health Board, Waitemata District Health Board, Counties Manukau District Health board and the Plunket Society were approached by the researcher (RVW) between September 2012 and December 2012 and asked to distribute the questionnaire among their teams. Furthermore, questionnaires were distributed to paediatricians during the Paediatric Society of New Zealand 64th Annual Scientific Meeting (November 2012).

Data collection

Beliefs, attitudes and expectations of healthcare professionals were assessed using a self-completed questionnaire. The questionnaire was offered web-based and paper-based. The questionnaire started with background characteristics of the participants (age, gender, profession, experience). Next, the following constructs were included in the questionnaire
1) experience: "experience with natural recovery of and helmet therapy in infants with skull deformation"; four questions: two yes/no questions and two questions with answers on a 5 point Likert scale (1—very inexperienced, 5—very experienced);

Table 1. Healthcare professionals involved in early detection and referral of infants with skull deformation in the Netherlands and New Zealand

	THE NETHERLANDS	NEW ZEALAND
EARLY DETECTION	**Preventive Child Health Care: Physicians** 2nd week to 4th year *Referral for paediatric physical therapy or paediatrician*	**Well Child / Tamariki Ora providers: Midwives** First 4-6 weeks of life *Report to GP and Well Baby provider for 6-week check.* **Child health nurses (Plunket nurses)** 6th week to 5th year *Referral to GP or paediatrician*
TREATMENT REFERRAL	**Paediatricians / medical doctors** *Referral for (paediatric) physical therapy / helmet therapy*	**Paediatricians / medical doctors** *Referral for (paediatric) physical therapy / helmet therapy*

2) beliefs: statements regarding "perceived burden of the skull deformation" to infants (four questions) and their parents (four questions) and "perceived burden of helmet therapy" to infants (one question) and their parents (two questions), (Likert scale 1—disagree, 5—agree);
3) expectations: "expected recovery when awaiting the natural course and when applying helmet therapy"; two questions with answers on a 5 point Likert scale (1—no recovery at all, 5—complete recovery);
4) attitudes: "perceived preference of parents towards natural recovery and helmet therapy" (two questions, Likert scale 1—mostly negative, 5—mostly positive) and "own preference for treatment" (one yes/no question whether the person has a preference, then a Likert scale 1—strong preference helmet therapy, 5—strong preference awaiting natural course).
The questionnaire was pilot tested in the Netherlands in a convenience sample of ten healthcare providers and small changes were made before it was finalized. The Dutch version was translated into English by the Dutch researchers in consultation with the New Zealand researchers (native English speakers). A web-based survey product (Limesurvey) was used to create the survey online. The web-based questionnaire is linked to a secured server at the University of Twente, the Netherlands.

Statistical analysis

Background characteristics were described for healthcare professionals of both countries separately.
Experience, beliefs, expectations and attitudes were presented for the Netherlands and New Zealand group using means and standard deviation for continuous variables, and counts and percentages in discrete variables. Groups were compared by means of the independent *t*-test or chi-square test and differences were calculated with 95% confidence intervals. All P values are two sided and significance was set at 5%. Data analysis was performed using SPSS (version 21.0).

RESULTS

In the Netherlands 314 healthcare professionals responded to the questionnaire and in New Zealand 73 healthcare professionals responded. In both countries more pediatricians/medical doctors compared to preventive child health care professionals were included in the study. Participants in The Netherlands did not differ by gender, age or experience compared with those in New Zealand (Table 2).

Experience

Healthcare professionals in New Zealand who participated in this study saw more new-borns each month compared to healthcare professionals in the Netherlands, but saw fewer cases with positional skull deformation under age 4 months. Dutch healthcare professionals were more often familiar with the natural course of skull deformation and with helmet therapy compared to their New Zealand colleagues (Table 3).

Beliefs, expectations and attitudes

Healthcare professionals of both countries had similar expectations of the recovery of skull deformation when awaiting its natural course, as well as when applying helmet therapy (Table 4). However, New Zealand professionals perceived the physical consequences of skull deformation as more severe for the child older than 1 year of age in comparison to Netherlands professionals. At the same time, New Zealand professionals perceived a larger physical burden of helmet therapy for the infant under 1 year of age and they expected a higher social and psychological burden of helmet therapy for parents during the time when the infants were under 1 year of age.

About two third of healthcare professionals expressed a preference for the management of SD; the majority of health professionals in the Netherlands and New Zealand preferred a wait-and-see regimen and this did not differ between the countries.
With regard to parental preferences for the management of skull deformation, healthcare professionals in New Zealand expected that parents had a more positive attitude about the natural course compared to the Netherlands healthcare professionals. There was no difference between the countries for expected parental attitude about helmet therapy. According to healthcare professionals in both countries, parents in the Netherlands had equally strong preferences for both options while parents in New Zealand had a preference for natural recovery.

Table 2. Background characteristics, presented as n (%)

	The Netherlands N=314	New Zealand N=73	P
Profession			
Pediatricians/medical doctors	180 (57)	46 (63)	.37
Preventive child health care	134 (43)	27 (37)	
Gender			
Male	81 (26)	23 (32)	.10
Female	233 (74)	50 (68)	
Age			
20-29 years	5 (2)	5 (8)	
30-39 years	67 (21)	13 (20)	
40-49 years	84 (27)	24 (33)	.07
50-59 years	120 (38)	25 (34)	
>59 years	38 (12)	6 (8)	
Experience as health professional ^			
<5 years	46 (16)	9 (14)	
5-14 years	91 (31)	23 (37)	
15-24 years	86 (29)	20 (28)	.15
25-34 years	69 (23)	16 (22)	
>35 years	3 (1)	4 (6)	

Groups were compared using *t* test or χ^2 test.
^ n=20 missing (5%)

Table 3. Experience of healthcare professionals, presented as mean (SD) or n (%)

	The Netherlands		New Zealand		New Zealand – The Netherlands	
	N		N		Mean difference (95% CI)	P
New-borns seen each month	285	8.7 (9.5)	57	15.8 (15.9)	7.1 (2.7 to 11.5)	<.01
Infants with skull deformation*	283	6.6 (11.1)	42	1.9 (2.4)	-4.7 (-6.2 to -3.2)	<.01
Familiar with the natural course (yes)	295	279 (95%)	71	62 (87%)	0.4 (0.2 to 0.9)†	.04
*Self-reported level of experience with natural course^*	279	3.7 (0.9)	55	3.6 (1.0)	-0.1 (-0.4 to 0.2)	.50
Familiar with helmet therapy (yes)	295	289 (98%)	69	61 (88%)	0.2 (0.1 to 0.5)†	<.01
*Self-reported level of experience with helmet therapy^*	289	3.0 (1.0)	61	1.4 (0.8)	-1.6 (-1.9 to 1.3)	<.01

Groups were compared using *t* test or χ^2 test.
*In The Netherlands <6 months, New Zealand <4 months
^Measurements on Likert scale, range 1-5. Higher numbers indicate more experience with management strategies in SD
† Odds ratio (95% confidence interval).

Table 4. Healthcare professionals' beliefs about the burden of positional skull deformation (PSD) and helmet therapy (HT) to the child and its parents, expectations for recovery and attitudes

	The Netherlands (n=314)		New Zealand (n=71)		New Zealand – The Netherlands	
	N	Mean (SD)	N	Mean (SD)	Mean difference (95% CI)	*p*
BELIEFS*						
Concerning the child						
Physical burden PSD <1y	285	2.2 (1.1)	65	2.2 (1.2)	0.0 (-0.3 to 0.3)	.89
Physical burden of HT <1y	278	2.6 (1.1)	38	3.2 (1.5)	0.6 (0.1 to 1.1)	<.01
Physical burden PSD >1y	267	2.2 (1.1)	66	2.6 (1.5)	0.4 (0.0 to 0.8)	.03
Social burden PSD >1y	259	2.7 (1.1)	66	2.7 (1.5)	0.0 (-0.4 to 0.4)	.87
Psychological burden PSD >1y	255	2.8 (1.2)	64	2.8 (1.4)	0.0 (-0.3 to 0.4)	.82
Concerning the parents						
Social burden PSD <1y	276	3.1 (1.1)	69	2.8 (1.2)	-0.3 (-0.6 to 0.0)	.05
Psychological burden PSD <1y	273	3.3 (1.1)	68	3.2 (1.3)	-0.1 (-0.4 to 0.2)	.62
Social burden HT < 1y	272	3.2 (1.1)	50	4.0 (1.0)	0.8 (0.5 to 1.1)	<.01
Psychological burden HT <1y	270	3.2 (1.0)	47	4.0 (1.0)	0.8 (0.5 to 1.2)	<.01
Social burden PSD >1y	255	2.7 (1.1)	66	2.9 (1.4)	0.2 (-0.1 to 0.5)	.22
Psychological burden PSD >1y	255	2.9 (1.1)	65	3.1 (1.3)	0.2 (-0.1 to 0.6)	.17
EXPECTATIONS^						
Expected recovery natural course	277	3.6 (0.6)	54	3.5 (0.8)	-0.2 (-0.4 to 0.1)	.17
Expected recovery helmet therapy	283	3.9 (0.6)	25	3.8 (1.0)	-0.1 (-0.5 to 0.3)	.53
ATTITUDES†						
Perception parents natural course	266	3.3 (1.0)	20	4.3 (0.9)	1.0 (0.7 to 1.3)	<.01
Perception parents helmet therapy	273	3.3 (1.0)	47	2.7 (1.5)	-0.6 (-1.3 to 0.1)	.09
Preference for treatment (yes)	281	184 (66%)	52	36 (69%)	1.2 (0.6 to 2.2)§	.60
Natural course‡		136 (83%)		31 (94%)	0.5 (0.2 to 1.9)§	.11
Helmet therapy‡		28 (17%)		2 (6%)		

Groups were compared using *t* test or χ^2 test.
*Measurements on Likert scale, range 1 to 5. Higher numbers indicate a higher perceived burden by the healthcare professionals.
^ Measurements on Likert scale 1 — no recovery at all, 5—complete recovery.
† Measurements on Likert scale, 1— mostly negative, 5— mostly positive, or n (%).
‡ Only health professionals indicating they had a treatment preference ('yes') were selected. Some filled out 3 on the Likert scale '1— strong preference helmet, 5—strong preference natural course' (n=20). These were set to missing values.
§ Odds ratio (95% confidence interval).

DISCUSSION

The aim of our study was to compare the beliefs, attitudes and expectations of healthcare professionals involved in infant healthcare in the Netherlands with those in New Zealand. The results indicate that healthcare professionals in both countries had similar expectations with regard to the effect of treatment of positional skull deformation using either helmet therapy or awaiting the outcome of the natural course.

When asked about their preference for treatment, Dutch healthcare professionals were slightly more likely to prefer helmet therapy compared to their New Zealand colleagues. However, in both countries the preference for helmet therapy was low. Given the equality in expectations of effectiveness, a higher preference for helmet in the Netherlands seemed unexpected. This might be explained by the difference in the beliefs about the long-term consequences of positional skull deformation as well as the consequences of helmet therapy. Both were perceived as more severe by healthcare professionals in New Zealand. If healthcare professionals placed more weight on the burden of therapy than on the consequences of the condition, this could explain the limited use of helmets in New Zealand. Another explanation of the low prescription rates could be the perceived attitudes of parents towards both management options. According to Dutch healthcare professionals, Dutch parents were equally positive about helmet therapy and natural course; according to their New Zealand colleagues, New Zealand parents were perceived to be more positive about awaiting the natural course compared to helmet therapy.

The similar expectations of healthcare professionals in both countries suggest they work from the same evidence base. However, the differences in beliefs and attitudes could be related to the studies that were carried out in the two countries and showed contradictory outcomes[14, 26, 28]. The different beliefs and attitudes could also simply be a consequence of the lack of experience with and availability of helmet therapy in New Zealand compared with the Netherlands. In the Netherlands, healthcare professionals often prescribe helmets, which results in a higher level of personal experience with the use and effects of the helmet.

