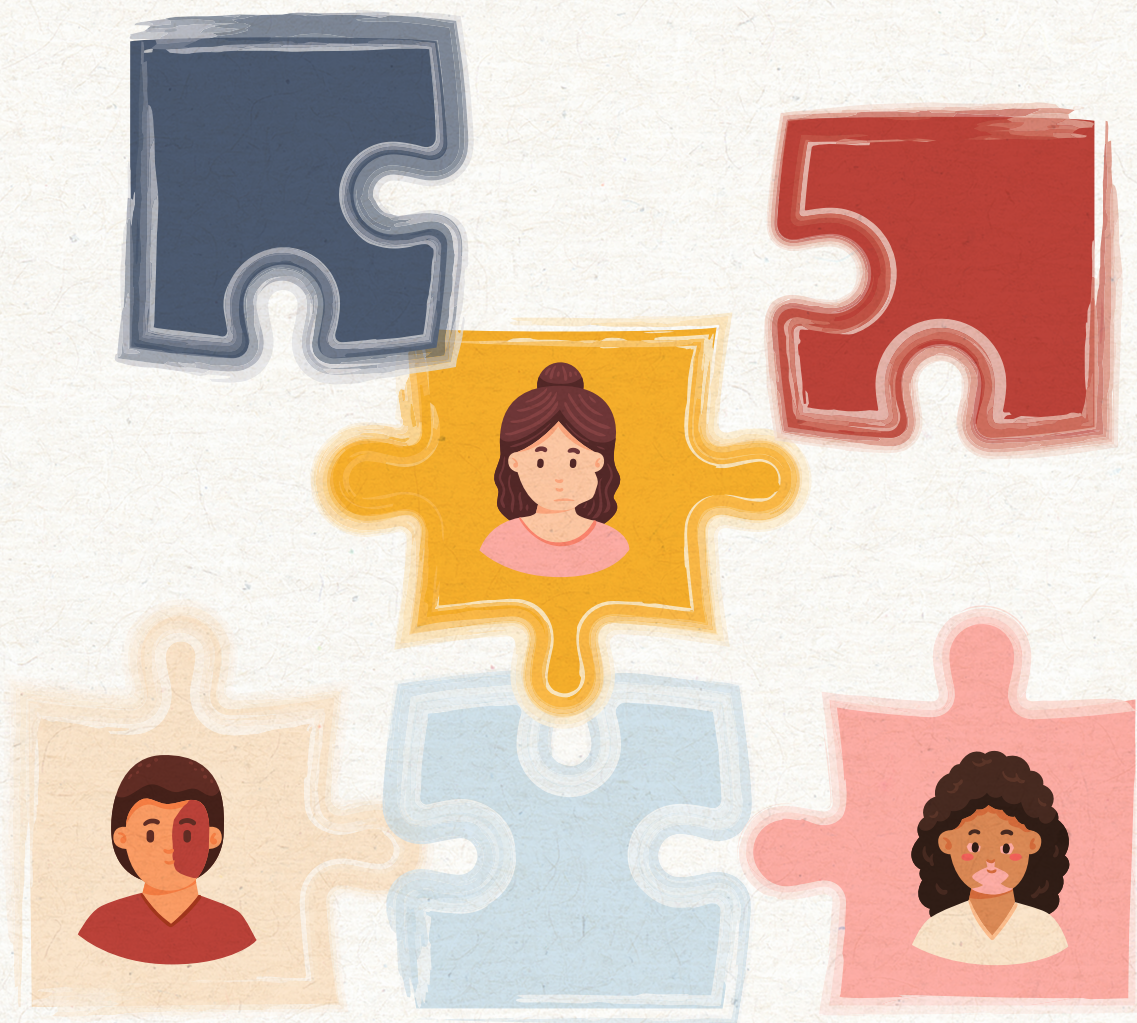


LIVING WITH A VISIBLE DIFFERENCE: Putting Together the Pieces of a Puzzle



Marije van Dalen

**Living with a Visible Difference:
Putting Together the Pieces of a Puzzle**

Leven met een zichtbare aandoening:
de legpuzzel compleet

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Leven met een zichtbare aandoening: de legpuzzel compleet

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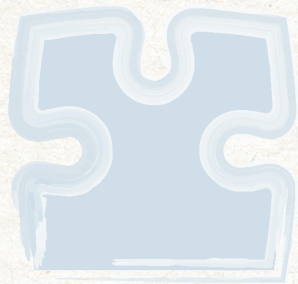
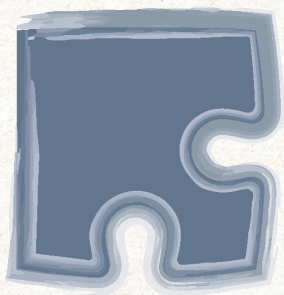
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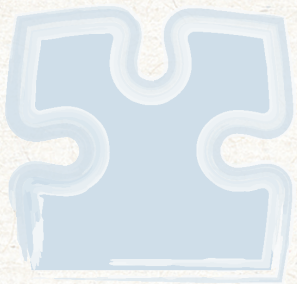
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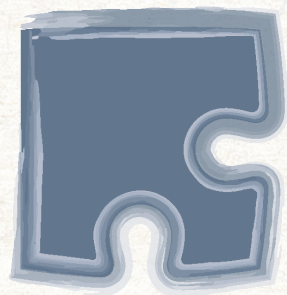
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CHAPTER 1

General introduction



Visible difference

The term visible difference covers a broad range of medical conditions or injuries that affect appearance. Visible differences can be congenital (i.e., cleft lip or craniosynostosis) or acquired later in life (i.e., burns or scars). Causes of visible differences can be divided into congenital conditions, skin conditions (i.e., psoriasis or acne), visible differences due to trauma (i.e., burns or scars), disease (i.e. cancer or meningitis) or medical treatment (i.e., surgery or radiotherapy).

There is no clear definition of what constitutes is a visible difference. As a result, a prevalence rate is hard to determine. Estimates are that 1 in 44 people have a visible difference on their face or body and that 1 in 111 people have a visible difference solely on their face (1). Around 1 in 124 children under 16 years old are said to have a visible difference (2). In The Netherlands, around 250.000 adolescents have a visible difference.

Lived experience

People with a visible difference commonly encounter challenging social situations and negative observer responses (3, 4). These include staring, unwanted comments and questions, teasing and bullying. As a consequence, people might avoid certain public places (2), social activities, such as going to parties, participating in sports and appearing in photos (5). Due to avoiding social activities, people might experience social isolation. Romantic concerns have also been reported (6-8).

The majority of people with a visible difference cope well, although around 30% report having psychological problems (9). These problems can be numerous, such as body image and self-esteem issues, anxiety and depression (10). These psychological problems are elaborated on later in this chapter.

Positive effects have also been reported. For instance, adults report having learned to place less value on appearance and more on other qualities people have, and becoming more resourceful and resilient (11).

Having a visible difference can also affect how people are perceived by others. For instance, children and adults with a visible difference are rated less favourably than those without a visible difference (12, 13). Children with a facial visible difference are rated as less likeable, less attractive, less happy, less good at school and less popular than children without a facial difference (13). Adults are rated as less honest, less employable, less trustworthy, less optimistic, less effective, less capable, less intelligent, less popular and less attractive (12).

In summary, living with a visible difference can severely impact one's life through adverse social experiences, negative observer responses and biases in others.

Consequently, many studies on psychosocial correlated of living with a visible difference have been done.

Severity of the condition or injury

The severity of a visible difference is often divided into the objective severity and subjective severity of a condition or injury. The objective severity, or objective visibility, is the severity as rated by medical professionals. The subjective severity, or subjective visibility, is the severity as rated by the person themselves or their caretakers. Intuitively, one might expect that the more visible a condition is, the more problems in psychological adjustment might be present. However, research has consistently shown that this is not the case for objective severity (14-21). Rather, a U-curve has been described, with people with a minor or very severe visible condition experiencing less psychological problems than people with a mild or average visible condition (14). The reason behind this is unclear, but it is hypothesised that observer responses are more unpredictable for people with a mild or average visible difference and that this causes psychological distress (14).

On the other hand, the subjective severity seems to be an important predictor of psychological problems (14, 16), with people experiencing their visible difference as highly visible consequently experiencing more psychological problems.

Psychosocial problems in children and adolescents living with a visible difference

Social environment. Living with a visible difference can have a critical impact on the social experiences of children and adolescents. For instance, the majority of children and adolescents with a visible difference report having been teased or bullied about their appearance, with estimates ranging from 43% to 75% (2, 22-25). However, there is also literature showing that children and adolescents with a craniofacial condition do not experience more teasing and bullying than unaffected peers (26).

Teasing or bullying has been found to occur more often in children or adolescents with a more severe visible difference (26) and additional medical or mental health problems (27). Children are most often bullied during primary school (23).

Being teased or bullied can influence how children and adolescents are perceived and can have negative consequences for psychological well-being. In the general population, children that are teased or bullied based on their appearance are perceived by classmates as less liked, less prosocial, less popular and less good looking (28). For people with a visible difference, teasing and bullying often has a negative influence and can be hurtful in nature (29). Furthermore, a quarter of children with burns report headaches or stomach-aches as a result of bullying (24).

Positive outcomes with regards to social experiences have also been reported, with adolescents with a visible cleft reporting more positive perceptions of close friendships and social acceptance (30) and boys with a cleft reporting fewer peer problems (27) when compared to unaffected peers.

Stigmatisation. Stigmatisation refers to *“the act of treating someone or something unfairly by publicly disapproving of them”* (31). These acts can be small (i.e., avoiding looking at people) or bigger and more overt (i.e., laughing or staring at people). Stigmatising behaviour consists of three facets, namely: confused or staring behaviour, hostile behaviour and an absence of friendly behaviour (32). These facets can be seen as reflecting social discomfort, social rejection and social acceptance respectively (33).

A large majority of children and adolescents with a facial visible difference experience stigmatising behaviour (34, 35), such as being stared at or hearing others talk about their appearance. Older children and children with a larger facial difference experience more stigmatising behaviour than younger children or children with a smaller facial difference (34). Furthermore, parents report significantly more absence of friendly behaviour and more hostile behaviour towards their children than parents of children without a visible difference (34).

Studies differ on whether the amount of perceived stigmatisation differs per gender. Strauss, Ramsey (35) found that girls report more stigmatisation than males. More recent work, however, did not replicate this finding (36). Studies did show that children who experience more stigmatisation are at risk for internalising behaviour problems, a lower health-related quality of life (37), dissatisfaction with facial appearance and body image disturbances (36).

Body Image. Body image is defined as *“a person’s perceptions, thoughts and feelings about his or her body”* (38). Body image embodies both the negative and positive aspects. Body dissatisfaction focuses on the negative aspects and is said to be *“a person’s negative thoughts and feelings about his or her body”* (38).

Body dissatisfaction has been shown to be related to negative psychosocial outcomes, such as (social) anxiety in adolescents (39) and college women (40). Furthermore, more body image disturbance, body dissatisfaction, body importance, and body change strategies to increase muscularity have all been linked to depressive symptoms in adolescence (41, 42).

Body dissatisfaction is very common in adolescence in general. In their study, Dion, Blackburn (43) found that in underweight girls, 37.5% of girls were dissatisfied with their body shape. For all other weight categories, the proportion of adolescents dissatisfied with their body shape ranged from 60.8 to 100%. So, the majority of

adolescents experience body dissatisfaction and are potentially at risk for a range of adverse psychosocial outcomes associated with body dissatisfaction (39-42).

Literature assessing body image and body dissatisfaction in people with a visible difference is mixed. When adults with a visible difference are compared to adults with an invisible mental illness, the former group experiences a more positive body image (44). For adolescents with craniofacial conditions, body image seems to be similar to non-affected peers (45). However, adolescent girls with a craniofacial condition report more appearance concerns and, when compared to boys with this condition, score in the clinical range for body image disturbance more often (36). In contrast to adolescents with craniofacial conditions, adolescents with acne experience a poorer body image when compared to unaffected peers (46).

Mental health. Literature on mental health in children and adolescents with a visible difference is mixed and lacks a clear overview. However, there are indications that these children and adolescents can experience internalising problems (10). For this reason we conducted meta-analysis, as described in **chapter 2** of this thesis.

Literature shows that the most common reasons for a referral to mental healthcare are problems with low self-esteem/confidence, experiencing or worrying about teasing, bullying or staring, body image/appearance concerns and social anxiety/avoidance (10). In adolescents depression or general low mood are frequent indications for referral. As the social environment, stigmatisation and body image have been described previously in this chapter, the next part focuses on (social) anxiety and depression.