It seems plausible that in a country such as the Netherlands where helmet therapy is marketed and often prescribed, opinions of parents and healthcare professionals are influenced.[33-35] It has also been hypothesized that parental concern may induce an increased need to act on skull deformation, thus driving treatment trends.[17, 30] A study in the Netherlands showed that when helmet therapy is freely available parental decision was mainly influenced by subjective variables (satisfaction with skull shape and expectations of treatment), rather than the objective severity of the condition.[31]

Other explanation could be the differences in the funding model of the health systems, an unequal financial situation, or dissimilarity in infants' health status.

The health care system differs between both countries. In New Zealand, the healthcare system is largely Government funded and the DHBs determine priorities for spending. Acute services and serious health problems clearly take priority. The pay for performance system in the Netherlands drives more treatments thus income. Also in the Netherlands 89% of the population have

supplementary private health insurance coverage, compared to 31% in New Zealand who have additional private health insurance coverage.[36]

Next, we see differences in the financial situation of both countries and their populations. The Netherlands has a higher GDP (2012: $43,146) compared to New Zealand (2012: $32,163) and spends a higher percentage of it on health (2011: NL 11.9%; NZ 10.3%).[37] This is in line with literature, describing that countries with social insurance systems tend to have a higher spending on health compared to countries with tax-funded insurance systems.[38] Also around 22% of the population in New Zealand consists of Māori and Pacific Island people, with their higher, more serious paediatric health needs; this might lessen concern about, and demand for, positional skull deformation treatment.

Finally, children's health status in New Zealand is at a lower level than that of the Netherlands. In New Zealand, serious health conditions in childhood demand more attention than cosmetic conditions. Especially in a tax-based system in which care has to be prioritized, prescription of care becomes a resource issue and a cosmetic treatment would be less likely to be funded.

Strengths and limitations of study

Various healthcare professionals were included in this study. In the Netherlands, more healthcare professionals were included, compared to New Zealand; however, this was representative of the size of the population in both countries (4:1). In both countries, comparable strategies, such as changing the head position of the infant during sleep, increasing tummy time, using various ways to hold the infants and applying active repositioning strategies, are recommended for the prevention and treatment of skull deformation.[19, 20]

We used similar questionnaires to assess beliefs, expectations and attitudes in both countries. This questionnaire was pilot tested in the Netherlands; however, we did not pilot-test the New Zealand questionnaire. We did introduce a few slight changes in the questionnaire in order to tailor it to the practices and systems of each country. In addition, since helmet therapy is not standard treatment in New Zealand during the study period, we had New Zealand participants skip questions about helmet therapy when they answered negatively to the question 'Have you ever heard or read about helmet therapy in deformational plagiocephaly/brachycephaly?'. Therefore the response to questions about helmet therapy is lower in the New Zealand data compared to the Netherlands data. Lastly, in the Netherlands we used the term 'awaiting natural recovery', while we chose to use 'active repositioning' in the New Zealand questionnaire. This was done because in The Netherlands active repositioning is typically used preceding the helmet therapy, while in New Zealand this would be the alternative of helmet therapy. To make sure that similar constructs were measured, we used specific time frames (e.g. preference for treatment in 5 month-olds) in our question. However, this might have caused healthcare professionals in New Zealand to respond more positively to the question about parental attitudes towards the natural course (active repositioning), nevertheless, healthcare professionals' expectations of recovery were comparable between both countries.

Conclusions and recommendations

This study has provided an insight into views and practices between two seemingly similar countries that have developed dissimilar ways of treating positional skull deformities. We have shown several differences in beliefs and attitudes of healthcare professionals in New Zealand and the Netherlands and subsequently we have provided a range of arguments for the difference in treatment policies. Since January 2013, helmet therapy is not being covered by basic health insurance in the Netherlands. At that time, when the National Health Care Institute decided not to reimburse cosmetic treatments anymore, outcomes of the few existing prospective comparative studies tended to show positive results in favor of helmet therapy, although contradictory results were found. Very recently in 2014, a Dutch randomized controlled trial comparing helmet therapy to following the natural course of the condition showed no relevant and significant differences between the two options.[39] Perhaps in the Netherlands this will induce a shift towards the New Zealand situation, now the therapy is not covered by basic insurance.

In current times of economic restraint, health services are facing more and more restrictions in resources. Therefore, treatments need to be proven to be value for money, especially in conditions where there is no medical reason to treat. Accordingly, changes in practice should be based on the results of good research.

REFERENCES

1. Beal SM. Sudden infant death syndrome: epidemiological comparisons between South Australia and communities with a different incidence. *Aust. Paediatr. J.* 1986;22 Suppl 1:13-16.
2. de Jonge GA, Engelberts AC, Koomen-Liefting AJ, Kostense PJ. Cot death and prone sleeping position in The Netherlands. *BMJ.* 1989;298(6675):722.
3. Fleming PJ, Gilbert R, Azaz Y, et al. Interaction between bedding and sleeping position in the sudden infant death syndrome: a population based case-control study. *BMJ.* 1990; 301(6743):85-89.
4. Mitchell EA, Scragg R, Stewart AW, et al. Results from the first year of the New Zealand cot death study. *N. Z. Med. J.* 1991;104(906):71-76.
5. Dwyer T, Ponsonby AL, Newman NM, Gibbons LE. Prospective cohort study of prone sleeping position and sudden infant death syndrome. *Lancet.* 1991;337(8752):1244-1247.
6. de Jonge GA, Burgmeijer RJ, Engelberts AC, Hoogenboezem J, Kostense PJ, Sprij AJ. Sleeping position for infants and cot death in The Netherlands 1985-91. *Arch. Dis. Child.* 1993;69(6):660-663.
7. Mitchell EA, Aley P, Eastwood J. The national cot death prevention program in New Zealand. *Aust. J. Public Health.* 1992;16(2):158-161.
8. American Academy of Pediatrics Task Force on Infant Sleep Positioning and SIDS. Positioning and SIDS. *Pediatrics.* 1992;89(6 Pt 1):1120-1126.
9. Wennergren G, Alm B, Oyen N, et al. The decline in the incidence of SIDS in Scandinavia and its relation to risk-intervention campaigns. Nordic Epidemiological SIDS Study. *Acta Paediatr.* 1997;86(9):963-968.
10. Dwyer T, Ponsonby AL, Blizzard L, Newman NM, Cochrane JA. The contribution of changes in the prevalence of prone sleeping position to the decline in sudden infant death syndrome in Tasmania. *JAMA.* 1995;273(10):783-789.
11. Gilman EA, Cheng KK, Winter HR, Scragg R. Trends in rates and seasonal distribution of sudden infant deaths in England and Wales, 1988-92. *BMJ.* 1995;310(6980):631-632.
12. Mitchell EA, Brunt JM, Everard C. Reduction in mortality from sudden infant death syndrome in New Zealand: 1986-92. *Arch. Dis. Child.* 1994;70(4):291-294.
13. Engelberts AC, de Jonge GA, Kostense PJ. An analysis of trends in the incidence of sudden infant death in The Netherlands 1969-89. *J. Paediatr. Child Health.* 1991;27(6):329-333.
14. Hutchison BL, Hutchison LA, Thompson JM, Mitchell EA. Plagiocephaly and brachycephaly in the first two years of life: a prospective cohort study. *Pediatrics.* 2004;114(4):970-980.
15. Boere-Boonekamp MM, van der Linden-Kuiper LT. Positional preference: prevalence in infants and follow-up after two years. *Pediatrics.* 2001;107(2):339-343.
16. van Vlimmeren LA, van der Graaf Y, Boere-Boonekamp MM, L'Hoir MP, Helders PJ, Engelbert RH. Risk factors for deformational plagiocephaly at birth and at 7 weeks of age: a prospective cohort study. *Pediatrics.* 2007;119(2):e408-418.
17. Collett B, Breiger D, King D, Cunningham M, Speltz M. Neurodevelopmental implications of "deformational" plagiocephaly. *J. Dev. Behav. Pediatr.* 2005;26(5):379-389.

18. Hutchison BL, Stewart AW, Mitchell EA. Deformational plagiocephaly: a follow-up of head shape, parental concern and neurodevelopment at ages 3 and 4 years. *Arch. Dis. Child.* 2011;96(1):85-90.

19. Hutchison BL, Stewart AW, De Chalain TB, Mitchell EA. A randomized controlled trial of positioning treatments in infants with positional head shape deformities. *Acta Paediatr.* 2010;99(10):1556-1560.

20. van Vlimmeren LA, van der Graaf Y, Boere-Boonekamp MM, L'Hoir MP, Helders PJ, Engelbert RH. Effect of pediatric physical therapy on deformational plagiocephaly in children with positional preference: a randomized controlled trial. *Arch. Pediatr. Adolesc. Med.* 2008; 162(8):712-718.

21. Flannery AB, Looman WS, Kemper K. Evidence-based care of the child with deformational plagiocephaly, part II: management. *J. Pediatr. Health Care.* 2012;26(5):320-331.

22. Kluba S, Kraut W, Reinert S, Krimmel M. What is the optimal time to start helmet therapy in positional plagiocephaly? *Plast. Reconstr. Surg.* 2011;128(2):492-498.

23. Xia JJ, Kennedy KA, Teichgraeber JF, Wu KQ, Baumgartner JB, Gateno J. Nonsurgical treatment of deformational plagiocephaly: a systematic review. *Arch. Pediatr. Adolesc. Med.* 2008;162(8):719-727.

24. Kluba S, Kraut W, Calgeer B, Reinert S, Krimmel M. Treatment of positional plagiocephaly - Helmet or no helmet? *J. Craniomaxillofac. Surg.* 2014;42(5):683-8.

25. Lipira AB, Gordon S, Darvann TA, et al. Helmet versus active repositioning for plagiocephaly: a three-dimensional analysis. *Pediatrics.* 2010;126(4):e936-945.

26. Loveday BP, de Chalain TB. Active counterpositioning or orthotic device to treat positional plagiocephaly? *J. Craniofac. Surg.* 2001;12(4):308-313.

27. Mulliken JB, Vander Woude DL, Hansen M, LaBrie RA, Scott RM. Analysis of posterior plagiocephaly: deformational versus synostotic. *Plast. Reconstr. Surg.* 1999;103(2):371-380.

28. Vles JS, Colla C, Weber JW, Beuls E, Wilmink J, Kingma H. Helmet versus nonhelmet treatment in nonsynostotic positional posterior plagiocephaly. *J. Craniofac. Surg.* 2000; 11(6):572-574.

29. Lee A, Van Pelt AE, Kane AA, et al. Comparison of perceptions and treatment practices between neurosurgeons and plastic surgeons for infants with deformational plagiocephaly. *Journal of Neurosurgery: Pediatrics.* 2010;5(4):368-374.

30. Naidoo SD, Cheng AL. Long-term satisfaction and parental decision making about treatment of deformational plagiocephaly. *J. Craniofac. Surg.* 2014;25(1):160-165.

31. van Wijk RM, van Til JA, Groothuis-Oudshoorn CG, L'Hoir M P, Boere-Boonekamp MM, IJzerman MJ. Parents' decision for helmet therapy in infants with skull deformation. *Childs Nerv. Syst.* 2014;30(7):1225-1232.

32. van Wijk RM, Boere-Boonekamp MM, Groothuis-Oudshoorn CG, van Vlimmeren LA, IJzerman MJ. HElmet therapy Assessment in infants with Deformed Skulls (HEADS): protocol for a randomised controlled trial. *Trials.* 2012;13:108.

33. Collett BR. Helmet therapy for positional plagiocephaly and brachycephaly. *BMJ.* 2014;348:g2906.

34. Sheu SU, Ethen MK, Scheuerle AE, Langlois PH. Investigation into an increase in plagiocephaly in Texas from 1999 to 2007. *Arch. Pediatr. Adolesc. Med.* 2011;165(8):708-713.

35. Shweikeh F, Nuno M, Danielpour M, Krieger MD, Drazin D. Positional plagiocephaly: an analysis of the literature on the effectiveness of current guidelines. *Neurosurg. Focus.* 2013; 35(4):E1.

36. OECD Health Statistics. Health at a Glance 2013. 2013.

37. OECD Health Statistics. Health expenditure and financing. 2013.

38. Tenbensel T, Eagle S, Ashton T. Comparing health policy agendas across eleven high income countries: islands of difference in a sea of similarity. Health Policy. 2012;106(1):29-36.

39. van Wijk RM, van Vlimmeren LA, Groothuis-Oudshoorn CG, Van der Ploeg CP, IJzerman MJ, Boere-Boonekamp MM. Helmet therapy in infants with positional skull deformation: randomised controlled trial. *BMJ.* 2014;348:g2741

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CHAPTER 8

General Discussion

GENERAL DISCUSSION

The primary aim of this thesis was to provide a stronger evidence base to improve decision-making for the treatment of infants with positional skull deformation. The main findings were presented in this thesis. Predictors for response to pediatric physical therapy at the start of therapy were determined, of which the most important were the infant's age and the presence of skull deformation.[1] Furthermore, the results of the HEADS study showed that helmet therapy does not add benefit compared to the natural course of positional skull deformation in infants with moderate or severe skull deformation.[2]

The secondary aim of this thesis was to gain a better understanding of the decision making for treatment by parents and professionals. It is described that subjective measures as 'parental (dis) satisfaction with the infant's appearance' and '(high) expectations of the helmet therapy' are the most important predictors for the decision for treatment.[3] Finally, the thesis provided insight into possible mechanisms of the different prescription rates of helmet therapy in the Netherlands compared to New Zealand where hardly any helmet therapy is prescribed. Healthcare professionals' beliefs and attitudes varied between countries, but health systems, the financial situation and children's' health status were expected to play important roles in the prescription of helmet therapy too.

Societal impact

The HEADS study meets the demands of many researchers and clinicians for a randomized controlled trial into the effects of helmet therapy.[4-8] The outcomes have been published in the high impact journal *BMJ*.[2] This publication not only represented a scientific impact, but also accounted for a considerable societal impact. The outcomes received significant lay press attention, both nationally and internationally. The most relevant publications are described in Table 1. The results have been published in lay press in more than 50 releases in different countries during the first month after publication.

Table 1. Summary of most prominent outreach related to the BMJ publication, released at 2 May 2014

Date	Source	Type	Country
1 May 2014	BBC News	Website	United Kingdom
2 May 2014	New York Times	Newspaper	United States
2 May 2014	Ned 1 'EenVandaag' (Current Affairs)	Television	The Netherlands
2 May 2014	New York CBS News	Television	United States
3 May 2014	NBS Nightly News	Television	United States
6 May 2014	Deutsches Ärzteblatt	Website	Germany
6 May 2014	NRC	Newspaper	The Netherlands
8 May 2014	Volkskrant	Newspaper	The Netherlands
10 May 2014	Radio 1 'Nieuwsshow'	Radio	The Netherlands

The paper also received five rapid responses during the first month after publication at the *BMJ* website from Germany, Switzerland, Spain and the United States. Furthermore, healthcare professionals and researchers from the Netherlands, Germany, United Kingdom, United States, Brazil, and Argentina provided feedback and requested more detailed information from the research team. Items about the RCT outcomes on websites also generated many comments from parents and healthcare professionals.

Hence, the outcomes have certainly not been adopted without discussion. Next to very positive reactions, the *BMJ* paper also received criticism from different stakeholders, including orthotists and parents. Parents were concerned about the established lack of evidence base for helmet therapy, in particular because they used non-clinical factors to base their decision on in addition to the (perceived) severity of skull deformation.[3, 10] Also, clear and high quality evidence seemed no guarantee that healthcare professionals will provide evidence-based care.

Parental perspective

Many parents have approached the research team during the study with questions for information about the effectiveness of helmet therapy. The HEADS study fulfilled this need for information among parents, and consequently many parents reacted positively to the study outcomes. At the time of the study it was unknown whether the parents' perception of the condition and expectations of treatment were realistic. Although, we already knew that subjective outcomes not always represented the objective outcomes in skull deformation.[11, 12] In reply to the publications, we noticed that some parents, who had used helmet therapy for their infants, did not believe the study results and were fully convinced that their infant did benefit from the treatment. Our evidence did not match their perception. In the paper on decision making we suggested that parents who chose for helmet therapy might have had extreme high expectations or irrational thoughts and emotions which cannot be substantiated. This could be supported by the fact that we found higher state anxiety levels, lower satisfaction scores and higher expectations of treatment effect in parents choosing for helmet therapy compared to parents who awaited natural course.

The critical responses of some parents to the first online publications about the RCT illustrate the challenge of explaining research to a lay public. It is important to pay attention to a clear message to present the implications of the study outcome, that encompasses understanding for the parents' perspective. Merely presenting the lack of added value of helmet therapy found using anthropometric outcomes is not sufficient.[13] Parents who decide for helmet therapy are more concerned than parents who await natural recovery.[3] Since concern can drive treatment trends it is important to address this issue. The fact that parents showed high satisfaction scores or low levels of concern at the long term, irrespective of treatment modality,[3, 10, 14] is therefore very important to incorporate in the message to reassure parents for the future.

We always described helmet therapy as a preference-sensitive treatment. This was based on the fact that there is no medical reason for treatment and there was no convincing evidence about

the best treatment modality. With the current knowledge, helmet therapy in healthy infants of 5 to 6 months old with moderate or severe skull deformation can be considered an unnecessary use of resources. It is important that healthcare professionals balance parental concern and dissatisfaction, with objective measures and evidence from research.[15]

Healthcare professionals' responses

The unique study design of the HEADS study was praised by many healthcare professionals and researchers. Pediatricians mentioned they expect that using the results from the HEADS RCT supports parents in decision-making. We hypothesize that the real world evidence from the nRCT provides additional insight to healthcare professionals.
In both the RCT and nRCT we reported a wide range of measures, including anthropometric measurement of the skull, parent-reported outcomes, treatment compliance, fitting of the helmet, side effects and costs of treatment. None of the prospective comparative studies that have been published to date have used such a comprehensive set of outcomes, while this is vital to generalize study outcome.[16, 17]

However, the results also received critical notes from orthotists providing helmet therapy in the United States and the United Kingdom. They criticized the high rates of reported fitting problems (73%), and question the quality of the helmets studied in the HEADS study. Accordingly they claim to have better helmets that are more likely to be beneficial. A comparable issue arises around the reported side effects; all parents in both the RCT and the nRCT reported one or more side effects. However, parents were satisfied with the fit of the helmet, represented by a mean score of 3.8 out of 5 in the RCT and nRCT. It is important to bear in mind that the fit of the helmet and side effects are parent-reported outcomes and that they were combined from two assessments (8 months and 12 months). Therefore, they might account for a wide range of issues. Probably not all of these fitting issues and side effects should be considered as a major problem, based on the high parental satisfaction score with the fit of the helmet. Moreover most of the issues could have been resolved easily by the manufacturer. It may be expected that independent, doctor-reported outcomes, like in the study of Wilbrand et al.[18], would represent the more problematic fitting issues and side effects and result in lower rates.

Nevertheless, the reported rate of fitting issues with the helmet and side effects could be considered rather high. However, reported fitting issues and side effects are, to our opinion, no argument for not accepting the study results. We described four reasons for this claim Firstly, in the HEADS study only experienced orthotists provided helmet therapy. Secondly, two types of helmets were studied: one is from the largest helmet manufacturer of the Netherlands with over 15 years of experience and a production of over 2000 helmets a year, using a helmet made out of one solid whole with several inner layers; the helmet of a second manufacturer consisted of two 'half shells' connected by a 'hinge' and the fit can be adjusted by Velcro-strap

fastening. By some the second helmet could be perceived as an active molding helmet.[19, 20] Both helmets had very similar outcomes in the RCT, though this should be interpreted with caution as the RCT was not designed and powered to perform subgroup analyses for different helmets. Thirdly, the treatment effects found in the RCT and nRCT are very comparable to that of a recent non-randomized study of Lipra et al. (2010) in the United States comparing helmet therapy (n=35) to repositioning (n=35). Both groups showed similar baseline values. The authors found no significant different improvement between both groups using a caliper. A more detailed 3D assessment found significant differences, but it could be questioned whether these differences are clinically meaningful.[16] More recently, in 2013, Kluba et al. compared 62 infants who underwent helmet therapy with 66 infants who received no helmet (natural course) in a non-randomized study in Germany. Infants in the helmet group started with a much more severe deformational plagiocephaly compared to infants in the natural course group. The helmet therapy group achieved more improvement compared to the natural course group (relative improvement: helmet therapy 68%, natural course 31%).[21] However, presenting relative improvement is not enough, since our study determined that the only significant and strongest predictor for improvement was the baseline value of skull deformation. It is important to adjust for the baseline values in the final analysis of the treatment effect. This makes the outcomes of Kluba et al. hard to value. In other studies that showed a significant better outcome in the helmet therapy group the clinical relevance of the difference in outcome could be questioned.[5] Fourthly and finally, most parents in the HEADS study show low concern for the future and high satisfaction with the long-term head-shape after treatment, similar to previous studies.[2, 10, 14, 22, 23] These subjective outcome measures should always be incorporated in a study towards treatment of a cosmetic condition.[16]

The fact that the outcomes of the RCT were also found in the nRCT, the comparable effect found for the two helmet types in our RCT, and the lack of convincing evidence in previous observational studies, confirms our conclusion that outcomes are expected to hold for all types of custom-made helmets comprising a rigid plastic shell with a foam lining that are designed to fit snugly over the infant's head and leaving room for skull growth at the flattened area.

Policy making

In many countries, helmet therapy is not covered in standard health care; in the United Kingdom helmet therapy is not covered in the National Health Service[8], in the United States in many states Medicaid does not cover helmet therapy[6] and also in the Netherlands the National Health Care Institute decided not to reimburse cosmetic treatments anymore from 2013 on. Additionally, several private insurance companies do not cover the helmets, so many parents were wondering whether it is worth it to pay out of pocket for the helmet. The HEADS study provides them with the very clear recommendation not to start helmet therapy in healthy infants with moderate or severe positional skull deformation. Pediatric departments who decided not to prescribe helmet therapy based on the lack of evidence, felt supported by the RCT results.[24]

In addition to healthcare professionals, also health policy makers have shown interest in the HEADS study. Medicaid, who provides free health care in the United States from a limited budget from the government, was seeing requests for helmets increase at rising costs.[25] Therefore, the Medicaid Evidence-based Decisions (MED) Project requested a review of evidence on helmet therapy for positional skull deformation. The MED Project was established at the Center for Evidence-based Policy in 2006 at the Oregon Health and Science University as a self-governing collaboration of state Medicaid agencies and their partners. Their review incorporated the outcomes of the HEADS study as their strongest piece of evidence. Based on the MED Project's conclusions, at least in one state the Medicaid medical director has adopted a non-coverage policy for helmet therapy and helmets are seen as not medically necessary.

The low coverage rate of helmet therapy in many countries, together with the new evidence from this thesis, might induce a shift towards much lower prescription rates, like in New Zealand. In the early 2000's, New Zealand studies suggested that helmet therapy was redundant in the recovery of positional skull deformation. This, together with a government funded healthcare system, a worse children's health status and less optimal financial situation compared to the Netherlands could explain that helmet therapy is rarely prescribed in New Zealand (chapter 7), in contrary to the Netherlands.

Implications of the thesis

Evidence on effects and costs of treatment is not always enough to influence healthcare practice. Clinical decisions should include the patient's circumstances and treatment options, scientific evidence of these treatment options and accordingly the patient's preferences.[15] Especially in preference-sensitive treatments, like helmet therapy, other factors besides effectiveness may be important as well. Therefore, the HEADS study included cost-effectiveness as well as parents' decision making outcomes and tried to explain treatment policy of healthcare professionals. These findings will be integrated in the implications of the present thesis.