(Social) anxiety. Studies on anxiety problems in general found higher anxiety levels for children and adolescents with alopecia areata (47), hirsutism (48), neurofibromatosis type 1 (NF1) (49) when compared to unaffected peers. Other studies did not find a difference for children and adolescents with acne (19), vitiligo (50), alopecia areata (48), atopic eczema (51), cleft lip and/or palate (25), port wine stain (52) and prominent ears (52). However, studies often included small study samples and had lacked power. So no firm conclusions regarding levels of anxiety can be drawn from these studies.

Regarding social anxiety in adolescents with a visible difference, little research has been conducted. This is remarkable, since in clinical practice, social anxiety is highly prevalent in adolescents with a visible difference. For adolescents with NF1 no differences in social anxiety were observed, when compared to peers (49). In adolescents with craniofacial conditions, adolescents with lower social competence experience more social anxiety (53). However, these studies included 24 and 15 participants respectively, so results must be interpreted with extreme caution.

Depressive symptoms. Study results on depressive symptoms in children and adolescents with a visible difference are mixed. When compared to unaffected peers, higher rates of depressive symptoms have been found in children, but not adolescents, with vitiligo (50), children, but not adolescents, with alopecia areata (47), adolescents with atopic eczema (51) and children and adolescents with a cleft lip and/or palate (25). A meta-analysis showed that children and adolescents with atopic dermatitis were more likely to be diagnosed with depression than unaffected peers (54). Conversely, no difference in depressive symptoms have been found for children and adolescents with alopecia areata (48), adolescents with hirsutism (55), children with a port-wine stain (52) and children with prominent ears (52).

As with studies on anxiety, study samples often are small and studies thus lack power. More research is needed to determine the prevalence of depression in children and adolescents with a visible difference. This is why we conducted a meta-analysis in **chapter 2**.

Externalising problems. Studies on externalising problems in children have mainly used the Child Behaviour Checklist (CBCL) (56) and, in adolescents, the Strengths and Difficulties Questionnaire (SDQ) (57). These studies have yielded mixed results. When compared to normative data, more externalising problems have been found in adolescents with a cleft (25). Similar externalising problems have been found in pre-schoolers with craniofacial microsomia (58), children with craniofacial microsomia (59), children with a cleft (27), children with a congenital melanocytic nevus (60), children with port-wine stains or prominent ears (52), children with atopic eczema (20), children with chronic idiopathic urticarial (61), children with a range of facial differences (37), adolescents with a range of craniofacial anomalies (62) and adolescents with moebius syndrome (63). And lastly, fewer externalising problems have been reported in children with a range of craniofacial anomalies (62) and in adolescents with a cleft (64).

In sum, evidence seems to point towards similar levels of externalising problems for children and adolescents with a visible difference when compared to normative data. This thesis presents study outcomes on emotional and behavioural problems in children with a visible difference in **chapter 3**.

Available interventions

While research has shown that people with a visible difference may experience adverse psychosocial outcomes, there is a dearth of evidence-based interventions. This is true both for interventions aimed at adults (65-67) and adolescents (68). However, research often lacks a solid design and has low overall methodological quality, yielding small effect sizes. The paucity of literature available offers some support for interventions involving Social Skills Training (SST), Cognitive Behavioural

Therapy (CBT; 65, 67, 68) and techniques for managing anxiety (66). After starting work on this thesis, Acceptance and Commitment Therapy has also been argued to be effective in addressing appearance-related distress (69).

Young People Face IT

In an attempt to teach adolescents with a visible difference adaptive coping skills through an effective intervention focussing on improving emotional resilience, Young People's (YP) Face IT was developed. YP Face IT (Dutch: *Face IT voor jongeren*) was developed in the UK, in collaboration with adolescents, clinical experts and the charity Changing Faces (70). It is a self-help intervention aimed at helping adolescents cope with some of the main problems they may experience, such as anxiety, depression, low self-esteem and appearance-related distress. YP Face IT was based on an intervention for adults, named Face IT (71), which was proven to be effective at reducing anxiety, depression and appearance concerns (71).

YP Face IT combines SST with CBT. The intervention consists of seven weekly sessions and an additional booster session after six weeks, repeating what the adolescent has learned during the weekly sessions. Sessions 1-3 sessions focus on improving social skills using SST, sessions 4-6 focus on unhelpful thoughts and behaviours using CBT techniques and session 7 is a summary of all learned techniques. Session 8 is a booster quiz, six weeks after session 7. The entire intervention takes 13 weeks to complete.

Each session consists of different exercises, videos and activities and takes 45-60 minutes to complete. In addition to the weekly sessions, adolescents are asked to complete small homework assignments between sessions. These take about 10 minutes to complete and help adolescents practice the techniques discussed in the sessions. Participants have access to an online journal in which they can write about their experiences and answer the homework assignments.

YP Face IT is designed as a self-help program for adolescents with subclinical psychological symptoms. Answers to homework assignments and progress in the session is monitored in the background by a psychologist. Should an adolescents experience acute psychological symptoms, possibly reflecting a psychological disorder, the psychologist can intervene and refer to other, more appropriate care.

In an acceptability and feasibility study in the UK, the intervention was found to be acceptable, with most of the adolescents thinking it would help improve their confidence and self-acceptance and help develop new skills in dealing with difficult social situations (70). However, a study amongst adolescents with burns in the USA (72) reported that despite experiencing appearance-related distress, motivation to

complete YP Face IT was low. Parents have reported that YP Face IT can help them in starting conversations around appearance-related issues (73).

As part of this thesis, YP Face IT was translated to Dutch and named *Face IT voor jongeren*. A screenshot of the homepage is shown in Figure 1. Part II of the current thesis focuses on testing the acceptability and feasibility (**chapter 4**), and effectivity (**chapters 5 & 6**) of this intervention for Dutch adolescents.

Parenting a child with a visible difference

Studying the family is important as a visible difference or medical condition impacts the entire family (74). Furthermore, parents and children can also influence each other. For instance, children of parents with more parenting stress are reported to have more externalising symptoms (75). A bidirectional relationship between parenting stress and child behaviour problems has also been confirmed (76).

Parents of children with a visible difference face several challenges. They may have to face medical treatment and possible hospitalizations of their child and have to cope with negative social feedback related to the child's appearance (77, 78). This may upset parents and cause stress (79, 80) (80). Regarding parents of children with a chronic illness, meta-analyses (81, 82) showed that these parents experience more parenting stress, anxiety and depression compared to parents of healthy children or compared to normative data.

Parents of children with a visible difference also report adverse psychosocial outcomes. Qualitative studies have also shown that having a child with a skin condition can affect parents' decision to have more children (79). Also, 66% of parents experience comments from strangers (83) and experience distress in relation to their child's medical condition (84). In a study of mothers with a child with a cleft lip and palate evidence of psychological distress was found in 38% of mothers (85). Evidence of severe psychological problems was found in 24% of mothers. Furthermore, mothers of children with burns experience more psychopathology than mothers of unaffected children (86). Contrasting findings have been reported by Berger and Dalton (87). They showed that parents of adolescents with a cleft lip did not differ from other parents on psychological well-being.

Although there is evidence to indicate that parents of children with a visible difference are at risk for adverse psychosocial outcomes, there is a paucity of interventions. A recent review found only 15 studies on interventions for parents of a child with a visible difference (88), with 12 reporting positive outcomes of the intervention studied.

Figure 1. Screenshot of the Face IT voor jongeren homepage

FACE IT VOOR JONGEREN
Online support voor jongeren met aandoeningen of ietsel wat hun uiterlijk beïnvloedt

home | over | sessies | forum | team | ouders | professionals | contact | links

login

NU MEEDOEN
Als je mee wilt doen aan onderzoek om deze website te testen, neem contact op met:
face.it.voor.jongeren@erasmusmc.nl

Over
Deze website is ontworpen door jongeren en gebruikt verschillende activiteiten, illustraties, foto's, video's en adviezen van jongeren met een zichtbare aandoening.
lezen

Begin nu!
Beginnen is makkelijk en simpel. Als je jonger bent dan 18 jaar, hebben we toestemming voor je deelname nodig van je ouders of verzorgers.
lezen

Forum
Dit is een plek waar je andere jongeren met een zichtbare aandoening kunt ontmoeten en ervaringen kunt delen. Je kunt je ervaringen van Face IT voor jongeren delen, praten over zorgen die je hebt of anderen steunen in hun zorgen.
lezen

Beoordelen
Ik denk dat Face IT voor jongeren echt kan helpen. Het is geweldig dat jongeren vaardigheden geleerd worden om hun zelfvertrouwen in sociale situaties te vergroten en om te horen over anderen met dezelfde zorgen die hun problemen hebben overwonnen.
Amanda Redding, 17 jaar
volgende

afspelen **afspelen** **afspelen**

sessie 1 Veel voorkomende problemen	sessie 2 Verbeter je sociale vaardigheden	sessie 3 Wees niet angstig, begin een gesprek	sessie 4 Denken, voelen, doen
sessie 5 SMART doelen	sessie 6 Overwin je angst	sessie 7 Je vooruitgang bekijken	sessie 8 Face IT voor jongeren quiz

Face IT is er om jou te helpen. | We horen graag van jou: | T: 010-7037251 | E: face.it.voor.jongeren@erasmusmc.nl

In summary, parents of children with a visible difference can be at risk for experiencing psychosocial problems. However, studies on this topic are scarce and more research is needed to determine the etiology of psychological problems and the ways in which parents should receive psychosocial support. Therefore, we conducted a study to assess distress and parenting stress in a large sample of parents of a child with a visible difference (**chapter 7**).

Aims and outline of this thesis

The overall aim of this thesis is to study psychological problems in children and adolescents with a visible difference and their parents. A second aim is to improve psychological well-being of adolescents with a visible difference through the online psychological intervention, YP Face IT.

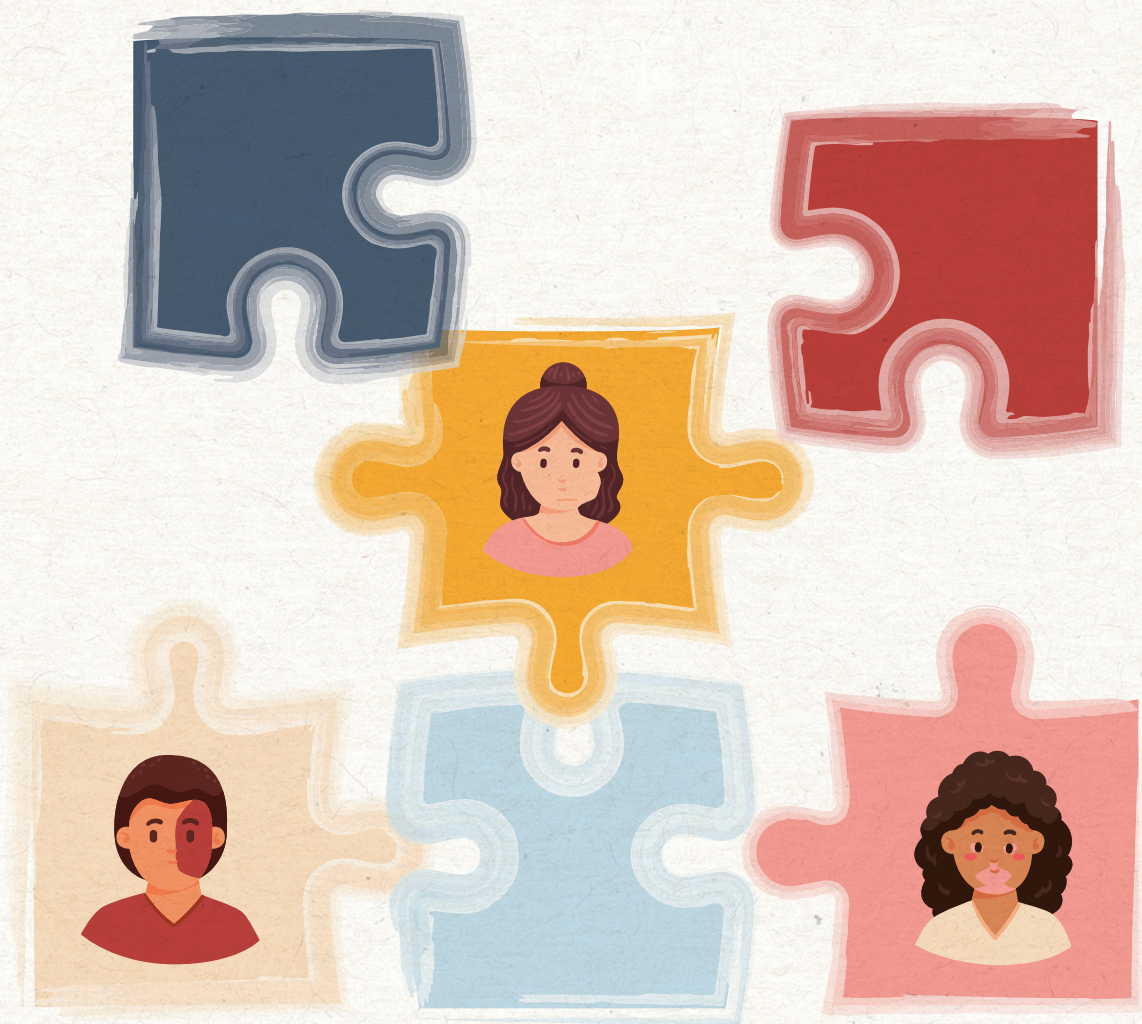
This thesis consists of three parts. **Part I** focuses on the psychosocial problems of children and adolescents living with a visible difference. **Chapter 2** outlines a systematic review and meta-analysis into the prevalence of symptoms of anxiety and depression in adolescents with a visible difference. The aim of this study was to assess whether adolescents with a visible difference experienced more symptoms of anxiety and depression than unaffected peers. **Chapter 3** describes a cross-sectional study into emotional and behavioural problems in children with a cleft lip with or without palate or children with a visible infantile haemangioma. The aim was to assess whether these children exhibited more emotional and behavioural problems than children of the same age and gender. Furthermore, we aimed to understand what factors influenced these emotional and behavioural problems.