Implications for clinical guidelines

Despite the increased attention for positional skull deformation during the last decades, no evidence-based guideline exists. Several reviews tried to give an overview of available evidence for the treatment of positional skull deformation and some provide a clinical decision tool.[4, 6, 7, 26] Most recommendations for treatment are based on outcomes of non-randomized or even non-controlled studies, in an infant population where preventive measures were not taken systematically before commencing helmet treatment. To our knowledge, the Netherlands is the only country with an integrated care guideline regarding the positional preference and positional skull deformation. This guideline was published by the Netherlands Centre of Preventive Child Health Care in 2012.[27] The guideline included preventive measures, recommendations for healthcare

professionals to timely detect a positional preference or positional skull deformation, and described a follow-up policy, either within preventive child health care or by referring to other healthcare professionals. The HEADS study results can be used in addition to the current guideline.

> *We suggest that professionals working in preventive child health care should follow the guideline and ideally refer infants with persistent positional preference or positional skull deformation before 3 months of age to the pediatric physical therapist.*
> *Pediatric physical therapists should be alert to infants presenting with a clear skull deformation or infants of parents who are unsatisfied with their infant's appearance (either posture or shape of the head).*[1]

It could be expected that these infants benefit from more individualized, intensive treatment. We believe that the current pediatric physical therapy practice leaves room for improvement based on the high prevalence of positional preference and positional skull deformation, malleability of the young infants' skull and the potential of therapy when started before 3 months of age.

The Preventive Child Health Care guideline also advises healthcare professionals to be reluctant in prescribing helmet therapy, aside from using helmets in scientific studies. Furthermore the guideline prescribed that 1) parents should be provided with the evidence from literature about the suggested short-term effects of helmet therapy and 2) the lack of information about the long-term consequences and potential side effects should be discussed.

> *Therefore, we suggest that the guideline's main advice regarding the prescription of helmet therapy can be strengthened using the outcomes of the HEADS study; helmet therapy should be discouraged in healthy infants with moderate or severe positional skull deformation.*[2]
> *Next, it is important that professionals are familiar with the parents' perspective regarding the condition and treatment to be able to balance medical information with parents' expectations, values and beliefs.*[3, 13, 23]

Anthropometric outcomes showed that only about 25% of infants show full recovery at 24 months of age. Meanwhile, parents in the RCT and nRCT show high to very high satisfaction scores with the shape of their infant's head, no matter whether their infants received helmet therapy or not.[2]

> *It would be justified to advice healthcare professionals to reassure parents based on the information that parents are, in general, satisfied with their child's long-term head shape, despite the fact that not all infants fully recover from their skull deformation.*[2, 10, 14, 22, 23]

In 2017, the guideline will be revised and the outcomes of the HEADS study can be incorporated. In the meantime, an appendix to the current version of the guideline can be written and offered to the guideline administrator.

Implications for research

Randomized controlled trials (RCTs) are widely accepted as the gold standard in comparative effectiveness research.[28, 29] The random allocation and concealment of treatments reduce bias, making the RCT the most reliable design to determine the exact treatment effects. By minimizing the possibility of bias, the internal validity of these studies is ensured. However, the generalizability of study outcomes may be limited.[30] Before RCT study results can be implemented, it is necessary to determine whether the results are valid in clinical practice and to whom the results apply.[17] Pragmatic RCTs, like the HEADS pragmatic RCT, can be the answer to the lack of generalizability of RCTs because interventions are studied in routine, everyday practice with no or minimal blinding and the intervention is randomly allocated to participants.[13, 31-33] In studies towards the treatment of a non-medical condition, the decision for treatment is preference sensitive. This complicates the inclusion of participants in a (pragmatic) RCT. Preliminary studies of RCT participation using a questionnaire about preferences with regard to a hypothetical trial, are likely to provide an overestimation.[34] A pilot study of the HEADS study estimated a participation rate that was twice as high as actual participation.[35]

> *When studying preference-sensitive treatments that are widely available, it could be expected that preliminary assessment of hypothetical participation in a randomized controlled study is likely to provide an overestimation of the willingness to participate in real-life.*

More challenges of a randomized study design can be described. In studies with low recruitment rates the study sample might not be representative of the target population. Next, minimal or no blinding may lead to the situation where participants are assigned to a preferred or non-preferred treatment, causing over- or underestimation of the treatment effect, respectively.[30] For example, observational studies are often accused of presenting an overestimation of the treatment effect.[36] Apart from this, research participation itself can affect trial outcomes. When people (either participants or healthcare professionals) are aware of the fact they are being monitored, they tend to improve their behavior to get better results; the Hawthorne effect.[37, 38] The effect could be expected to be more prominent when participation has a distinct influence on the participant e.g. in unblinded, random allocation of treatment and frequent follow-up assessments. Finally, in RCTs, patients are forced into a treatment arm which limits external validity as we do not know what would happen in real-life. In addition, a medical decision taken after consulting parents for their preferences could possibly yield better therapy adherence and thereby a larger effect size than in an RCT.

Researchers who study standard care, should take into account that therapy compliance is likely to be better in a non-randomized study, compared to a randomized controlled trial (chapter 6).

Nevertheless, the direction nor the magnitude of potential differences in treatment effects found in observational studies in comparison to RCT's could be predicted.[39]
Finally, although theoretically superior, there are also studies that show that outcomes of RCTs are comparable to outcomes of the intervention in daily practice.[30, 40-44] In the debate about advantages and disadvantages of RCTs versus observational studies, it is advised to study non-participants parallel to an RCT, to compare outcomes and asses the generalizability of the RCT.[41, 45, 46] In the HEADS study, the non-randomized study results strengthened the results of the RCT.

We recommend the nested RCT design for future studies into standard care to allow robust comparison of RCT results with real-world data.

Implications for policy makers

In an atmosphere where costs of healthcare are rising, and at the same time, budgets are getting more tight, treatments need to be proven to be value for money, especially in conditions where there is no medical reason to treat. Accordingly, changes in practice should be based on the results of good research. In the case of positional skull deformation pediatric physical therapy is regarded the only therapy that is proven to be effective to prevent or diminish the deformation of the young infant's skull.[47] The HEADS study provides additional evidence with the potential to improve outcomes after pediatric physical therapy. Furthermore, this study represents the third RCT with regard to the treatment of positional skull deformation.[47, 48]
We concluded that helmet therapy should be discouraged as a standard treatment for healthy infants with moderate to severe skull deformation. Additionally, we mentioned the importance of healthcare professionals balancing parental concern and dissatisfaction, with objective measures and evidence from research.[15] However, this introduces a challenge in a country as The Netherlands, where pay for performance by diagnosis-related group was implemented for contracting hospitals. This system drives more treatment en thus income. It could be suggested that healthcare professionals should be rewarded for explaining the current evidence to parents and discouraging helmet therapy. This prevents overtreatment and thereby unnecessary costs, which is interesting from the health economic perspective.

However, discouraging helmet therapy, is not the ultimate answer for the problem of positional skull deformation. We know from the HEADS study, that the majority of infants with a moderate to severe skull deformation at 5 months do not show full recovery at 2 years of age, irrespective of treatment modality. This demands a shift of attention towards the earlier phase of the condition.

The low rate of infants showing full recovery in the HEADS study, urges the need for (financial support for) high quality studies with regard to prevention measures, early detection and early treatment for positional skull deformation. Next, results need to be implemented in evidence-based, integrated care guidelines. This should lead to fewer concerned parents and a focus on evidence-based prevention and treatment.

The importance of incorporating advices concerning the preventive measures for positional skull deformation and sudden infant death syndrome, is stressed by a study in the United States.[49] In the United States, it has been described that the preventive measures with regard to sudden infant death syndrome (supine sleeping position) in combination with the advice with regard to positional preference (tummy time when infant is awake and under supervision) still lack clarity. Various sources provided inconsistent information. Also, parents reported barriers in implementing the preventive advice. Resulting in unnecessary cases of positional skull deformation.

Recommendations

Positional skull deformation is a cosmetic condition since there is no medical reason to treat. Without evidence for the effectiveness of treatment, the decision for helmet therapy has been preference-sensitive; did parents feel a need to act, and what option did they prefer? The HEADS study adds required evidence regarding the treatment of positional preference and provides insight in parents' decision-making and healthcare professionals' preferences.
The evidence, presented in this dissertation, should induce a shift from preference-based decision making for treatment of positional skull deformation at 5 to 6 months, towards evidence-based decision making in which helmet therapy is being discouraged. The parents' need to treat may still exist, but helmet therapy does not add benefit compared to naturals course. Treatment can therefore be considered an unnecessary use of resources. Healthcare professionals are expected not to prescribe helmet therapy in healthy infants of 5 to 6 months old with moderate or severe skull deformation. Instead they can reassure parents using the high satisfaction scores reported by parents who awaited natural course the present study, and in several other studies.[2, 10, 14] Insurance companies may likely change their reimbursement policy.

Furthermore, we recommend that healthcare professionals and researchers focus on primary prevention, early detection and early treatment of positional preference or positional skull deformation.[50] Evidence for effective prevention measures is needed to provide a uniform message in addition to the Back to Sleep advice. Predictors of response to pediatric physical therapy, as reported in this thesis, can be used to increase the potential of this treatment.[1]

The valuable collection of evidence from the HEADS study however, does not ensure a change in healthcare practice. Results need to be implemented to make sure the evidence reaches the relevant population of parents, healthcare professional and policy makers and accordingly will be adopted by all stakeholders. Ideally, the evidence of both the effectiveness of treatment and the parents' and healthcare professionals' perspective will be incorporated in national integrated care guidelines for the prevention and treatment of positional skull deformation. The present chapter included suggestions how the main findings of this dissertation should be used in practice. Next, results need to be communicated through scientific publications, publications in (national) specialist journals, magazines and website directed at young parents, and media (e.g. lay press, television, radio). The thesis will also be actively spread among healthcare professionals, youth health care organizations, policy makers and insurance companies and could complemented by lectures or training sessions.

Finally, we can expand the current body of knowledge with future work within the HEADS study. The study data provide excellent opportunities to assess risk factors for positional skull deformation, study motor development in affected infants, investigate the stability of treatment preferences, compare elicit and stated preferences and determine the value of consultation of various stakeholders (o.a. healthcare professionals and the internet) in decision-making.

REFERENCES

1. van Wijk RM, Pelsma M, Groothuis-Oudshoorn CG, IJzerman MJ, van Vlimmeren LA, Boere-Boonekamp MM. Response to Pediatric Physical Therapy in Infants With Positional Preference and Skull Deformation. Phys Ther. 2014;94(9).

2. van Wijk RM, van Vlimmeren LA, Groothuis-Oudshoorn CG, Van der Ploeg CP, IJzerman MJ, Boere-Boonekamp MM. Helmet therapy in infants with positional skull deformation: randomised controlled trial. *BMJ.* 2014;348:g2741.

3. van Wijk RM, van Til JA, Groothuis-Oudshoorn CG, L'Hoir MP, Boere-Boonekamp MM, IJzerman MJ. Parents' decision for helmet therapy in infants with skull deformation. Childs Nerv Syst. 2014;30(7):1225-1232.

4. Flannery AB, Looman WS, Kemper K. Evidence-based care of the child with deformational plagiocephaly, part II: management. *J. Pediatr. Health Care.* Sep-Oct 2012;26(5):320-331.

5. Goh JL, Bauer DF, Durham SR, Stotland MA. Orthotic (helmet) therapy in the treatment of plagiocephaly. *Neurosurg. Focus.* 2013;35(4):E2.

6. Robinson S, Proctor M. Diagnosis and management of deformational plagiocephaly. *J. Neurosurg. Pediatr.* 2009;3(4):284-295.

7. Xia JJ, Kennedy KA, Teichgraeber JF, Wu KQ, Baumgartner JB, Gateno J. Nonsurgical treatment of deformational plagiocephaly: a systematic review. *Arch. Pediatr. Adolesc. Med.* 2008;162(8):719-727.

8. Singh A, Wacogne I. What is the role of helmet therapy in positional plagiocephaly? *Arch. Dis. Child.* 2008;93(9):807-809.

9. Helmet therapy in infants with positional skull deformation: randomised controlled trial - Recent rapid responses. http://www.bmj.com/content/348/bmj.g2741?tab=responses. Accessed 26 May, 2014.

10. Naidoo SD, Cheng AL. Long-term satisfaction and parental decision making about treatment of deformational plagiocephaly. *J. Craniofac. Surg.* 2014;25(1):160-165.

11. Feijen M, Schuckman M, Habets E, van der Hulst R. Positional plagiocephaly and brachycephaly: is there a correlation between subjective and objective assessment of cranial shape? *J. Craniofac. Surg.* 2012;23(4):998-1001.

12. Katzel EB, Koltz PF, Sbitany H, Girotto JA. Treatment of plagiocephaly with helmet molding therapy: do actual results mimic perception? *Cleft Palate. Craniofac. J.* 2011;48(2):205-209.

13. Mullins CD, Vandigo J, Zheng Z, Wicks P. Patient-Centeredness in the Design of Clinical Trials. *Value Health.* 2014.

14. Hutchison BL, Stewart AW, Mitchell EA. Deformational plagiocephaly: a follow-up of head shape, parental concern and neurodevelopment at ages 3 and 4 years. *Arch. Dis. Child.* 2011;96(1):85-90.

15. Haynes RB, Devereaux PJ, Guyatt GH. Physicians' and patients' choices in evidence based practice. *BMJ.* 2002;324(7350):1350.

16. Lipira AB, Gordon S, Darvann TA, et al. Helmet versus active repositioning for plagiocephaly: a three-dimensional analysis. *Pediatrics.* 2010;126(4):e936-945.

17. Rothwell PM. External validity of randomised controlled trials: "To whom do the results of this trial apply?". *The Lancet.* 2005;365(9453):82-93.

18. Wilbrand JF, Wilbrand M, Malik CY, et al. Complications in helmet therapy. *J. Craniomaxillofac. Surg.* Jun 2012;40(4):341-346.

19. Lee WT, Richards K, Redhed J, Papay FA. A pneumatic orthotic cranial molding helmet for correcting positional plagiocephaly. *J. Craniofac. Surg.* 2006;17(1):139-144.

20. Littlefield TR, Beals SP, Manwaring KH, et al. Treatment of craniofacial asymmetry with dynamic orthotic cranioplasty. *J. Craniofac. Surg.* 1998;9(1):11-17; discussion 18-19.

21. Kluba S, Kraut W, Calgeer B, Reinert S, Krimmel M. Treatment of positional plagiocephaly - Helmet or no helmet? *J. Craniomaxillofac. Surg.* 2014;42(5):683-8

22. Govaert B, Michels A, Colla C, van der Hulst R. Molding therapy of positional plagiocephaly: subjective outcome and quality of life. *J. Craniofac. Surg.* 2008;19(1):56-58.

23. Steinbok P, Lam D, Singh S, Mortenson PA, Singhal A. Long-term outcome of infants with positional occipital plagiocephaly. *Childs Nerv. Syst.* 2007;23(11):1275-1283.

24. Brand PLP. Koppiekoppie. *Medisch Contact.* Vol 21; 2014:1068.

25. Shweikeh F, Nuno M, Danielpour M, Krieger MD, Drazin D. Positional plagiocephaly: an analysis of the literature on the effectiveness of current guidelines. *Neurosurg. Focus.* 2013; 35(4):E1.

26. Bialocerkowski AE, Vladusic SL, Howell SM. Conservative interventions for positional plagiocephaly: a systematic review. *Dev. Med. Child Neurol.* 2005;47(8):563-570.

27. Nederlands Centrum Jeugdgezondheid. *JGZ-richtlijn Preventie, signalering en aanpak van voorkeurshouding en schedelvervorming.* Utrecht: TNO innovation for life;2012.

28. Abel U, Koch A. The role of randomization in clinical studies: myths and beliefs. *J. Clin. Epidemiol.* 1999;52(6):487-497.

29. Dreyfuss D. Is it better to consent to an RCT or to care? Muetadeltaepsilonnu alphagammaalphanu ("nothing in excess"). *Intensive Care Med.* 2005;31(3):345-355.

30. King M, Nazareth I, Lampe F, et al. Impact of participant and physician intervention preferences on randomized trials: a systematic review. *JAMA.* 2005;293(9):1089-1099.

31. Macpherson H. Pragmatic clinical trials. *Complement. Ther. Med.* 2004;12(2-3):136-140.

32. Schwartz D, Lellouch J. Explanatory and pragmatic attitudes in therapeutical trials. *J. Chronic Dis.* 1967;20(8):637-648.

33. Porzsolt F, Eisemann M, Habs M, Wyer P. Form follows function: pragmatic controlled trials (PCTs) have to answer different questions and require different designs than randomized controlled trials (RCTs). *Z Gesundh Wiss.* 2013;21(3):307-313.

34. Weinstein SL, Dolan LA, Wright JG, Dobbs MB. Design of the Bracing in Adolescent Idiopathic Scoliosis Trial (BrAIST). *Spine (Phila Pa 1976).* 2013;38(21):1832-1841.

35. van Wijk RM, Boere-Boonekamp MM, Groothuis-Oudshoorn CG, van Vlimmeren LA, IJzerman MJ. HElmet therapy Assessment in infants with Deformed Skulls (HEADS): protocol for a randomised controlled trial. *Trials.* 2012;13:108.

36. Guyatt GH, DiCenso A, Farewell V, Willan A, Griffith L. Randomized trials versus observational studies in adolescent pregnancy prevention. *J. Clin. Epidemiol.* 2000;53(2):167-174.

37. McCambridge J, Witton J, Elbourne DR. Systematic review of the Hawthorne effect: New concepts are needed to study research participation effects. *J. Clin. Epidemiol.* 2014;67(3):267-277.

38. McCarney R, Warner J, Iliffe S, van Haselen R, Griffin M, Fisher P. The Hawthorne Effect: a randomised, controlled trial. *BMC Med. Res. Methodol.* 2007;7:30.

39. Odgaard-Jensen J, Vist GE, Timmer A, et al. Randomisation to protect against selection bias in healthcare trials. *Cochrane Database Syst. Rev.* 2011(4):MR000012.

40. Benson K, Hartz AJ. A comparison of observational studies and randomized, controlled trials. *N. Engl. J. Med.* 2000;342(25):1878-1886.

41. Rovers MM, Straatman H, Ingels K, van der Wilt GJ, van den Broek P, Zielhuis GA. Generalizability of trial results based on randomized versus nonrandomized allocation of OME infants to ventilation tubes or watchful waiting. *J. Clin. Epidemiol.* 2001;54(8):789-794.

42. Vist GE, Hagen KB, Devereaux PJ, Bryant D, Kristoffersen DT, Oxman AD. Systematic review to determine whether participation in a trial influences outcome. *BMJ.* 2005;330(7501):1175.

43. Concato J, Shah N, Horwitz RI. Randomized, controlled trials, observational studies, and the hierarchy of research designs. *N. Engl. J. Med.* 2000;342(25):1887-1892.

44. McKee M, Britton A, Black N, McPherson K, Sanderson C, Bain C. Methods in health services research. Interpreting the evidence: choosing between randomised and non-randomised studies. *BMJ.* 1999;319(7205):312-315.

45. Bower P, King M, Nazareth I, Lampe F, Sibbald B. Patient preferences in randomised controlled trials: conceptual framework and implications for research. *Soc. Sci. Med.* 2005;61(3):685-695.

46. Torgerson DJ, Klaber-Moffett J, Russell IT. Patient preferences in randomised trials: threat or opportunity? *J. Health Serv. Res. Policy.* 1996;1(4):194-197.

47. van Vlimmeren LA, van der Graaf Y, Boere-Boonekamp MM, L'Hoir MP, Helders PJ, Engelbert RH. Effect of pediatric physical therapy on deformational plagiocephaly in children with positional preference: a randomized controlled trial. *Arch. Pediatr. Adolesc. Med.* 2008; 162(8):712-718.

48. Hutchison BL, Stewart AW, De Chalain TB, Mitchell EA. A randomized controlled trial of positioning treatments in infants with positional head shape deformities. *Acta Paediatr.* 2010;99(10):1556-1560.

49. Koren A, Reece SM, Kahn-D'angelo L, Medeiros D. Parental information and behaviors and provider practices related to tummy time and back to sleep. *J. Pediatr. Health Care.* 2010; 24(4):222-230.

50. Collett BR. Helmet therapy for positional plagiocephaly and brachycephaly. *BMJ.* 2014;348:g2906.

SUMMARY / SAMENVATTING

SUMMARY

Background and aims of the dissertation

Positional skull deformation is a prevalent condition in infants under 6 months of age. Since parents were advised to put their baby's on their back to sleep to prevent sudden infants death syndrome, an increase of the prevalence of positional preference and skull deformation has been reported. Positional skull deformation (hereafter: skull deformation) can develop when infants show insufficient variation in lying positions, and is generally considered as a cosmetic condition. Most parents are concerned for their infant's future appearance when a deformation is diagnosed. The long-term consequences of skull deformation remain unclear, however the shape of the skull seems to improve when infants grow older. Despite, parental concern and anxiety may drive treatment trends.

The increasing prevalence of skull deformation in the 1990s caused an international interest in the condition's etiology and treatment option. After two decades it remains unclear what the best treatment plan is for infants with skull deformation. Pediatric physical therapy has been proven to be effective in young infants, however not all infants show full recovery. In infants with moderate or severe skull deformation at 5 to 6 months of age, often helmet therapy is started. A helmet is a cranial orthosis made up of a rigid plastic shell with a foam lining. The helmet is custom-made and fits closely to the infant's skull, but leaves room for the skull to grow at the flattened area.

Helmet therapy is a controversial treatment since there is no convincing evidence for its effectiveness and treatment is expensive. It is unknown on what basis healthcare professionals prescribe the treatment and parents start helmet therapy in their infants.

The primary aim of this dissertation was to provide a stronger evidence base for the treatment of skull deformation. A second aim was a better understanding of the decision for treatment by parents and preferences for treatment of professionals. This should lead to evidence-based decision-making by parents and professionals in the future regarding treatment for infants with skull deformation, more efficient health care, less infants with persistent skull deformation and less concerned parents. All aims of the dissertation were met in the HEADS (HElmet therapy Assessment in Deformed Skulls) study.

Study design

The design of the HEADS study fits the chain of care in treatment of skull deformation in infants (Figure 1) and is described in **chapter 2**. The study started as a large cohort study for infants aged two to four months with positional preference and/ or skull deformation. In this cohort, predictors for the effectiveness of pediatric physical therapy could be studied. After the first follow-up assessment at the age of five months a randomized controlled trial (RCT) started, in

which the effects of helmet therapy and the natural course of skull deformation were compared in infants with moderate or severe skull deformation. In parallel with the RCT, a non-randomized controlled trial (nRCT) was carried out. In this study the effects of treatment in daily clinical practice were determined and parents could start the preferred treatment for skull deformation (helmet therapy or awaiting natural course). Next to the effectiveness of treatment, treatment preferences of parents and professionals were explored in the HEADS study.
Nesting the RCT in a follow-up study made it possible to focus on various aspects of treatment and determine the generalizability of study outcomes.