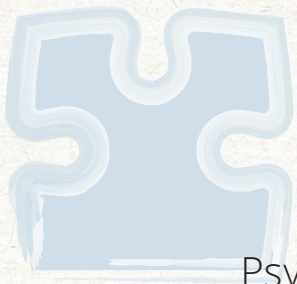
Next, **part II** describes studies on the Dutch version of YP Face IT (*Face IT voor jongeren*). **Chapter 4** describes a qualitative acceptability and feasibility study on YP Face IT. We sought to understand whether YP Face IT was acceptable and feasible to Dutch adolescents. More specifically, we sought their opinion on the therapeutic content of YP Face IT, structure and presentation of YP Face IT, usefulness of YP Face IT and on study procedures. **Chapter 5** describes the trial design for a Randomised Controlled Trial (RCT) on YP Face IT. **Chapter 6** describes the results of this RCT, combined with data from a similar Norwegian RCT. In this chapter we sought to assess whether YP Face IT was effective at improving body esteem in Dutch and Norwegian adolescents.

Finally, **part III** focuses on parents of a child with a visible difference. **Chapter 7** describes the results of a cross-sectional study on distress and parenting stress in parents of children with a cleft lip with or without palate or visible infantile haemangioma. We aimed to assess whether these parents experience more distress

and parenting stress than parents in the general population. Furthermore, we aimed to assess what factors influence the severity of distress and parenting stress.

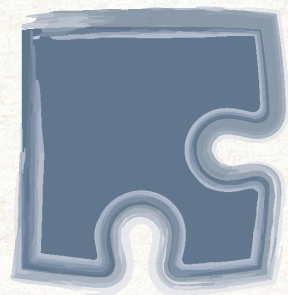
Chapter 8 presents a general discussion of the findings presented in this thesis, including the clinical implications and suggestions for future studies.

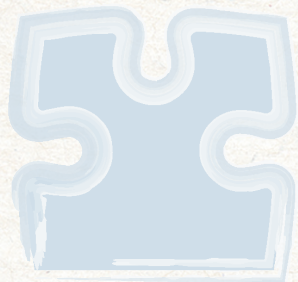
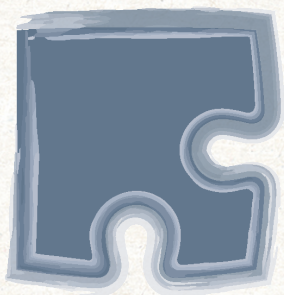




PART I

Psychosocial correlates in children and adolescents with a visible difference





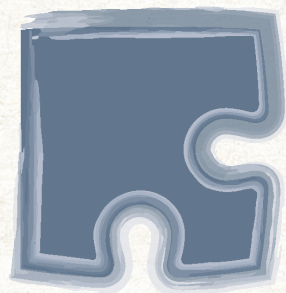


CHAPTER 2

Anxiety and depression in adolescents with a visible difference: a systematic review and meta-analysis

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Body Image, 2020, 33, 38-46



Abstract

Living with a visible difference can entail challenging social situations, associated with psychosocial symptoms. However, it is not clear whether adolescents with a visible difference experience more anxiety and depression than unaffected peers. We aim to determine whether adolescents with a visible difference experience more symptoms of anxiety and depression than unaffected peers. A literature search was conducted in Embase, Medline Ovid, Web of Science, Cochrane CENTRAL, PsycINFO Ovid, and Google Scholar. Meta-analyses were done using random-effects models to calculate a standardised mean difference. Analyses for subgroups were used to study causes of visible difference. Eleven studies were identified ($n = 1075$, weighted mean age = 15.80). Compared to unaffected peers, adolescents with a visible difference experience more symptoms of anxiety (SMD = 0.253, 95% CI [0.024, 0.482], $p = .030$), but not depression (SMD = 0.236, 95% CI [-0.126, 0.599], $p = .202$). Adolescents with a skin condition did not experience more symptoms of anxiety (SMD = 0.149, 95% CI [-0.070, 0.369], $p = .182$) or depression (SMD = 0.090, 95% CI [-0.082, 0.262], $p = .305$) when compared to unaffected peers. Overall, more symptoms of anxiety are found in adolescents with a visible difference compared to peers. No differences in anxiety or depression were found for skin differences. Screening for anxiety is recommended.

Keywords: Anxiety/Anxiety disorders; Depression; Visible differences; SAD/social anxiety disorder/social phobia.

1. Introduction

Approximately 1 in 44 people have a condition or injury that results in a socially undesirable impact on their physical appearance (1). These appearance altering conditions are often referred to as a visible difference or disfigurement and can result from congenital conditions (e.g., cleft lip and palate, craniofacial conditions), skin conditions (e.g., vitiligo, psoriasis and acne), trauma (e.g., burns, scars), disease (e.g., cancer, meningitis and alopecia areata) or medical treatment (e.g., surgery or radiotherapy). The term visible difference is a relatively new term, with the first mention in the literature occurring in 2004 (9).

One important aspect in visible differences is negative observer responses. Having a visible difference can lead to challenging social situations and negative observer responses, such as staring, teasing, and receiving unwanted comments (4, 34). These experiences can be distressing, and individuals often develop a fear of being negatively evaluated based on their appearance (89). This can result in avoidance of social activities such as going to parties, participating in sports and appearing in photos (5). Concerns around developing romantic relationships can also greatly impact self-esteem in adolescents and adults with a visible difference (8). Furthermore, a study by Moss (14) shows that the severity of the visible difference is not directly related to the amount of psychological distress. Rather, the subjective severity of the visible difference predicts psychological distress.

A possible consequence of negative observer responses are symptoms of anxiety and depression. In the general population, anxiety and depression are the second and third most common disorders in adolescence (90) and are thus considered a major cause for mental health-related disability. A review of prevalence rates shows a mean prevalence of 10.7% for anxiety and 6.1% for depressive disorders in adolescence (90). However, 12-month prevalence rates as high as 8.2% for depression and 24.9% for anxiety in adolescence have been reported (91). Also, prevalence rates of depression and anxiety disorders seem to increase throughout childhood and adolescence (92, 93), with girls experiencing more anxiety and depression (94). Being diagnosed with an anxiety or depressive disorder in childhood can also have implications for adulthood. For instance, studies show that depression in adolescence predicts depression in adulthood, as do some types of anxiety disorders (95).

Another important aspect of visible differences in adolescence is body image. Body dissatisfaction, the discrepancy between the perceived body shape and the ideal body shape, is very common in adolescence (43). In their study, Dion et al. (43) found that in underweight girls, 62.5% of girls were satisfied with their body shape. For all other weight categories, the proportion of adolescents satisfied with their

body shape ranged from 39.2% to 0%. So, the majority of adolescents experience body dissatisfaction. Body dissatisfaction has been shown to be related to negative psychosocial outcomes, such as (social) anxiety in adolescents (39) and college women (40). Furthermore, a greater body image disturbance, body dissatisfaction, body importance, and body change strategies to increase muscularity, sex, and stress have all been linked to depressive symptoms in adolescence (41, 42).

Literature assessing body image in visible differences is mixed. For adolescents with craniofacial conditions, body image seems to be similar to non-affected peers (45). On the other hand, adolescents with acne experience a poorer body image when compared to peers (46). When adults with a visible difference are compared to adults with an invisible mental illness, the former group experiences a more positive body image (44), indicating that a nonvisible condition might be associated with a poorer body image than a visible condition. In sum, a poor body image is related to anxiety and depression. However, it remains debatable whether the body image of adolescents with a visible difference is negatively affected by their appearance.

In a European survey concerning visible difference, 116 psychosocial specialists from 15 countries reported that up to 83% of their referrals for adolescents with a visible difference were related to social anxiety and up to 79% of referrals were related to depressed mood (10). In an adult sample of 458 persons with a visible difference from 15 outpatient clinics in the United Kingdom, 48% experienced subclinical or clinical symptoms of anxiety and up to 27.5% experienced subclinical or clinical symptoms of depression (5). In this study, persons attending burns, eye, and hand clinics had the lowest anxiety scores, while persons seeking elective plastic surgery had the highest anxiety scores. Furthermore, hand patients had the lowest depression scores, while persons seeking elective plastic surgery had the highest depression scores.

When looking at symptoms of anxiety and depression in adolescents, studies are inconsistent. Studies have either reported no significant differences between adolescents with a visible difference and unaffected peers (e.g. 19, 96) or significantly more anxiety and depressive symptoms in adolescents with a visible difference when compared to unaffected peers (e.g. 51, 97).

In sum, depression and anxiety are common psychological disorders. However, due to inconsistent findings, the question of whether adolescents with a visible difference experience more anxiety and depressive symptoms than unaffected peers has not been systematically explored. Therefore, the aim of the current meta-analysis is 1) to determine whether adolescents (12 – 18 years old) with a visible difference suffer more symptoms of anxiety and depression than unaffected peers

and 2) to determine the influence of the cause of visible difference on anxiety and depression in these adolescents.

This meta-analysis can contribute to the knowledge regarding the psychosocial impact of having a visible difference. To date, it is not known whether adolescents with a visible difference resulting from a wide variety of conditions and injuries, present with the same psychosocial symptoms, or whether this differs by cause of visible difference.

2. Method

This meta-analysis was performed according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement (98). The meta-analysis was registered prospectively in the international prospective register of systematic reviews, PROSPERO, registration number CRD42018110201.

2.1. Eligibility Criteria

Studies were included if they met the following eligibility criteria: (a) sample with a mean age between 12 and 18, (b) sample with a visible difference, (c) quantitative data on anxiety and/or depression from a validated questionnaire, (d) data reported by adolescents or parents, and (e) a control group of unaffected peers. Studies were excluded if (a) they were published in a non-English language, (b) they reported on a sample with cognitive developmental delay, (c) they reported on a traumatic event less than three months before the study (e.g., studies on psychological well-being in burn victims with burns sustained less than three months before were excluded),¹ (d) the visible difference was caused by self-harming, and (e) they described case reports, case series, qualitative studies, dissertations or review papers, and conference abstracts.

2.2. Information Sources and Search

As there was no clear picture on how many articles a search solely on anxiety and depression would yield, a broader search focusing on social and emotional aspects of visible differences in adolescence was done. A research librarian conducted a search using Embase, Medline Ovid, Web of Science, Cochrane CENTRAL, PsycINFO Ovid, and Google Scholar. The search was conducted in June 2018 and updated in February and April 2019. The search included terms relating to visible difference or disfigurement and the following relevant medical conditions: neurofibromatosis, limb malformation, eczema, psoriasis, epidermolysis bullosa, vitiligo, skin haemangioma, albinism, port-wine stains, ectodermal dysplasia, scars, stoma, wheelchair, amputation, burns, paralysis, hirsutism, cerebral palsy, craniofacial

¹ After this period, potential post-traumatic stress symptoms will have declined (99).

malformations, and cleft lip. These terms were combined with terms relating to anxiety and depression, and adolescence. The search excluded conference abstracts, letters and editorials, and was limited to articles written in English. The full search is displayed in the Supplementary Material.