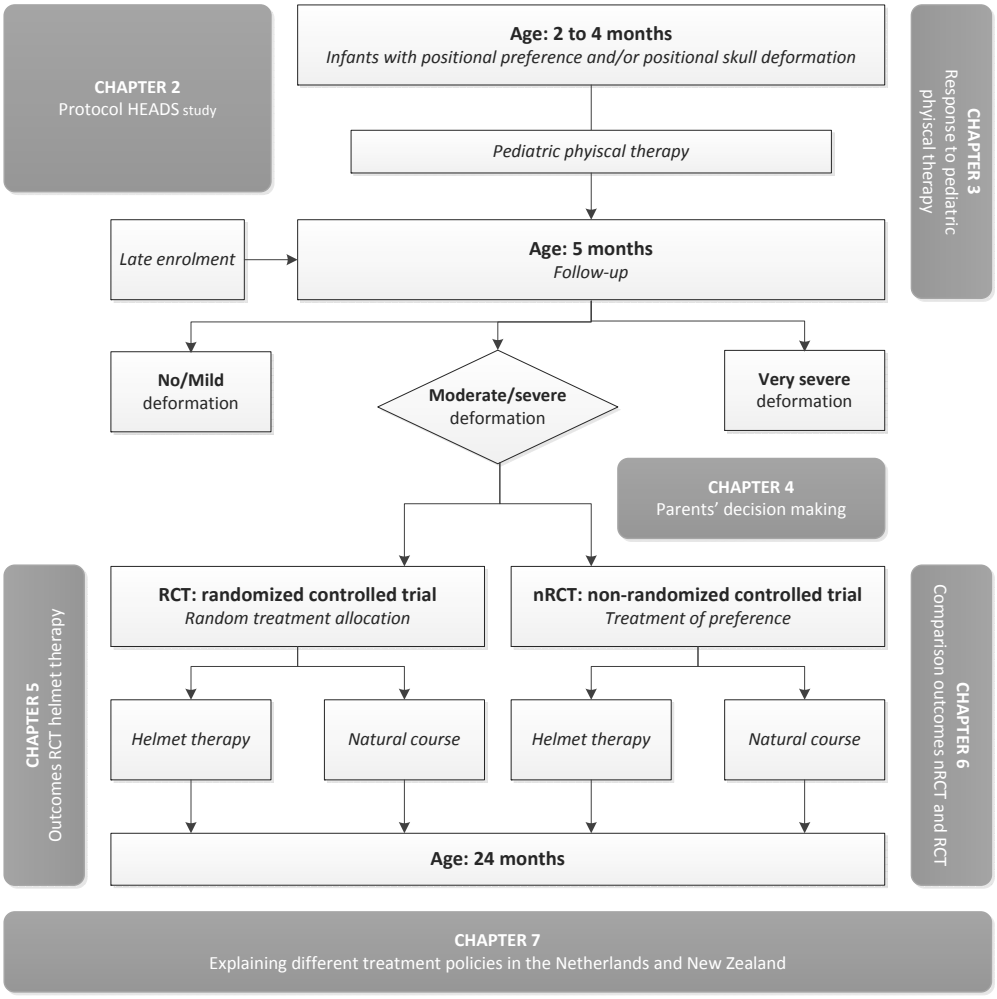


Figure 1. Flow chart HEADS study and thesis chapters

Pediatric physical therapy

In **chapter 3**, the results of a study into predictors for the response to pediatric physical therapy were described. In the HEADS study 657 infants with positional preference or skull deformation at 2 to 4 months of age started pediatric physical therapy and were followed up. At age 5 months, 45% of the infants presented with moderate or severe skull deformation. This group was compared to infants from the cohort who had no or mild skull deformation at 5 months of age. Infants presenting with skull deformation at baseline and infants who start therapy at an older age (>3 months) were more likely to respond poorly to treatment. An older age at the start of therapy allows less time for pediatric physical therapy to improve the infant's skull deformation. To reduce the possible burden of treatment of skull deformation for infants at a later age and prevent parental concern, infants with persistent positional preference or skull deformation should ideally be referred to the pediatric physical therapist before 3 months of age. Pediatric physical therapists should be alert to infants presenting with a clear skull deformation or infants of parents who are unsatisfied with their infant's appearance, since these infants are more likely to respond poorly to pediatric physical therapy.

Parents' decision making

Chapter 4 provides insights into parental decision-making for treatment of 5-month-old infants with skull deformation. Completed questionnaires of 186 parents were analyzed; 67 parents chose to start helmet therapy and 119 parents awaited the natural course. It is concluded that the parents' decision to start helmet therapy for their infant is mostly influenced by the expected additional value of helmet therapy compared to the natural course of skull deformation and their (dis)satisfaction with their infant's appearance. Contrary to what was expected, anxiety, decision uncertainty and the parents' perception of adverse events ultimately did not influence decision making.

Helmet therapy

In **chapter 5** the results of the first randomized controlled trial (n=84) comparing helmet therapy started at age 6 months, to the natural course of skull deformation were presented. In this study, 84 infants of with moderate or severe skull deformation at 5 to 6 months of age were randomized into the helmet therapy arm, or the natural course arm. Neither significant nor clinically meaningful differences in improvement of skull shape at 24 months of age were found. Parents of all infants in the helmet therapy group reported one or more side effects of treatment, like skin irritation, augmented sweating or feeling hindered in cuddling. No influence of the helmet on the infants' motor development, quality of life, sleeping, or crying was determined. Overall, parents in both groups were satisfied to very satisfied with the shape of their child's skull shape at 24 months of age. A cost study within the RCT, showed that the total costs per infant treated with

a helmet were substantially higher (n=20, €1401; £1157; $1935) than for infants in whom the natural course of skull deformation was awaited (n=14, €157). Based on the equal effectiveness of helmet therapy compared with the natural course, the high prevalence of side effects and the high costs of treatment, the use of helmet therapy is discouraged as a standard treatment for healthy infants with moderate or severe skull deformation.

The majority of eligible non-participants of the RCT were followed-up in the parallel non-randomized controlled trial (nRCT), that is described in **chapter 6**. In 265 infants in the nRCT, the real-world effects of helmet therapy (n=89) were compared to the natural course (n=176) when parents chose a preferred treatment option. The study population of both studies were comparable. Despite a better therapy compliance in the nRCT, the effects of treatment were comparable to the nRCT. Additionally, the combined sample of imputed RCT and nRCT data showed no relation of treatment with the change in skull shape. Only the severity of skull deformation at baseline was related to improvement in skull deformation; the more severe the deformation was at baseline, the more improvement in skull shape at 24 months. Costs in the nRCT were €1577 for helmet therapy and €177 for natural course.
It was concluded that the effects and costs of treatment in the real-world nRCT confirmed the findings of the RCT.

Healthcare professionals' views

Both nationally and internationally differences exist in the prescription of helmet therapy. In the Netherlands 1% to 2% of all infants received helmet therapy for positional skull deformation in the recent years while in New Zealand hardly any helmets are prescribed. Both countries show a comparable prevalence of the condition. In **chapter 7** we explored the reasons for this variation in therapy policy. In a study comparing the views of 387 healthcare professionals regarding positional skull deformation and its treatment between both countries, differences in beliefs and attitudes with regard to consequences of helmet therapy and the natural course of skull deformation were found. Healthcare professionals in New-Zealand (n=73) perceived the consequences of positional skull deformation and helmet therapy in infants younger than 1 year old as more burdensome, compared to the Dutch healthcare professionals (n=314). Next, according to healthcare professionals, New Zealand parents are more positive about the natural course than Dutch parents are. This could explain the different prescription rates in both countries. However no differences in expectations of recovery of helmet therapy or natural course could be determined. It is speculated that the differences in prescription rates might also relate to differences in the funding model of the health systems, dissimilarity in infants' health status and a contradictory evidence base in both countries with regard to skull deformation and treatment.

Discussion

The societal impact and implications of the evidence presented in this dissertation were discussed in **chapter 8**.

The study results of the RCT into helmet therapy has received significant media attention, both nationally and internationally. The responses from the various stakeholders were used in combination with the additional outcomes from the HEADS study to provide recommendation to implement study results. In the general discussion, it was concluded that the evidence presented in this dissertation should induce a shift from preference-based decision making for treatment of skull deformation at 5 to 6 months, towards evidence-based decision making in which helmet therapy is being discouraged. Healthcare professionals are being challenged to balance parental concern and dissatisfaction, with objective measures and evidence from research.

Furthermore, the majority of infants with a moderate or severe skull deformation at 5 months do not show full recovery at 2 years of age, irrespective of treatment modality. It was stated that a focus of attention is needed towards primary prevention, early detection and early treatment of positional preference and skull deformation using repositioning strategies. Predictors for outcome of pediatric physical therapy reported in this study can be used to increase the potential of this treatment. This should lead to fewer infants who develop skull deformation, less parental concern and anxiety and a decreased care consumption.

The nested study design of the HEADS study made it possible to assess the effectiveness of treatment in an RCT and allow robust comparison of the RCT results with real-world data. This design is recommended for future studies, aiming to compare different types of standard care.

This dissertation may affect decisions of parents, policymakers, insurance companies, and a wide range of clinicians such as pediatricians, general practitioners, youth healthcare professionals, pediatric physiotherapists, orthotists, pediatric neurosurgeons, and craniofacial surgeons, both nationally and internationally.