2.3. Study Selection

Studies were selected if they met the inclusion criteria. First, two reviewers (MvD and YK or FH) independently assessed title and abstract. The reviewers agreed on 88.6% of the references. Discrepancies were resolved using consensus. Second, two reviewers (MvD and YK or FH) independently assessed the full text for eligibility. Reviewer agreement was 90.0% for the second step. Discrepancies were again resolved using consensus. Third, MvD checked the reference list of included articles for additional relevant references. Any references deemed relevant were first screened based on title and abstract. If still relevant, the full-text was read. When the article met the inclusion and exclusion criteria, it was included in the review. Endnote X9 was used to manage references.

2.4. Data Collection Process and Data Items

Data collection was completed independently by two reviewers (MvD and YK), using a data extraction form. The following data were extracted: year of publication, medical condition involved, sample size, percentage male, mean age of the sample, age range, mean score, and standard deviation.

2.5. Quality and Risk of Bias

Quality and risk of bias were assessed using the NIH Quality Assessment for Observational Cohort and Cross-sectional studies (100). This checklist includes 14 questions with *yes*, *no* or *cannot determine/not reported/not applicable* responses. For cross-sectional studies, only 7 questions are applicable. Hence, we rated 5.5 to 7 (>80%) points as good, 4.5 or 5 (60-80%) points as fair and 4 points or less (<60%) as poor quality. Quality assessment was performed independently by two reviewers (MvD and YK). Discrepancies were resolved by consensus.

2.6. Data Synthesis and Statistical Analyses

Comprehensive Meta-Analysis (CMA), version 2 was used for meta-analysis. Because of the high likelihood of between-study heterogeneity, a random-effects model was employed. Means and standard deviations of the samples were used to compute an effect size, the standardized mean difference (SMD). When means and standard deviations were not available, medians were transformed to means and *SDs* using the interquartile range, as described by Wan, Wang, Liu, and Tong (101).

Separate meta-analyses were conducted for anxiety and depression, using the SMD as effect measure. Heterogeneity was assessed using the I^2 -statistic, with values

≥75% indicating considerable heterogeneity (102). Publication bias was assessed by visual inspection of a funnel plot and Egger's regression. To assess whether cause of visible difference influenced the results (Aim 2), analyses for subgroups were performed. Subgroups were defined based on the cause of visible difference: (1) congenital conditions, (2) skin conditions, (3) trauma, (4) disease, or (5) medical treatment. When two or more studies were present in a subgroup, a meta-analysis for the subgroup was conducted.

3. Results

3.1. Study Selection

After removing duplicate articles, the database search yielded 4764 records. One additional record was identified through the reference lists of included articles. The title/abstract was screened in all 4765 records, 4098 articles did not meet the inclusion criteria. Thereafter 676 full-text articles were assessed for eligibility, of which 147 records met the inclusion criteria and focussed on social and emotional aspects of a visible difference. Of the 147 articles focusing on social and emotional aspects of a visible difference, 11 were included in the meta-analyses. Of the 136 articles excluded, most did not focus on anxiety and/or depression ($n = 91$). Figure 1 details the selection process.

3.2. Study Characteristics

Eleven studies were included in the meta-analyses, as displayed in Table 1. These studies included a total of 1075 adolescents with a visible difference and 2375 unaffected peers. Of the adolescents with a visible difference, 47.61% were male. Of the unaffected peers, 44.82% percent were male. One study included females only (55). The number of adolescents with a visible difference per study ranged from 15 to 385, with a median sample size of 44. The weighted mean age was 15.80. One study did not report a mean age (103). The youngest participants were 7 years old, the oldest 20 years old. Six studies investigated a skin condition (acne, vitiligo, alopecia, hirsutism, and atopic eczema), two investigated a congenital condition (cleft lip or cleft lip and palate [CL/P] and neurofibromatosis type 1 [NF1]), two investigated a visible difference due to trauma (burns), and one investigated a visible difference due to disease (cutaneous leishmaniasis). All studies included self-report measures, and none included parent or proxy reports.

Figure 1. Flow chart displaying the selection process

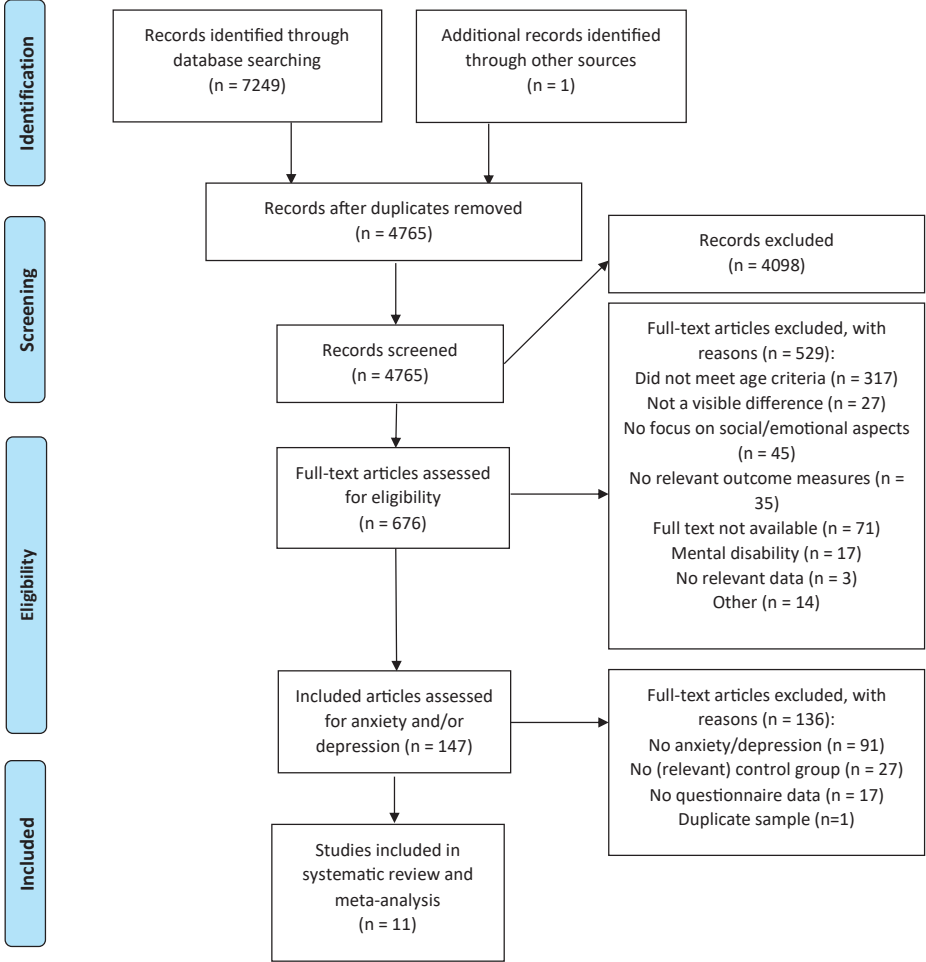


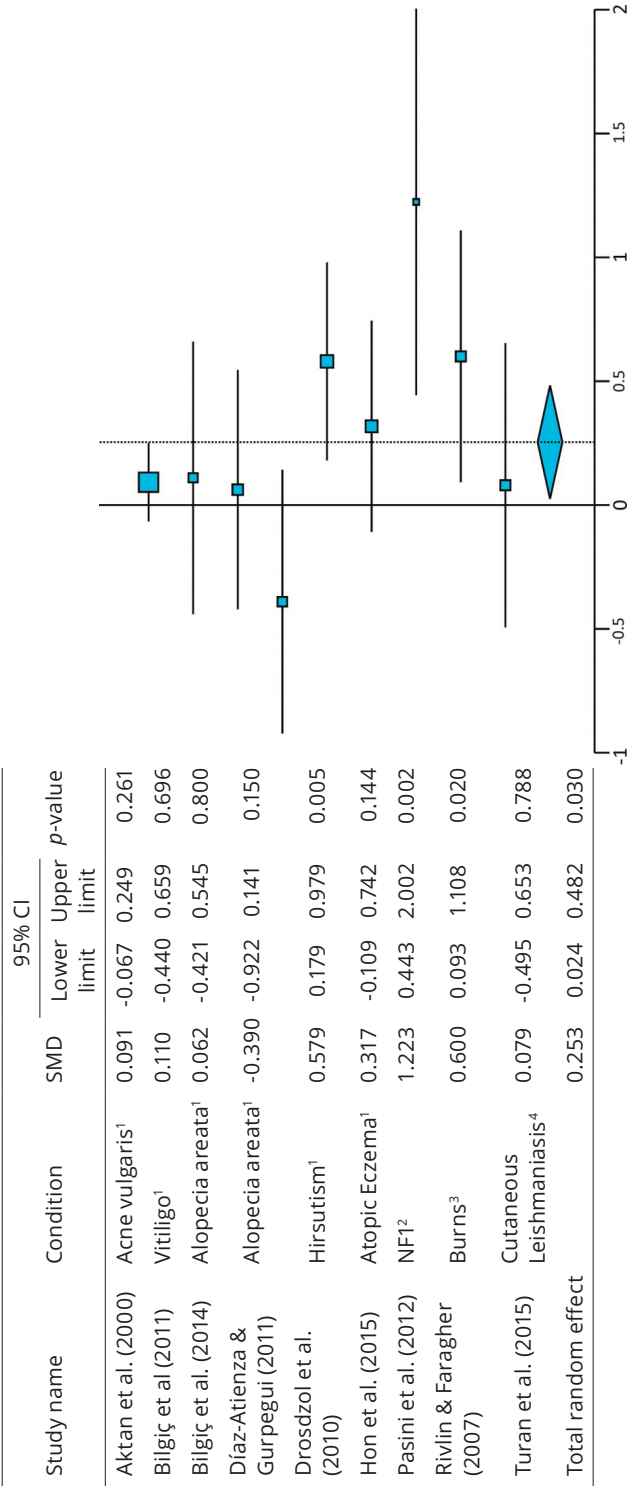
Table 1. Overview of study characteristics

Study	Type of condition	Condition	% male	Mean age (range)	Quality score	Outcome	Instrument	Visible difference		Healthy controls			
								Sample size	Mean	SD	Sample size	Mean	SD
Aktan et al. (2000)	Skin condition	Acne vulgaris	67.6	16.1 (14-20)	2.5	Anxiety	HADS	308	8.00	4.05	308	7.62	4.34
						Depression	HADS		4.54	2.82		4.73	2.82
Bilgiç et al. (2011)	Skin condition	Vitiligo	44.0	15.72 (13-18)	6.0	Anxiety	STAI-C: trait anxiety	25	37.16	6.93	26	36.46	5.83
						Depression	CDI		12.76	7.99		12.04	7.33
Bilgiç et al. (2014)	Skin condition	Alopecia areata	61.8	14.6 (13-18)	4.5	Anxiety	STAI-C: trait anxiety	34	35.60	6.80	32	35.20	6.00
						Depression	CDI		11.50	7.00		10.50	7.20
Díaz-Atienza and Gurpegui (2011)	Skin condition	Alopecia areata	52.0	12.2 (7-19)	3.0	Anxiety	STAI-C: trait anxiety	31	12.20	6.90	25	15.00	7.50
						Depression	CDI		9.80	5.30		9.70	4.70
Drosdzol et al. (2010)	Skin condition	Hirsutism	0	16.44 (13-18)	5.0	Anxiety	HADS	50	5.00*	3.82*	50	3.00*	3.05*
						Depression	HADS		2.17*	3.82*		1.50*	2.29*
Feragen et al. (2016)	Congenital	Cleft lip (and palate)	60.2	16 (16)	4.0	Depression	HSCL-7	385	1.46	0.43	1808	1.75	.57
Hon et al. (2015)	Skin condition	Atopic eczema	58.0	16.0 (14.4-18.2)	1.0	Anxiety	DASS-42	120	4.67*	4.50*	26	3.33*	2.35*
						Depression	DASS-42		3.67*	5.25*		1.33*	3.14*
Pasini et al. (2012)	Congenital	NF1	33.3	13.4 (9-18)	3.0	Anxiety	MASC	15	48.90	7.00	15	40.70	6.40
Pope et al. (2007)	Trauma	Burns	36.1	15.1 (11-19)	2.5	Depression	BDI-II	36	10.37	9.73	41	10.10	7.92
Rivlin and Faragher (2007)	Trauma	Burns	50.0	13.5 (9-16)	3.5	Anxiety	Short form - MAS	44	6.55	3.35	24	4.55	3.30
Turan et al. (2015)	Disease	Cutaneous leishmaniasis	53.7	NR (13-18)	4.5	Anxiety	STAI-C: trait anxiety	54	36.41	40.50	20	33.90	10.87
						Depression	CDI		14.25	4.76		4.50	2.46

Note. NR, Not reported; NF1, Neurofibromatosis type 1; BDI, Beck Depression Inventory; CDI, Children's Depression Inventory; DASS-42, Depression Anxiety Stress Scale - 42; HADS, Hospital Anxiety and Depression Scale; HSCL-7, the Hopkins Symptoms Checklist - 7; MASC, Multidimensional Anxiety Scale for Children; short form-MAS, short form Manifest Anxiety Scale; STAI-C, State Trait Anxiety Inventory for Children.