SAMENVATTING

Achtergrond en doelen van dit proefschrift

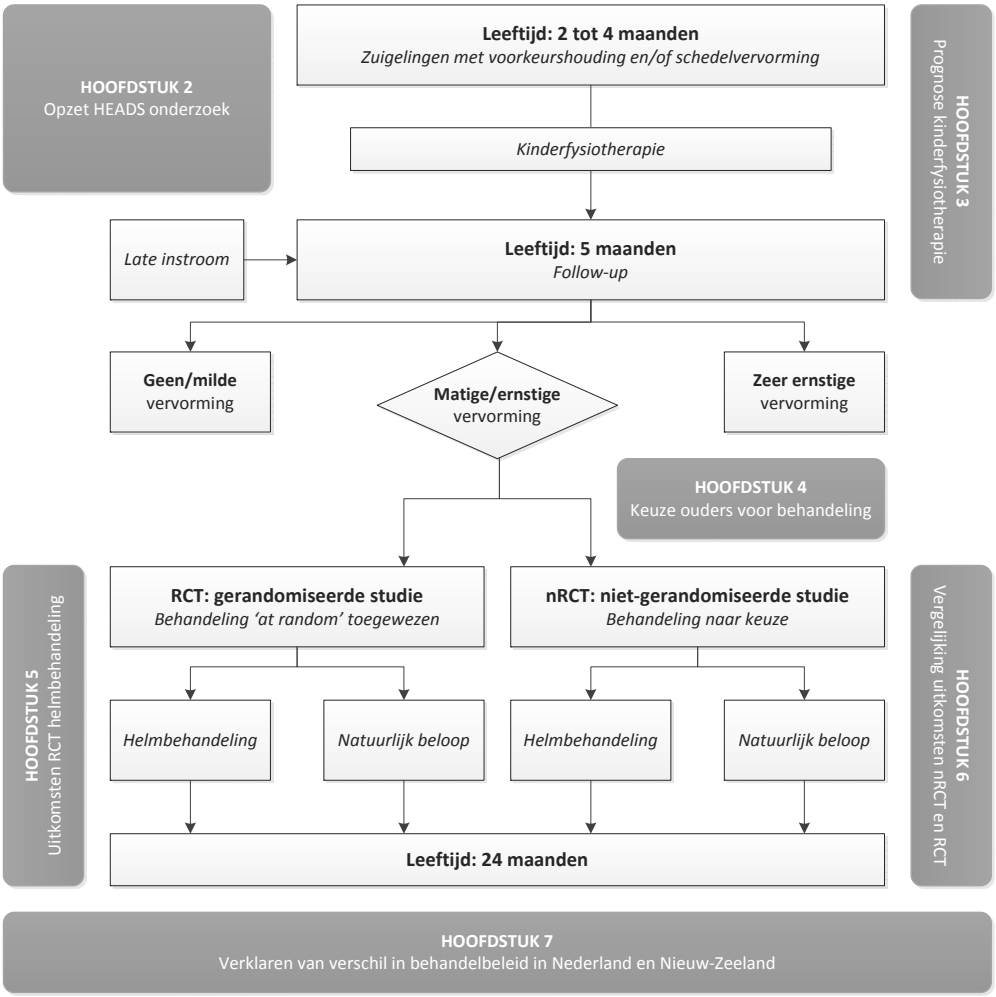
Positionele schedelvervorming komt vaak voor bij kinderen jonger dan 6 maanden. Na de invoering van het advies aan ouders om zuigelingen op de rug te laten slapen ter vermindering van het risico op wiegendood eind jaren '80, is het aantal gevallen van voorkeurshouding en schedelvervorming sterk toegenomen. Positionele schedelvervorming (hierna 'schedelvervorming') kan ontstaan door eenzijdige ligposities en wordt gezien als een cosmetisch probleem. Veel ouders van kinderen met schedelvervorming zijn bezorgd over het uiterlijk en de toekomst van hun kind, al zijn de consequenties voor het kind op de lange termijn nog niet bekend. Wel is uit onderzoek gebleken dat het natuurlijk beloop bij het merendeel van de kinderen gunstig is en de schedelvervorming bij de meeste kinderen verbetert. Desondanks zijn de zorgen en angsten van ouders vaak aanleiding om over te gaan tot behandeling.
De sterke toename van de prevalentie van schedelvervorming in de jaren '90 zorgde voor wereldwijde aandacht voor het ontstaan van deze aandoening en mogelijkheden tot behandeling. Twee decennia later blijkt er echter nog veel onduidelijkheid te bestaan over de meest optimale behandeling bij schedelvervorming. Kinderfysiotherapie is bewezen effectief bij jonge zuigelingen met een voorkeurshouding, maar niet bij alle kinderen kan schedelvervorming voorkomen of succesvol behandeld worden. Bij kinderen met een matige of ernstige schedelvervorming op de leeftijd van 5 tot 6 maanden wordt vaak gestart met helmbehandeling. De redressiehelm bestaat uit een harde kunststof buitenlaag en een zachte binnenlaag of binnenlagen. De helm wordt pasgemaakt op het hoofd van de zuigeling en sluit nauw aan op de schedel waar deze de gewenste vorm heeft, maar laat ruimte voor verdere schedelgroei op de plaats van de afplatting. De toepassing van de helm is controversieel: er is geen overtuigende evidentie voor de effectiviteit van de helm en de kosten van behandeling zijn hoog. Over de redenen waarom zorgprofessionals de helmbehandeling voorschrijven en ouders voor behandeling kiezen is nog weinig bekend.
Het hoofddoel van dit proefschrift was het bijdragen aan de evidentie voor de behandeling van schedelvervorming. Bijkomende doelen waren inzicht krijgen in de manier waarop ouders beslissen over het al dan niet starten met helmtherapie, en hoe behandelaars denken over de aanpak van schedelvervorming. De nieuwe kennis moet leiden tot evidence-based beslissingen voor behandeling, en daarmee tot effectievere en efficiëntere zorg. De doelen van dit proefschrift werden bereikt door uitvoering van het HEADS (HElmet therapy Assessment in Deformed Skulls) onderzoek.

Opzet van het onderzoek

De opzet van het HEADS onderzoek sluit aan bij de verschillende fasen in de keten van zorg bij zuigelingen met schedelvervorming (Figuur 1) en wordt beschreven in **hoofdstuk 2**. Het onderzoek startte als grote cohortstudie bij zuigelingen met een voorkeurshouding en/of schedelvervorming op de leeftijd van 2 tot 4 maanden. In dit cohort konden prognostische factoren voor de effectiviteit van kinderfysiotherapie worden onderzocht. Na de vervolgmeting bij 5 maanden, startte een gerandomiseerde, gecontroleerde studie (RCT) waarin de effectiviteit van helmbehandeling werd vergeleken met het natuurlijk beloop bij kinderen met matige tot ernstige schedelvervorming. De behandeling werd 'at random' toegewezen. Parallel aan de RCT werd een niet-gerandomiseerde, gecontroleerde studie (nRCT) uitgevoerd. In deze studie konden ouders zelf de behandeling van schedelvervorming kiezen (helmbehandeling of afwachten van het natuurlijk beloop), waarmee een inschatting van het effect van de helmbehandeling in de dagelijkse praktijk kon worden gegeven. Naast de effectiviteit van behandeling, werden de voorkeuren voor behandeling van ouders en behandelaars onderzocht.
Het inbedden van een RCT in een cohortstudie, maakte het mogelijk om diverse aspecten van de behandeling van schedelvervorming te bestuderen en uitspraken te doen over de generaliseerbaarheid van de studie uitkomsten.

Kinderfysiotherapie

In **hoofdstuk 3** worden de resultaten van een onderzoek naar voorspellers voor de effectiviteit van kinderfysiotherapie beschreven. Van de 657 zuigelingen die binnen het HEADS onderzoek vanaf de leeftijd van 2 tot 4 maanden voor voorkeurshouding en/of schedelvervorming werden behandeld door een kinderfysiotherapeut, had 45% op de leeftijd van 5 maanden nog een matige of ernstige schedelvervorming. Deze kinderen werden vergeleken met de kinderen uit het cohort die bij 5 maanden geen, of milde schedelvervorming hadden. Zuigelingen die bij de start van de behandeling al schedelvervorming hadden en zuigelingen die na de leeftijd van 3 maanden startten met kinderfysiotherapie, hadden minder kans op een goede uitkomst na de kinderfysiotherapie behandeling. Het later starten van de behandeling zorgde er voor dat de periode kinderfysiotherapie te kort was om effectief te kunnen zijn. Zuigelingen met voorkeurshouding en/of schedelvervorming zouden vóór de leeftijd van 3 maanden verwezen moeten worden naar de kinderfysiotherapeut om (helm)behandeling op latere leeftijd te voorkomen en zorgen van ouders te verminderen. Daarnaast moeten kinderfysiotherapeuten alert zijn op zuigelingen die bij aanvang van de therapie schedelvervorming hebben, aangezien deze kinderen minder kans hebben op herstel door kinderfysiotherapie.



Figuur 1. Flow chart HEADS onderzoek en hoofdstukken van dit proefschrift

Keuze voor behandeling door ouders

Hoofdstuk 4 geeft inzicht in hoe ouders de beslissing nemen voor de behandeling van schedelvervorming bij kinderen op de leeftijd van 5 à 6 maanden. Er werden gegevens van 186 ouders geanalyseerd; 67 ouders kozen om te starten met helmbehandeling en 119 ouders wachtten het natuurlijk beloop af. De conclusie was dat de keuze van ouders om te starten met helmbehandeling voornamelijk was gebaseerd op de verwachte toegevoegde waarde van de helm ten opzichte van het natuurlijk beloop en hun (on)tevredenheid met het uiterlijk van hun kind. In tegenstelling tot wat verwacht werd, hadden angstgeneigdheid, onzekerheid over de beslissing en perceptie met betrekking tot bijwerkingen uiteindelijk geen invloed op de keuze voor behandeling.

Helmbehandeling

De resultaten van wereldwijd de eerste RCT naar het effect van helmbehandeling vergeleken met het afwachten van het natuurlijk beloop, staan beschreven in **hoofdstuk 5**. In dit onderzoek zijn 84 zuigelingen met matige tot ernstige schedelvervorming op de leeftijd van 5 à 6 maanden 'at random' toegewezen aan een groep die helmbehandeling kreeg (n=42), of een groep waarbij het natuurlijk beloop werd afgewacht (n=42). Er werden geen significante of klinisch relevante verschillen tussen de groepen gevonden voor het herstel van de schedelvervorming op de leeftijd van 24 maanden. Van alle kinderen die helmbehandeling kregen, rapporteerden de ouders één of meer bijwerkingen van de helm, zoals huidirritatie, overmatig zweten of het niet kunnen knuffelen van hun kind. De behandeling had geen invloed op de motorische ontwikkeling, de kwaliteit van leven, het slapen of het huilen van het kind. Gemiddeld waren ouders in beide groepen van het onderzoek tevreden tot zeer tevreden over de vorm van het hoofd van hun kind op de leeftijd van 24 maanden. De RCT toonde tevens aan dat de totale kosten van behandeling per kind hoger waren voor de helm (n=20, €1401; £1157; $1935), dan voor het afwachten van het natuurlijk beloop (n=14, €157).
Omdat de helmbehandeling geen toegevoegde waarde ten opzichte van het natuurlijk beloop van schedelvervorming heeft, er veel bijwerkingen zijn en de therapiekosten hoog zijn, wordt het gebruik van de helm bij gezonde zuigelingen van 5 tot 6 maanden oud met matige tot ernstige schedelvervorming afgeraden.

De meeste zuigelingen met matige tot ernstige schedelvervorming op de leeftijd van 5 à 6 maanden in het HEADS onderzoek die niet deelnamen aan de RCT, zijn gevolgd in de parallel uitgevoerde nRCT die beschreven wordt in **hoofdstuk 6**. Bij 265 kinderen in de nRCT werd het effect van helmbehandeling (n=89) ten opzichte van het natuurlijk beloop (n=176) onderzocht in de dagelijkse praktijk, waarbij ouders zelf de keuze maakten voor een van beide opties. De onderzoekspopulatie van de nRCT was vergelijkbaar met de populatie die deelnam aan de RCT. Ondanks een hogere therapietrouw in de nRCT, waren de effecten van behandeling vergelijkbaar met die in de RCT. Analyse van samengevoegde data uit de RCT en de nRCT liet evenmin een toegevoegd effect van helmbehandeling op het natuurlijk beloop zien. Alleen de ernst van de schedelvervorming bij 6 maanden was gerelateerd aan de verbetering van de schedelvorm tussen 6 en 24 maanden; hoe groter de afwijking was bij 6 maanden, hoe groter de verbetering bij 24 maanden. In zowel de RCT als de nRCT bereikte het merendeel van de kinderen geen volledig herstel op de leeftijd 24 maanden. Toch waren de meeste ouders zeer tevreden met de vorm van het hoofd van kind, ongeacht de gevolgde behandeling. De kosten voor behandeling in de nRCT waren €1577 voor helmbehandeling (n=49) en €177 voor het afwachten van het natuurlijk beloop (n=36).
De effecten en kosten van behandeling die werden gevonden in de dagelijkse praktijk van de nRCT bevestigden de uitkomsten en conclusie van de RCT.

Mening van zorgprofessionals

Zowel nationaal, als internationaal, bestaan er verschillen in het voorschrijven van helmbehandeling. In Nederland ondergaat 1% tot 2% van alle zuigelingen helmbehandeling in verband met schedelvervorming. In Nieuw-Zeeland daarentegen, worden zelden helmen voorgeschreven, terwijl schedelvervorming in beide landen vrijwel even vaak voorkomt. In **hoofdstuk 7** staat beschreven hoe dit verschil in voorschrijfbeleid verklaard kan worden. In een vragenlijstonderzoek naar de mening van 387 zorgprofessionals over schedelvervorming en de behandeling ervan, zijn verschillen gevonden tussen beide landen in de overtuigingen en opvattingen met betrekking tot de gevolgen van helmbehandeling en het afwachten van het natuurlijk beloop van schedelvervorming. Zorgprofessionals in Nieuw-Zeeland (n=73) vonden de mogelijk nadelige gevolgen van schedelvervorming en van helmbehandeling bij kinderen jonger dan 1 jaar groter dan Nederlandse zorgprofessionals (n=314). Daarnaast was de mening van ouders over het afwachten van het natuurlijk beloop volgens Nieuw-Zeelandse zorgprofessionals positiever dan volgens de Nederlandse zorgprofessionals. Dit zou het verschil in behandelbeleid tussen beide landen kunnen verklaren. Er werd echter geen verschil gevonden in de verwachtingen over de mate van herstel bij de beide opties. Verondersteld wordt dat het verschil in het voorschrijven van behandeling ook beïnvloed kan zijn door de verschillende financieringssystemen voor zorg in beide landen, een verschillend niveau van de gezondheidsstatus van zuigelingen en tegenstrijdige uitkomsten van studies in beide landen op het gebied van schedelvervorming en de behandeling ervan.