* Scores calculated using the method described by Wan et al. (2014).

Figure 2. Meta-analysis for anxiety



Note. 1. Visible difference due to skin disease; 2. Congenital visible difference; 3. Visible difference due to trauma; 4. Visible difference due to disease; NF1, Neurofibromatosis type 1.

Table 2. Quality assessment of included studies

	1. Research question	2. Study population	3. Participation rate	4. Recruitment	5. Power	6. Outcome measures	7. Confounders	Total score
Aktan et al. (2000)	1	0.5	CD	0	0	1	NR	2.5
Bilgiç et al. (2011)	1	1	1	1	0	1	NR	5
Bilgiç et al. (2014)	1	0.5	CD	0.5	0	1	1	4
Díaz-Atienza & Gurpegui (2011)	1	1	CD	0.5	0	1	NR	3.5
Drosdzol et al. (2010)	1	1	1	1	0	1	NR	6
Feragen et al. (2016)	1	1	1	0	0	1	NR	4
Hon et al. (2015)	0.5	0	CD	CD	0	0.5	NR	1
Pasini et al. (2012)	1	0.5	CD	0	0	1	NR	2.5
Pope et al. (2007)	1	0.5	1	CD	0	1	0.5	4
Rivlin & Faragher (2007)	0.5	0.5	0	1	0	1	0.5	3.5
Turan et al. (2015)	1	1	CD	0.5	0	1	1	4.5

Note. CD: Cannot Determine; NR: Not Reported. 1. Was the research question or objective in this paper clearly stated? 2. Was the study population clearly specified and defined? 3. Was the participation rate of eligible persons at least 50%? 4. Were all subjects selected or recruited from the same or similar populations? Were inclusion and exclusion criteria for being in the study prespecified and applied uniformly to all participants? 5. Was a sample size justification, power description, or variance and effect estimates provided? 6. Were the exposure outcome measures clearly defined, valid, reliable and implemented consistently across all study participants? 7. Were key potential confounding variables measured and adjusted statistically for their impact on the relationship between exposure and outcome?

3.3. Study Quality/Risk of Bias

The quality assessment is shown in Table 2. The mean quality score was 3.59 (range 1.0 – 6.0), which can be considered poor quality. Overall, eight studies were considered to be of poor quality (7, 19, 47-49, 51, 96, 97). Two studies were of fair quality (50, 103) and one study was of good quality (55). None of the studies achieved a maximum score of seven points.

3.4. Anxiety Symptoms

A meta-analysis was run to estimate whether adolescents with a visible difference experience more symptoms of anxiety than unaffected peers. Nine studies reported on symptoms of anxiety (19, 47-51, 55, 97, 103), with five different instruments. The studies included 653 participants, with a weighted mean age of 15.45, and 526 controls. One study did not report a mean age (103).

Figure 2 shows the meta-analysis for anxiety. Results show that adolescents with a visible difference experience significantly more anxiety than unaffected peers (SMD = 0.253, 95% CI [0.024, 0.482], $p = .030$), with a small effect size. Some level of heterogeneity was observed ($I^2 = 59.55\%$, $p = .011$). Inspection of the funnel plot indicated a symmetric funnel plot, with Egger's regression being non-significant, $t(7) = 1.10$, $p = .307$. This indicates an absence of publication bias.

Meta-analysis for subgroups of visible differences showed that adolescents with a skin condition did not differ significantly from unaffected peers (SMD = 0.149, 95% CI [-0.070, 0.369], $p = .182$). There was no significant heterogeneity ($I^2 = 47.76\%$, $p = .088$). The funnel plot showed a symmetric shape.

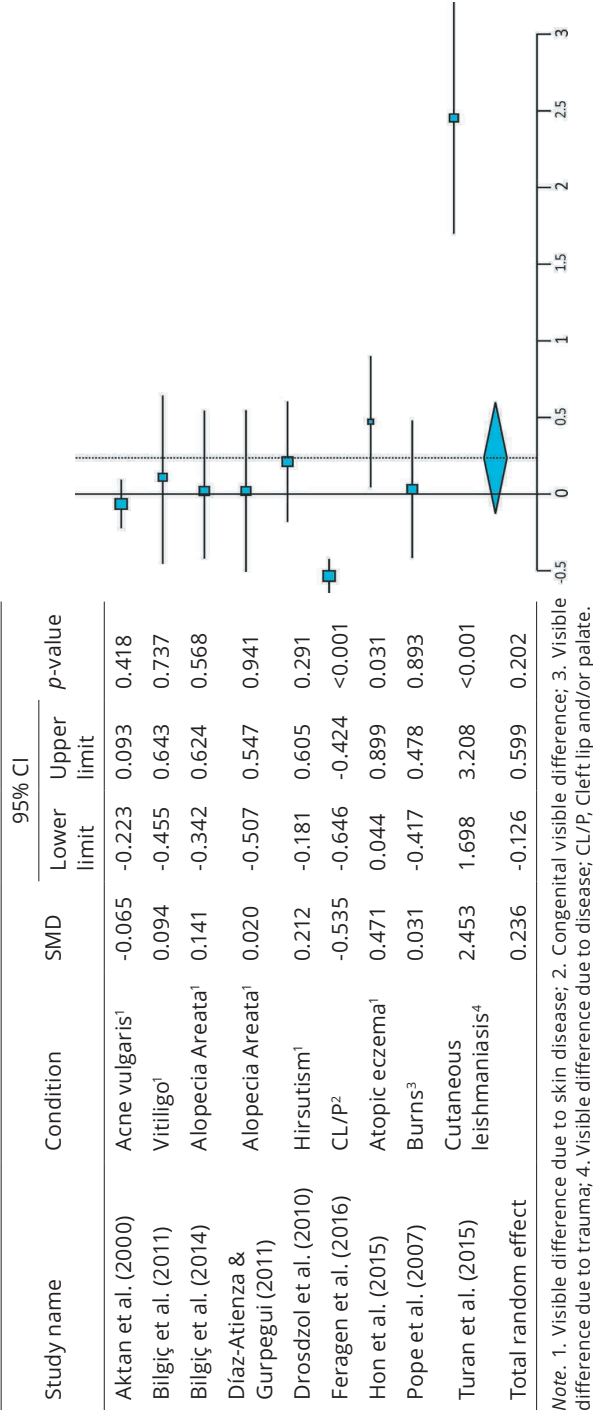
Meta-analyses for subgroups could only be run for skin conditions, as only one study investigated a congenital condition (NF1) (49), one study investigated trauma (burns) (97) and one study investigated a disease (cutaneous leishmaniasis) (103). These studies showed that adolescents with a congenital visible difference (SMD = 1.223, 95% CI [0.443, 2.002], $p = .002$) and a visible difference due to trauma (SMD = 0.600, 95% CI [0.093, 1.108], $p = .020$) experienced more anxiety than unaffected peers. Adolescents with a visible difference due to disease did not experience more anxiety (SMD = 0.079, 95% CI [-0.495, 0.653], $p = .788$).

3.5. Depressive Symptoms

A meta-analysis was run to estimate whether adolescents with a visible difference experience more depressive symptoms than peers. Nine studies reported on depressive symptoms (7, 19, 47, 48, 50, 51, 55, 96, 103), with five different instruments. The studies included 1017 participants, with a weighted mean age of 15.84, and 2336 controls.

Figure 3 shows the meta-analysis for depression. Results showed that adolescents with a visible difference did not experience significantly more depressive symptoms than unaffected peers (SMD = 0.236, 95% CI [-0.126, 0.599], $p = .202$). A high level of heterogeneity was observed ($I^2 = 92.19\%$, $p < .001$). The funnel plot was asymmetric, with more studies reporting a positive result. Egger's regression was significant, indicating publication bias, $t(7) = 3.51$, $p = .010$. The funnel plot showed one outlier (103). Removal of this outlier resulted in a considerable decrease of the effect size (SMD = 0.018, 95% CI [-0.267, 0.303], $p = .902$). Heterogeneity was still high ($I^2 = 86.78\%$, $p < .001$).

Figure 3. Meta-analysis for depression



Meta-analysis for subgroups based on cause of visible difference showed that adolescents with a skin condition did not experience significantly more depressive symptoms than unaffected peers (SMD = 0.090, 95% CI [-0.082, 0.262], $p = .305$). There was no significant heterogeneity ($I^2 = 23.79\%$, $p = .255$).

Meta-analyses for subgroups were not run for visible difference due to disease (cutaneous leishmaniasis), congenital conditions (CL/P) or trauma (burns), as these categories included only one study each. These studies show that adolescents with a visible difference due to disease (SMD = 2.453, 95% CI [1.698, 3.208], $p < .001$) experience more depressive symptoms than unaffected peers. Adolescents with a congenital condition experience fewer depressive symptoms than unaffected peers (SMD = -0.535, 95% CI [-0.646, -0.424], $p < .001$). Adolescents with a visible difference due to trauma do not differ from unaffected peers concerning depressive symptoms (SMD = 0.031, 95% CI [-.417, .478], $p = .893$).

4. Discussion

In this meta-analysis we compared adolescents with a visible difference to unaffected peers and looked at different causes of visible difference.

Our first research question asked whether adolescents with a visible difference experience more symptoms of anxiety and depression than unaffected peers. Results showed that this was true for anxiety but not for depression. For anxiety a small effect size was found, indicating slightly elevated anxiety for adolescents with a visible difference. For depression, a non-significant result was found.

The results found for depression seem to be largely driven by Turan et al. (103), reporting an extraordinary effect size of 2.453. As anxiety and depression are often seen as comorbid conditions (104), it is noteworthy that when looking at symptoms of anxiety, the same study does not seem to find any effect, with an effect size of 0.079. However, in their study they note a mean of 36.41 with a standard deviation of 40.50 for adolescents with cutaneous leishmaniasis, and a mean of 33.90 with a standard deviation of 10.87 for controls. Given that the possible range of the STAI-C is 20-80, these results seem highly unlikely. Furthermore, Turan et al. (103) have reported a p -value of .143, while the same results in our meta-analysis yield a p -value of .788. This is a striking and remarkable difference. Without this outlier, the effect for depression is not significant (SMD = 0.018, $p = .902$).

Our second research question concerned the effect of the cause of visible difference on symptoms of anxiety and depression. Due to the small number of studies found, we were only able to determine the effects of skin conditions on anxiety and depression. Results showed that adolescents with a skin condition did not

differ in symptoms of anxiety and depression when compared to unaffected peers. Both analyses included 568 adolescents with a visible difference, gathered from six different studies and five different skin conditions. A retrospective power calculation following guidelines as proposed by Valentine, Pigott, and Rothstein (105) shows that both analyses were underpowered. Hence, we cannot firmly say that the lack of a significant finding is free of type II errors.

The finding that adolescents with a skin difference do not experience more anxiety than unaffected peers, while the overall group of adolescents with a visible difference does experience more anxiety than unaffected peers is striking. A direct comparison of the different causes of visible differences is not possible, due to the low amount of studies available. However, a possible explanation may be that a selection bias has influenced the results. Most participants with skin conditions included in the current meta-analysis experience acne or eczema. These are conditions that often have a mild presentation. For instance, only 6.5% of adolescents with eczema have severe eczema (106) and moderate to severe acne vulgaris is reported in only 15-20% of young people with acne (107). Similarly, articles included in the current meta-analysis reported few participants with a severe condition. For example, severe acne was found in only 2.1% of adolescents with acne (19). It could be that the relatively mild symptoms of the condition have a low impact on the psychosocial well-being of the adolescents studied.

When looking at the different subgroups, it is notable that the results for congenital visible difference are divergent. The congenital condition NF1 shows a big effect ($SMD = 1.223$) with adolescents with NF1 experiencing more symptoms of anxiety than unaffected peers. The congenital condition CL/P shows the opposite effect ($SMD = -0.535$), with unaffected peers experiencing more depression than adolescents with CL/P. Conclusions pertaining congenital visible difference are hard to make. More research on psychological problems in congenital visible difference is needed to examine how this group compares to unaffected peers.

The current results provide insight into symptoms of anxiety and depression in adolescents with a visible difference. However, this meta-analysis does not provide insight into the cause of these findings. One possible explanation might lie in the social situations experienced by adolescents with a visible difference. Different studies show that people with a visible difference commonly experience adverse social experiences (4, 34). These social situations might be experienced as stigmatising. Stigmatisation, in turn, has been shown to affect quality of life and psychological adjustment in children with a facial difference (37). Furthermore, a relation exists between stigmatisation and poorer mental health (108). Following this line of reasoning, adverse social experiences might lead to psychological problems. In support of this, studies have found higher levels of social anxiety

in adults with a visible difference (109), but more research is needed to warrant a definite conclusion.

Another possible explanation is that adolescents with a visible difference often have a chronic medical condition. Anxiety and depression are reported to occur regularly in chronically-ill children and adolescents (110, 111). In adults, chronic medical conditions are also associated with occurrence of major depressive disorder and anxiety disorders (112). The increased symptoms of anxiety we found might thus be related to the underlying medical condition instead of the visible difference itself.

For medical practitioners, we recommend them to pay attention to the psychological aspects of dealing with a visible difference. More specifically, questions should be asked as to whether the adolescent experiences anxiety. Furthermore, it could be beneficial to screen all adolescents with a visible difference on symptoms of anxiety prior to their medical appointment, using computerised questionnaires. During the appointment, the medical practitioner could then enquire about the anxiety symptoms. In this way, adolescents that are in need of extra psychological care may be identified. Early intervention would then be possible and later adverse outcomes may be reduced. For those delivering psychological care, we recommend focusing on anxiety when determining the psychological burden of dealing with a visible difference. More research is needed to establish the cause of anxiety in adolescents with a visible difference, but treatment could focus on the role of negative observer responses and body image in the aetiology of the psychological complaints.

This study also has some strengths and limitations. A particular strength of this study is the thorough literature search conducted. As it was a broad literature search, articles that were not indexed by the terms anxiety or depression might still have been found in the search.

However, despite the extensive literature search conducted, only 11 articles could be included in this meta-analysis. In combination with the relatively high heterogeneity, interpretation of current results should be made with caution. The results that have been found in this study might not generalise to the entire population of adolescents with a visible difference. Another limitation is that the studies included in the meta-analyses did not focus specifically on visible difference, with the exception of Feragen et al. (7). We included medical conditions that are presumed to be associated with a visible difference, but it was impossible to check whether a visible difference existed. Hence, confounders may have influenced the results.

Following these limitations, future research should study anxiety and depression in adolescents with a visible difference more extensively. To provide a clear picture on the symptoms of anxiety and depression, future studies should include a bigger

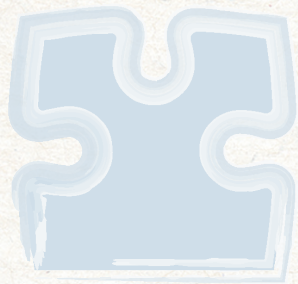
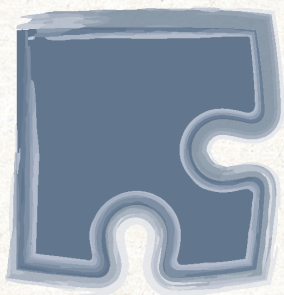
sample size and use questionnaires as well as clinical interviews. Furthermore, to directly compare the causes of visible differences, efforts should be made to study all causes of visible differences in one sample. These results could help to gain insight into whether the clinical presentation of symptoms differs depending on the cause.

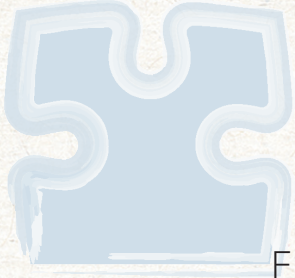
In conclusion, this meta-analysis shows that adolescents with a visible difference experience more symptoms of anxiety, but not depression when compared to unaffected peers. It is not yet clear how different causes of visible difference influence symptoms of anxiety and depression. Future research is needed to further examine anxiety and depression in adolescents with a visible difference.

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Data availability statement: The data that support the findings of this study are available from the corresponding author upon reasonable request.



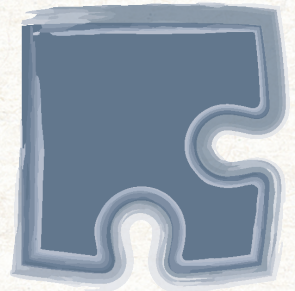


CHAPTER 3

Emotional and behavioural problems
in children with a cleft lip with or without palate
or an infantile haemangioma

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Abstract

Objective: Life can be challenging for children with a visible difference due to a medical condition and they might be at risk for emotional and behavioural problems. This study examines emotional and behavioural problems in children with a Cleft Lip with or without Palate (CL±P) or an Infantile Haemangioma (IH) in relation to the visibility of the condition, the presence of additional condition-related problems and parental affect. **Setting:** This cross-sectional study took place in an academic medical hospital in Rotterdam, The Netherlands. **Participants:** A total of 309 parents (Mean age=40.34, 44.00% male) of 182 children with CL±P and 48 parents (Mean age=39.21, 37.50% male) of 33 children with an IH completed questionnaires. Children were 1.5 to 12 years old. **Results:** Parents reported fewer child emotional and behavioural problems compared to normative data. Problems reported were mainly related to learning difficulties and parent gender, while visibility of the condition had no significant influence. Parental negative affect was related to child internalising problems. Parental positive affect was not related to any of the outcome measures. **Conclusions:** Parents reported fewer problems for their children compared to normative data. This is inconsistent with previous research, showing similar or worse scores for these children compared to peers. Our findings may be explained by a protective parenting style, a response shift in parents or problems developing at a later point in life.

Keywords: Visible differences; Cleft lip; Capillary Hemangioma; Vascular Malformations; Vascular Tissue Neoplasms; Child behavior.

1. Introduction

In societies that place high demands on physical appearance, coping with a visible difference due to a medical condition, such as cleft lip with or without palate (CL±P) or an infantile haemangioma (IH), can be challenging. Children with a visible difference that is present from birth or early infancy are at risk for negative social interactions, including stigmatisation and bullying (79). These social interactions may be associated with emotional and behavioural problems and can negatively impact the overall quality of life of children with a visible difference (25, 113).

CL±P is one of the most common craniofacial anomalies with 1 occurrence per 700-1100 live births (114, 115). IH is the most common vascular tumour with an estimated incidence of 2.0% to 4.5% in infants, often located in the head and neck area (116-118). Both conditions are visible from birth or shortly after, may cause significant functional problems during infancy and leave permanent scars (115, 119). Nonetheless, the nature of the visible differences and functional problems may be different, potentially associated with variation in emotional and behavioural functioning.

A range of findings has been reported regarding emotional and behavioural problems in children with CL±P (120). Some studies report an increased number of psychological difficulties in children with CL±P compared to children from the general population (121-124), while other studies suggest that children with CL±P do not have more psychological difficulties (125-127). The nature and the extent of emotional and behavioural problems vary according to the child's age and gender (121, 122, 128). Furthermore, emotional and behavioural problems may be more prevalent in children with visible cleft as opposed to children with a nonvisible cleft (129).

Previous studies suggest that children with IH have an average or a better quality of life than children without IH (130, 131). Nonetheless, parents report that their school-aged children with IH exhibit more negative emotions compared to peers (130). In addition, children with an IH experience negative observer responses such as staring, when the IH is at a visible location or medically complicated (130). Yet, research has not found elevated levels of emotional or behavioural problems in children with IH (132-134). However, small sample sizes may have led to inconclusive results. Furthermore, associations between emotional and behavioural problems and visibility or additional medical problems were not explored.

Following concerns about the impact of the visible medical conditions CL±P and IH, an investigation of emotional and behavioural problems in these patient groups is highly relevant. Conclusions about why some patients with CL±P or IH,

but not others, experience mental health problems are hard to draw (128, 135). Adjustment to living with a visible difference involves a complex interplay of physical, sociocultural and psychological factors (136, 137). It is commonly assumed that the degree of visibility of a medical condition is directly associated with mental health problems in children with visible differences. However, results in the literature are variable (138). It has been suggested that the relationship between visibility and mental health problems follow an inverted U-shape, with individuals with minor or major visibility experiencing less stress (14). Additionally, parent-reported or child-reported subjective visibility of a child's medical condition may be a more appropriate indicator of a child's emotional and behavioural problems than clinician-reported visibility of a child's medical condition (14, 30).

Children develop within the broader context of their family. Parents may also be emotionally affected by having a child with a visible difference (136). In turn, parental emotions may influence emotional and behavioural problems in their children. For example, children of parents with psychopathology have an elevated risk for developing psychiatric symptoms (139). Similarly, parenting stress is associated with increased parent-reported emotional and behavioural problems in children with CL±P or IH (140). On the other hand, parental positive affect promotes child development (141).

Additional medical difficulties could also play a role in emotional and behavioural problems of children with CL±P or IH (130, 138). IH may be life- or function-threatening during infancy, obstructing vital organs and causing feeding difficulties. (119). Feeding problems in infants can impact parent-child interaction and indirectly contribute to infant mental health (142). At school age, speech problems and academic problems in children with CL±P, such as learning disability, low academic achievement and grade retention, are also associated with emotional and behavioural problems (143, 144).

Finally, child behavioural problems vary according to a child's age, gender and socio-economic status (145). Parental characteristics, such as parent age and gender also play a role in the assessment of child emotional and behavioural problems (146, 147). Therefore, these variables have to be taken into account as covariates when identifying the association between emotional and behavioural problems and the visibility of CL±P or IH, parental affect and condition-related difficulties.

Our aim was to answer the following two research questions:

- 1) Do children with CL±P or IH experience different levels of emotional and behavioural problems compared to children in the general population?
- 2) Which factors are associated with emotional and behavioural problems in children with CL±P or IH?

We expect that parent-perceived visibility of the medical condition, parental affect and additional condition-related difficulties (i.e., feeding problems, eating problems, learning difficulties and psychosocial problems) are associated with emotional and behavioural problems in children with CL±P or IH, when corrected for child age, child gender, parent age, parent gender and socio-economic status.

2. Method

This study was part of a larger project assessing parental well-being as described in (140). Ethical approval for this study was obtained from the Medical Ethics Review Committee Erasmus MC, Rotterdam, the Netherlands (MEC-2006-185 and MEC-2008-191). This study was conducted in accordance with the Declaration of Helsinki (148). This article was written in accordance with the STROBE guidelines (149).

2.1. Sample and procedure

Recruitment took place at the Department of Dermatology in the Centre of Paediatric Dermatology and the Department of Oral and Maxillofacial surgery of the Erasmus MC Sophia Children's Hospital, The Netherlands. Recruitment took place from 2008 until 2011 and data was later analysed and reported in 2019 and 2020 by a PhD student. Parents were included in the study if they 1) had sufficient knowledge of the Dutch language and 2) had a child between 0 and 12 years of age with CL±P (isolated cleft palate excluded due to the nonvisible nature) or an IH (regardless of location on the body). This age range was chosen as in The Netherlands children often make the transition to secondary education at age 12. For many parents and their children this is seen as the end of childhood and the start of adolescence. There were no additional exclusion criteria. For our analyses, children younger than 1.5 years were excluded.

Each family was sent an informed consent letter, two questionnaires and a prepaid envelope. Parents were explicitly asked to fill out the questionnaires independently from their partner. Children did not complete any questionnaires. As an incentive, parents received a small gift for their child. Reminders were sent after approximately one month and after 3 months.

2.2. Medical care at the Erasmus MC, The Netherlands

Cleft care was provided at the Erasmus MC Sophia Children's Hospital, The Netherlands by multidisciplinary teams with average cleft lip surgery at age of three months and cleft palate closure at average age of 12 months. The alveolar cleft is closed around 9-12 years of age. Access through speech therapy is guaranteed through the treating hospital. Patients are followed up regularly by the multidisciplinary team until age 22.

Medical care for patients with an IH was provided at the Centre for Vascular Anomalies Erasmus MC. Treatment (such as propranolol topical/systemic, prednisone, system/intralesional, surgery) was administered to children with IH. All treated IHs were either potentially life-threatening or had functional risk, local discomfort or severe cosmetic consequences. In case of treatment, follow-up is until the end of systemic treatment. If cosmetic surgery is a suspected possibility, the IHs or its residuals are re-evaluated at about age 3.