Discussie

In **hoofdstuk 8** worden de maatschappelijke impact en de implicaties van dit proefschrift besproken. De publicatie over de resultaten van de RCT naar helmbehandeling heeft veel aandacht in zowel de nationale als de internationale media gekregen. De reacties op de publicatie zijn, samen met de uitkomsten van de verschillende studies van het HEADS onderzoek, gebruikt om aanbevelingen te formuleren om de studieresultaten te implementeren. In de algemene discussie van dit proefschrift wordt gesteld dat een omslag dient plaats te vinden van het kiezen van behandeling bij schedelvervorming op basis van persoonlijke voorkeur, naar het evidence-based beslissen voor behandeling. Hierbij wordt het gebruik van de helm bij gezonde zuigelingen van 5 tot 6 maanden met een matige of ernstige schedelvervorming afgeraden. De uitdaging van zorgprofessionals ligt in het bespreekbaar maken van de zorgen en verwachtingen van ouders en in aanvulling hierop goed uitleg geven van de waarde van helmbehandeling op basis van wetenschappelijk bewijs.

In het HEADS onderzoek is aangetoond dat de meerderheid van de kinderen die op de leeftijd van 5 à 6 maanden een matig tot ernstige schedelvervorming had, geen volledig herstel bereikt bij 24 maanden, ongeacht de behandeling. In de algemene discussie wordt daarom geconcludeerd dat onderzoekers en behandelaars zich moeten richten op primaire preventie, vroegtijdige opsporing en behandeling van voorkeurshouding en schedelvervorming door middel van houdings- en hanteringsadviezen. Hierbij kunnen de voorspellers voor de effectiviteit van kinderfysiotherapie gebruikt worden om het potentieel van de kinderfysiotherapeutische behandeling optimaal te benutten. Dit zou moeten leiden tot minder kinderen die schedelvervorming ontwikkelen, minder zorgen en angsten bij ouders en daarmee minder zorggebruik.

De studieopzet van het HEADS onderzoek, waarbij een RCT genest is in een cohort studie, maakte het mogelijk om uitspraken te doen over zowel de effectiviteit van behandeling als de generaliseerbaarheid ervan. Deze opzet wordt daarom aanbevolen voor toekomstige studies die gericht zijn op het vergelijken van bestaande behandelingen.

Dit proefschrift kan zowel nationaal als internationaal invloed hebben op de beslissingen van ouders, beleidsmakers, verzekeraars en een breed spectrum aan zorgprofessionals en specialisten: kinderartsen, huisartsen, jeugdartsen, jeugdverpleegkundigen, kinder- fysiotherapeuten, helmbehandelaars, kinderneurochirurgen en craniofaciale chirurgen.

DANKWOORD
(ACKNOWLEDGEMENTS)

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Aan het einde van de rit, is het tijd om terug te kijken. Hoe ben ik hier gekomen en dankzij wie? Dit alles begint bij de eerste gesprekken voor een promotieplek op de Universiteit Twente met mijn promotor Maarten IJzerman en co-promotoren Magda Boere-Boonekamp en Leo van Vlimmeren. Na, in mijn beleving, pittige maar zeker ook leuke gesprekken kwam uiteindelijk de vraag of ik wel helemaal uit Maastricht naar Enschede wilde komen voor deze baan; ja!

Twee maanden nadat ik begon, zou het onderzoek al van start moeten gaan en ik sprong op de rijdende trein die we 'HEADS study' noemden. Het hele HEADS onderzoek was een uitdagender project dan ik had kunnen vermoeden. Desondanks lieten jullie me zelfstandig aan de slag gaan, maar stonden jullie me bij waar nodig.

Magda, bedankt voor je oog voor detail, me laten zien wat goed onderzoek doen is, me vrij laten en zelf de weg laten zoeken, maar me ook weer de goede kant op wijzen als ik iets te kort door de bocht ging. Op de een of andere manier voelde dat nooit als een vervelende 'terechtwijzing', maar gewoon als verbetering.
Leo, je onuitputtelijke enthousiasme, relativeringsvermogen, denken in mogelijkheden in plaats van problemen, hebben me altijd erg gemotiveerd. Ik hoop dat ik hier iets van mee kan nemen; iemand wijzen op wat goed gaat, werkt zo veel stimulerender dan wijzen op onvolkomenheden. Naast dat jullie me veel geleerd hebben op zowel vakinhoudelijk als organisatorisch gebied, was het ook op persoonlijk vlak een hele fijne samenwerking. Ik vind het een voorrecht dat ik onder jullie begeleiding mijn promotieonderzoek heb kunnen uitvoeren.

Daarnaast heb ik getroffen met Maarten als mijn promotor. Jouw abstractieniveau en andere blik op de materie, zorgden er soms voor dat alles voor mijn gevoel even compleet op zijn kop stond, maar er daarmee wel een essentiële slag gemaakt was. Je hebt me ook goed uitgedaagd door de lat hoog te leggen; publiceren in BMJ is mogelijk. Punt. En dat was het. Daarnaast heb je er voor gezorgd dat, wat er ook gebeurde, wij op de vakgroep in alle rust ons werk konden doen. Bedankt hiervoor!

Ook wil ik de projectgroepleden Monique 'l Hoir en Kitty van der Ploeg bedanken voor de fijne samenwerking en jullie input bij zowel de opzet van het HEADS onderzoek als de artikelen waar jullie bij betrokken waren. Raoul Engelbert en Léon van Adrichem, bedankt dat jullie als projectadviseurs aan de wieg hebben gestaan van het HEADS onderzoek.

De leden van de leescommissie wil ik graag bedanken voor hun bereidheid om mijn proefschrift en de verdediging ervan op wetenschappelijke waarde te beoordelen.

Ank en Marjon, wat fijn dat jullie me bij willen staan tijdens mijn verdediging en alles daaromheen! Ank, nadat wij 12 jaar geleden als de twee onafscheidelijk krullenbollen Maastricht onveilig maakten, ben ik erg blij dat jij als mede-promovenda nu mijn paranimf bent. Marjon, ik vond het bijzonder om jouw paranimf te zijn toen jij promoveerde en het was eigenlijk bijna vanzelfsprekend dat je nu de mijne bent. Bedankt!

Zoals gezegd, toen ik begon aan mijn promotieonderzoek reed de HEADS trein al in volle gang. Ongetwijfeld aangestoken door Leo's enthousiasme, meldden zich al snel vele kinderfysiotherapeuten om deel te nemen aan het HEADS onderzoek. Kinderfysiotherapeuten werkzaam in zowel kleine als grote praktijken in Drenthe, Overijssel, de Achterhoek en Apeldoorn en Arnhem, bedankt dat jullie het onderzoek uit hebben willen voeren. Een zestal kinderfysiotherapeuten heeft daarnaast gedurende twee jaar op zaterdagen de metingen van kinderen van 2 jaar verzorgd. Mirjam Eggen-Navis, Annelies Eijsink, Maaike Pelsma, Brenda Pennings-Diepenbroek, Nicole Strikker-Fontijn, Germette Timmerman-Schaap, en de kinderfysiotherapeuten die (toen nog) in opleiding waren, heel erg bedankt voor jullie nooit aflatende inzet, het meedenken als het allemaal iets anders liep dan gepland en de vele leuke zaterdagen. Ook wil ik graag alle ouders die met hun kind hebben meegedaan aan ons onderzoek ontzettend bedanken. Gedurende een kleine twee jaar waren er verschillende meetmomenten en lange vragenlijsten, en ik ben jullie dankbaar dat jullie het er allemaal voor over hebben gehad. Hierdoor hebben we een fantastische studie neer kunnen zetten.

Terwijl het HEADS onderzoek liep, maakte ik ook kennis met de rest van de net opgerichte vakgroep Health Technology and Services Research waar ik werkte. Vanaf de start van HTSR heb ik de vakgroep zien groeien en heb ik mezelf kunnen ontwikkelen. Marjon, Joris en Janine waren mijn mede promovendi, hoewel Janine al snel de felbegeerde titel binnen had. Marjon, het was meteen twee handen op een buik; een voorliefde voor slechte grappen, M&M's en sport (ter compensatie van hiervoor genoemde) zorgde ervoor dat het nooit saai was op onze kamer. Met Rolf en Jorien kwam er al snel een goede lokale invloed op de vakgroep. Bedankt voor alle ontspanning naast het werk. Annelies en Joke, bedankt dat ik altijd even langs kon komen om stoom af te blazen, en bedankt voor jullie hulp tijdens het onderzoek. Uiteraard waren er meer fijne collega's; ik heb me altijd erg thuis gevoeld op de vakgroep.

Ondertussen werd het onderzoek steeds complexer en op een bepaald moment liepen er vijf verschillende meetmomenten tegelijkertijd. Dit project management was niet gelukt zonder student-assistenten; Annemieke, Marieke, Evelien, Marloes en Adrienne. Wat leuk dat drie van jullie zelfs collega's zijn geworden! Daarnaast bleek dat niet alleen ikzelf het onderzoek interessant vond, maar ook afstuderende studenten. Maar liefst elf afstudeerders hebben een deelonderzoek binnen het HEADS onderzoek uitgevoerd. Dit werkte erg stimulerend omdat jullie vaak in korte tijd snel vooruit wilden en het was soms een hele uitdaging om jullie daarin bij te houden.

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It seemed like there was never a dull moment, yet I felt the need to get more out of my PhD. Therefore, I explored the options to go abroad and visit Ed Mitchell and Lynne Hutchison in Auckland, New Zealand. I had been citing them quite regularly in my papers and hoped to learn more about skull deformation and the New Zealand approach of the problem. Ed, thank you for having me visit and work in your department, your critical research approach and humor. It is an honor that your are taking part in my graduation committee. Lynne, you helped me out with so much more than just setting up the study with me. From the ethics applications and the trips to the various healthcare professionals to helping me settle in Auckland, thank you for everything. It has been a pleasure working with you.

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CURRICULUM VITAE

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Renske van Wijk was born on October 5, 1983 in Oosterhout, the Netherlands. She attended the Sint Oelbert gymnasium in 1996 and obtained her secondary school diploma in 2002. The same year, she started studying General Health Sciences at Maastricht University with Movement Sciences as a major, and Physiotherapy at Hogeschool Zuyd, Heerlen as a minor. She carried out an internship at Adelante Zorggroep and wrote her bachelor thesis about the concurrent validity of arm hand motor function tests in stroke patients. She obtained a Bachelor of Science in General Health Sciences and a Bachelor of Physiotherapy in 2007. The results of this thesis were included in a publication in *Journal of Rehabilitation Medicine* (2010).

In 2007 she started the Master Physical Activity and Health at Maastricht University. She visited the National Stroke Research Institute in Melbourne, Australia from April until September 2008 for her research internship. She graduated in November 2008 and her thesis results were published in an article about the feasibility of early rehabilitation after stroke in *Neurorehabilitation and Neural Repair* (2012).

In February 2009, she started working as a PhD candidate at the department of Health Technology and Services Research at the University of Twente. Her PhD project 'Deformational plagiocephaly: effects and costs of helmet treatment and a wait-and-see regimen', was funded by the Netherlands Organization for Health Research and Development (ZonMw). In September 2011 she visited The Department of Paediatrics of The University of Auckland, New Zealand for three months. She compared care for infants with skull deformation in New Zealand with the Netherlands, and tried to explain the differences in care between both countries. From February 2013 until June 2014 she worked for the Health Sciences bachelor program at the University of Twente and coordinated the implementation of project based learning. In July 2014, she started working at the Innovation Cluster of the Center for Medical Imaging North East Netherlands.

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