2.3. Instruments

2.3.1. Parent and child demographic characteristics. Demographic and participant characteristics were obtained using questionnaires and included age and ethnicity of children and parents and parental educational level as a proxy measure of socio-economic status. Parental education was divided into low, middle and high, based on the International Standard Classification of Education (ISCED) guidelines (150).

2.3.2. Child Emotional and Behavioural problems. Validated Dutch versions of the Child Behavior Checklist, designed for ages 1½-5 (CBCL 1½-5; Achenbach & Rescorla, 146) and ages 6-18 (CBCL 6-18; Achenbach & Rescorla, 151) were used to assess child emotional and behavioural problems, reported by parents. The CBCL 1½-5 consists of 100 items, the CBCL 6-18 has 120 items, both scored on a 3-point scale ranging from 0 (*not true*) to 2 (*very true or often true*).

For this study, the Total Problems scale and the Internalising and Externalising scales were used. The Total Problems scale is the sum of all items. To calculate the Internalising scale for the CBCL 1½-5 the syndrome scales Emotionally Reactive, Anxious/Depressed, Somatic Complaints and Withdrawn Behaviour were used. For the CBCL 6-18, the syndrome scales Anxious/Depressed, Withdrawn/Depressed and Somatic complaints were summed. The Internalising scale measures problems that are present mainly within the child. To calculate the Externalising scale on the CBCL 1½-5, the syndrome scales Attention Problems and Aggressive Behavior were summed. For the CBCL 6-18, the syndrome scales Rule Breaking Behavior and Aggressive behaviour were summed. The Externalising scale measures problems with regards to conflicts with others and the conflicts in the expectation others have of the child.

Raw scores can be converted to T-scores based on age (and gender for the CBCL 6-18). T-scores are normally distributed with a mean of 50 and a standard deviation of 10. T-scores of 60 to 63 (84th to 90th percentile) are considered borderline clinical range and scores above 64 are in the clinical range.

Internal consistencies for the scales range from $\alpha = .89$ to $\alpha = .99$ (146, 151). In the present study, Cronbach's alpha ranged between $\alpha = .84$ and $\alpha = .98$ for the CBCL 1½-5 and between $\alpha = .86$ and $\alpha = .98$ for the CBCL 6-18.

2.3.3. Parental positive and negative affect. To measure parental affect, the Dutch version of the Positive and Negative Affect Schedule was used (PANAS; 152). The PANAS consists of the subscales Positive Affect (PA) and Negative Affect (NA). PA refers to the extent to which a person feels enthusiastic, active and alert. High scores reflect a state of high energy, full concentration and pleasurable engagement. In contrast, NA refers to a general dimension of subjective emotional distress and includes a variety of aversive mood states, including anger, anxiety and disgust. High scores on the NA scale indicate more distress. Both scales consist of 10 items, using a five-point Likert scale ranging from 1 (*very slightly or not at all*) to 5 (*very much*). Parents were instructed to indicate how they had been feeling during the last two weeks. Scale scores are obtained by summing the item scores.

The PANAS has good psychometric properties, with $\alpha = .89$ for PA and $\alpha = .85$ for NA (153). In the present study, Cronbach's alphas were $\alpha = .89$ and $\alpha = .85$ for the PA and NA scales respectively.

2.3.4. Visibility. To assess the visibility of the condition, parents were asked two questions, both measured on a 5-point Likert scale: (1) "To what extent do you think your child's condition is visible?" and (2) "To what extent do you experience that bystanders look at your child's condition?" (both ranging from *not at all* to *very much*). Item scores were added to derive a total visibility score. The items correlated significantly ($r = .59, p < .001$) and the scale was reasonably reliable ($\alpha = .72$).

2.3.5. Additional condition-related difficulties. Three additional questions measured other problems related to the medical condition. Questions were asked on feeding problems (e.g., "Does your child have feeding problems?"), speech problems and learning difficulties. All items were rated on a 5-point Likert scale.

2.4 Statistical analysis

Statistical analyses were performed using Rstudio version 1.3.959 (154). Missing data was handled using multiple imputation. Multiple imputation was performed using the MICE package (155) in R.

The frequency of scores on the CBCL in the subclinical and clinical ranges was calculated. For children where both parents completed the questionnaires, a Pearson correlation was calculated to assess concordance. Additional analyses were run for parents' PANAS scores, comparing parents' scores to normative data. These are reported in the supplementary materials.

The first research question was tested using one sample *t*-tests to compare T-scores on the CBCL Total Problems, Internalising and Externalising scales to normative data. The T-scores were compared to a mean T-score of 50 with a standard deviation of 10. As one sample *t*-tests do not account for clustering in the data (i.e., two parents reporting on the same child), separate analyses were conducted for mothers and fathers.

The second research question was tested using Linear Mixed Models (LMM). In cases where both mother and father participated, there were two parent-reports for the same child. LMM account for this clustering in the data, so both parent-reports can be analysed in the same model. Three models were calculated. One for the Total Problems scale, one for the Internalising scale and one for the Externalising scale. Type of condition (CL±P or IH), parent-perceived visibility of the condition, parental affect, feeding difficulties, speech difficulties and learning difficulties were entered as predictors. To assess whether visibility was associated with a possible U-shape, as described by Moss (14), visibility was entered into the model with two splines. In addition, to test whether the predictors differed depending on the type of condition, an interaction term with condition was entered for all predictors. Child age, child gender, parent age, parent gender and socio-economic status were entered as covariates. A model with all covariates was computed, after which a second model was calculated excluding the non-significant predictors. Both models were subsequently compared using a likelihood ratio test to assess which model had a better fit to the data.

To account for multiple testing the False Discovery Rate (FDR) method as proposed by Benjamini and Hochberg (156) was used. All *p*-values were two-tailed and were compared to $\alpha = .05$.

3. Results

3.1. Participants

A total of 337 families with a child with CL±P and 72 families with a child with IH were approached. Four parents with a child with CL±P and four parents with a child with IH indicated that they did not have sufficient knowledge of the Dutch language. The response rate was 45.7% for CL±P and 34.0% for IH. A total of 357 questionnaires of parents of children older than 1.50 years were returned and analysed. Detailed sample characteristics are shown in Table 1. Overall, 203 mothers and 154 fathers of 215 children participated. Concerning CL±P, 40 (22.98%) children had an isolated cleft lip and 142 (78.02%) had a combined cleft lip and palate. Most clefts ($N = 137$, 75.69%) were unilateral. Concerning IH, 26 children (78.79%) had haemangiomas located on the face or on the head, 4 (12.12%) on the face and on the body and

3 (9.09%) on the body. Parents' concordance between Total, Internalizing and Externalizing scores on the CBCL ranged from $r = .62$ to $r = .67$.

Table 1. Descriptive statistics

	CL±P (N = 309)	IH (N = 48)
Parent gender, N (%)		
Male	136 (44.00)	18 (37.50)
Female	173 (56.00)	30 (62.50)
Parent age, mean (SD)	40.34 (6.30)	39.21 (5.37)
Age range	25.61 – 71.46	25.39 – 49.92
Child gender, N (%)		
Male	119 (65.38)	8 (24.24)
Female	63 (34.62)	25 (75.76)
Child age, mean (SD)	7.27 (2.71)	6.63 (2.79)
Age range	2.42 – 12.57	1.51 – 11.71
Parent Nationality, N (%)		
Dutch	301 (97.40)	46 (95.83)
Other/unknown	8 (2.60)	2 (4.17)
Parent Education, N (%)		
Low	34 (11.00)	4 (8.33)
Average	146 (47.25)	23 (47.92)
High	122 (39.48)	20 (41.67)
Other/unknown	7 (2.27)	1 (2.08)
Additional problems, mean (SD)		
Feeding problems	1.28 (0.79)	1.33 (0.99)
Speech problems	2.14 (1.18)	1 (0)
Learning difficulties	1.38 (0.90)	1.22 (0.49)

Note: CL±P = Cleft Lip with or without Palate, IH = Infantile Haemangioma

3.2. Comparison to norm group

Overall, 8.8 – 16.4% of children with CL±P was rated by their parent as experiencing subclinical or clinical problems. In children with IH this percentage was 0 - 5.6%.

To assess whether children with CL±P or IH experience more emotional- and behavioural problems than children in the general population, their scores on the CBCL were compared to the normative data. Results are shown in Table 2 and Table 3.

Table 2. Comparison of children with CL±P to normative data (one sample t-tests)

		Sample			Norm group		
		Parent	N	Subclinical score, N(%)	Clinical score, N(%)	Mean (SD)	Mean (SD)
Total problems	Mother	164	17 (10.4)	10 (6.10)	48.12 (10.64)	50 (10)	0.025
	Father	125	7 (5.60)	5 (4.00)	44.26 (10.44)	50 (10)	<.001
Internalising	Mother	164	14 (8.54)	12 (7.32)	47.39 (10.96)	50 (10)	0.003
	Father	125	4 (3.20)	7 (5.60)	44.15 (10.19)	50 (10)	<.001
Externalising	Mother	164	12 (7.32)	13 (7.93)	48.07 (10.12)	50 (10)	0.016
	Father	125	6 (4.80)	5 (4.00)	44.83 (10.04)	50 (10)	<.001
							Adjusted p-value
							Cohen's <i>d</i>

Table 3. Comparison of children with IH to normative data (one sample t-tests)

		Sample			Norm group		
		Parent	N	Subclinical score, N(%)	Clinical score, N(%)	Mean (SD)	Mean (SD)
Total problems	Mother	29	0 (0)	0 (0)	40.07 (9.51)	50 (10)	<.001
	Father	18	0 (0)	1 (5.56)	41.56 (11.38)	50 (10)	---
Internalising	Mother	29	1 (3.45)	0 (0)	41.55 (8.13)	50 (10)	<.001
	Father	18	0 (0)	1 (5.56)	42.28 (9.60)	50 (10)	.003
Externalising	Mother	29	1 (3.45)	0 (0)	40.72 (8.88)	50 (10)	<.001
	Father	18	0 (0)	1 (5.56)	42.00 (12.70)	50 (10)	---
							Adjusted p-value
							Cohen's <i>d</i>

Analyses were not performed for total and internalising problems for fathers of children with an IH, as these variables were not normally distributed and had a very low N. Non-parametric tests were not performed due to the low N.

Overall, parents of children with CL±P and IH reported less emotional and behavioural problems regarding their children than parents of children in the norm group. For parents of children with CL±P the effect sizes ranged from small to medium ($\delta = 0.18$ to $\delta = 0.57$; 157). For parents of children with IH the effect sizes range could all be classified as large ($\delta = 0.80$ to $\delta = 1.05$; 157).

3.3. Predictors and correlates of emotional- and behavioural problems

To assess what variables are related to the scores for total, internalising and externalising problems, linear mixed models were computed. For all three outcomes, the condition, parental positive affect, child age, child gender, parental age and SES (parental education) did not add significantly to the model. None of the interaction terms were significant, meaning that the type of condition (CL±P or IH) did not influence the relation between the predictors and the CBCL scores. Results can be seen in Table 4.

Table 4. Determinants of CBCL problem scales scores: results of linear mixed models

		Learning difficulties	Parent gender	PANAS NA
Total problems				
B		4.32	2.69	---
Std. Error		0.78	0.70	
<i>p</i> -value	Unadjusted	<.001	<.001	
	Adjusted	<.001	<.001	
Internalising problems				
B		2.96	2.24	0.38
Std. Error		0.73	0.73	0.10
<i>p</i> -value	Unadjusted	<.001	.002	<.001
	Adjusted	<.001	.003	<.001
Externalising problems				
B		3.03	2.29	---
Std. Error		0.74	0.74	
<i>p</i> -value	Unadjusted	<.001	.002	
	Adjusted	<.001	.003	

The model that best predicted total problems included learning difficulties ($t(106.62) = 5.51, p_{\text{adjusted}} = <.001$) and parent gender ($t(4126.41) = 3.83, p_{\text{adjusted}} = <.001$). Hence, parents reported more problems when the child had more learning difficulties and when the mother completed the questionnaires.

The model that best predicted internalising problems included the variables learning difficulties, parent gender and parental negative affect. Parents reported more internalising problems for their child when the child had more learning difficulties and when the parent themselves experienced more negative affect. Furthermore, fathers reported significantly less internalising problems than mothers.

The model that best predicted externalising problems included the variables learning difficulties ($t(352.29) = 4.07, p_{\text{adjusted}} = <.001$) and parent gender ($t(20,424.90) = 3.11, p_{\text{adjusted}} = .003$). Both variables were significantly related to externalising problems. Hence, parents of children with more learning difficulties and mothers reported more externalising problems.

4. Discussion

This study assessed parent-reported emotional and behavioural problems in children with the visible conditions CL±P or IH aged 1.5 to 12 years old. We expected more emotional and behavioural problems in both patient groups when compared to normative data of same-aged peers. Contrary to this expectation, the results of the current study indicated significantly fewer emotional and behavioural problems in children with CL±P and IH when compared to normative data. In the CL±P group, 8.8 - 16.4% of children experienced subclinical or clinical problems. In the IH group this percentage was 0 - 5.6%. As these represent scores in the 84th percentile or higher (146, 151), our sample has less children in the subclinical or clinical range than might be expected.

Current results are inconsistent with findings from some previous studies, which found either no significant differences with norm data (113, 126, 127, 134, 158), or significantly more emotional and behavioural problems in children with a visible difference (128, 159). The only previous study on Dutch children with an oral cleft found no differences in emotional and behavioural problems when compared to normative data (160). It remains unclear whether children with a visible difference are at risk for experiencing emotional and behavioural problems.

This study's current findings can be explained in several ways. A first explanation may be that children with CL±P or IH grow up in a protective environment. Parents may perceive children with a visible difference as more vulnerable, which could elicit a protective parenting style. Such overprotection has previously been shown

in a meta-analysis including parents of children with a chronic medical condition (161). Appropriate protection may facilitate positive emotional and behavioural development throughout childhood. Nonetheless, appropriate protection also includes a certain amount of autonomy support, which was recently associated with better child quality of life, less externalising behaviour and less anxiety in a meta-analysis (162). A second explanation is that emotional and behavioural difficulties in children with CL±P or IH are less prevalent during childhood than in puberty. This may be due to methodological differences between studies, with research in young children often using parent/caregiver reports, while research in adolescent populations often use self-reports. Moreover, body image plays a more prominent role in wellbeing during adolescence (163). Indeed, studies have shown that the majority of adolescents in the general population experience body dissatisfaction (164). Body dissatisfaction has been linked to negative outcomes such as social anxiety and school avoidance (165) and depressive symptoms (166) and could thus play a vital role in the origin of emotional- and behavioural problems. Its role in people with a visible difference remains unclear, but there are indications that satisfaction with appearance decreases with age for people with CL/P (158). A third possibility is that parents of children with CL±P or IH may exhibit a response shift. Response shift is a shift in an individual's perception of health and well-being, which can occur due to potentially challenging circumstances (e.g., parenting a child with a visible condition; 167). Possibly, parents of children with CL±P or IH have a more positive or a milder perception of emotional and behavioural problems than other parents and evaluate their child's behaviour in a more positive way.

The second research question involved an investigation of factors associated with emotional and behavioural problems in children with CL±P or IH. Our analyses led to three major results. First, learning difficulties and parent gender were related to all emotional and behavioural problem areas (i.e., total problems, internalising problems and externalising problems). Second, parental negative affect was associated with the child's internalising problems, but not with the child's externalising or total problems. Third, parent-reported subjective visibility was not associated with any of the emotional and behavioural problem areas. Lastly, the type of condition (CL±P or IH) did not influence the relation between the predictors and CBCL scores.

Consistent with our results, learning difficulties have previously been recognised as risk factor for emotional and behavioural problems and psychopathology (168, 169). In this study, the role of parent gender was similar to the general population, as described in the CBCL manual: mothers reported more child problems than fathers (145, 170). Possible explanations are a different parent-child interaction and differences between the roles of fathers and mothers within the family (145, 171).

Our finding that parental negative affect is associated with child internalising problems can be linked to previous research showing a relationship between parental stress and child emotional and behavioural problems. However, this relationship was not specific to internalising problems (140, 172). The association found in the current study may reflect the familial aggregation of anxiety and depression. Although the major source of familial aggregation seems genetic, parenting practices, including parental control, are also related to childhood anxiety (173, 174). Theoretical models including social learning theory (175) and attachment theory (176) emphasise the role of parenting in child development (177). Furthermore, common method variance may have played a role in the current study. The same informant completed questionnaires about both their parental affect and their children's emotional and behavioural problems. Parents with a more negative affect could have reported more emotional and behavioural problems in their children. Similarly, parents with internalising problems are prone to observe internalising problems in their children (178). Any correlations between informants (i.e., between the mother and father of the same child) were adjusted for in our statistical analyses.

Concerning the visibility of CL±P or IH, previous results on the association between visibility of a medical condition and emotional and behavioural problems have been mixed. Possibly, children and parents are used to the always present visible nature of CL±P or IH. This may not impact functioning as much as repeatedly recurring problems related to the medical condition.

The current study includes some strengths and limitations. Strengths of the current study were the sample size ($n = 357$) and number of fathers participating ($n = 154$). Fathers are often not included in other studies, especially when the target group involves children below the age of 3 (171). Mothers and fathers each provide a unique view of their child's development. This unique point of view was highlighted in the current study, in which mothers appointed different scores to their child's emotional and behavioural functioning than fathers. Hence multi-informant research is important in obtaining a detailed view of the child's development.

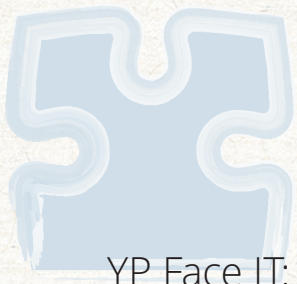
The current research involved a few limitations. First, this study was limited due to a low response rate of both patient groups (45.7% for children with CL±P and 34.0% for children with IH). Second, our sample was selected from a tertiary health care centre, which could entail more severe cases IH. Furthermore, our sample mostly involved highly educated parents. Therefore, parents in our study may have access to more resources to help their children with emotional or behavioural problems, compared to a more evenly distributed or lower educated group of families. Third, parents could have been influenced by a social desirability bias and completed the questionnaires to encompass less problems than they actually

experienced. However, questionnaires have a lower social desirability bias than other methods such as a face-to-face interview (179). Fourth, despite requesting parents to complete the questionnaires independently from each other, we cannot guarantee that all parents complied with these instructions, as the questionnaires were completed without supervision of the research team. Hence, some parents could have influenced each other during completion of the questionnaires. Fifth, this study was limited by the lack of a standardised measure of the functional impact of children's CL±P or IH diagnosis. Finally, treatment status was not accounted in the analysis.

To address the abovementioned limitations, we advise future research to include children from multiple health care settings, have a representative group of parents across a wider range of educational attainment, gather information about treatment status, and construct standardised measures to capture the impact of diagnoses. Furthermore, qualitative research is needed to assess specific concerns that might not have been addressed in our questionnaires. These studies can also help to indicate what factors, such as parenting style or a response shift, play a role in the aetiology of the current findings. In addition, replication across countries and cultures is needed.

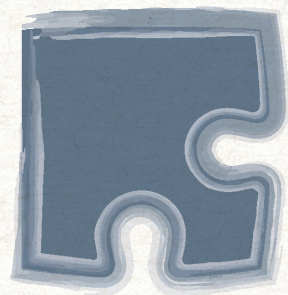
In conclusion, this study showed that parents of children with CL±P or IH report less emotional and behavioural problems in their children compared to the general population. Nonetheless, some children appear to be at risk. These include children with increased condition-specific problems and children of parents with heightened negative affect. To identify patients most at risk, we advise clinicians to use screening questionnaires in clinical follow-up. These can be used to offer timely psychological support.

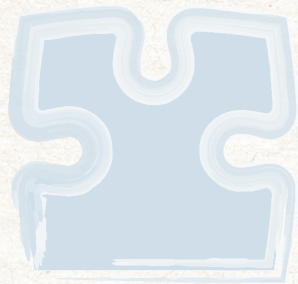
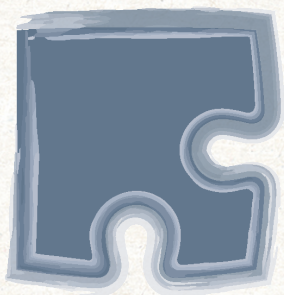


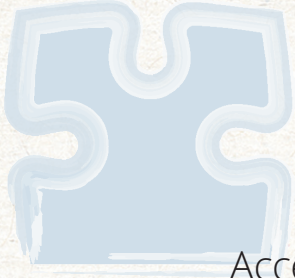


PART II

YP Face IT: an online psychosocial intervention
for adolescents with a visible difference





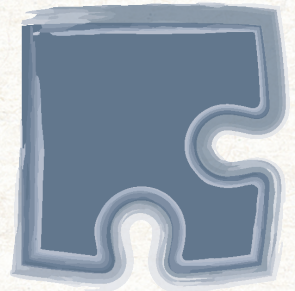


CHAPTER 4

Acceptability and feasibility of an online
psychosocial intervention for adolescents with a
visible difference: a mixed-method study

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Abstract

Introduction: Adolescents with a visible difference can experience difficult social situations, (e.g., people staring or making unwanted comments) and are at risk for mental health problems. Unfortunately, interventions for adolescents with a visible difference who experience appearance-related distress are scarce and lack an evidence-base. This study tests the acceptability and feasibility of YP Face IT, an innovative online psychological intervention, in Dutch adolescents. **Methods:** Adolescents aged 12-18 with a visible difference and access to an internet-enabled computer or tablet participated. They completed YP Face IT (eight sessions). Prior and directly after YP Face IT questionnaires were administered to inform future study design. After YP Face IT in-depth interviews took place to assess the acceptability and feasibility of YP Face IT and study procedures. **Results:** 15 adolescents consented to participation, one person dropped out after one session. Adolescents appreciated the intervention and would recommend it to other adolescents experiencing appearance-related distress. Everyone reported personal growth after following the sessions. Some struggled with motivation, but reminders by the website and research team were helpful. **Discussion:** The Dutch YP Face IT intervention is acceptable and feasible to use. An RCT should be conducted to assess the effectiveness of the intervention.

Keywords: eHealth, Body Image, Adolescent, Visible Difference, Psychosocial Intervention, Feasibility Study

1. Introduction

Living with a visible difference (i.e. disfigurement) can be very challenging, as it often concurs with difficult social situations, such as people that stare, ask unwanted questions or tease and bully. It is estimated that 1 in 44 people have a visible difference to the face or body and 1 in 111 have a visible difference that solely affects the face (1). A visible difference can be either congenital (e.g. cleft lip and palate, craniofacial conditions), result from a skin condition (e.g. vitiligo, psoriasis), trauma (e.g. burns, scars), disease (e.g. cancer, meningitis) or medical treatment (e.g. radiotherapy).

Studies that have focused on the psychosocial aspects of living with a visible difference have produced contradictory findings. Some studies show that adolescents with a cleft lip experience no additional psychosocial problems (87) and even perceive their friendship, social acceptance, appearance and emotional well-being in a more positive way than unaffected peers (30). In contrast, literature reviews show that a significant number of adolescents with a visible difference can experience adverse psychosocial outcomes (180-182). More specifically, they experience higher levels of self-consciousness in public situations, neuroticism (183), internalising symptoms (62, 182) and anxiety, depression and difficulties with social functioning (86). A recent meta-analysis shows that adolescents with a visible difference experience more anxiety than unaffected peers (184).

While research has shown that people with a visible difference may experience adverse psychosocial outcomes, available interventions are scarce and have not been thoroughly studied. This is true both for interventions aimed at adults (65-67) and adolescents (68). Research often lacks a robust design and has poor methodological quality, yielding small effect sizes. However, there is some support for interventions that include Social Skills Training (SST), Cognitive Behavioural Therapy (CBT; 65, 67, 68) and anxiety management techniques (66). These techniques are promising when it comes to ameliorating psychological distress in individuals with a visible difference.

In order to provide adolescents with a visible difference with an intervention to address psychosocial issues, Young People's (YP) Face IT was developed in collaboration with adolescents, clinical experts and the UK charity Changing Faces (www.yppfaceit.co.uk; 70). This intervention combines SST and CBT strategies and was derived from Face IT, an intervention aimed at adults (71). More information about YP Face IT is included in the methods section and in a trial design paper by van Dalen, Pasmans (185). In a Randomised Controlled Trial (RCT), Face IT was found to be effective at reducing anxiety, depression and appearance concerns (71). In a British acceptability and feasibility study YP Face IT was found to be acceptable to

adolescents, with most thinking it would help improve their confidence and self-acceptance, and help develop new skills in dealing with difficult social situations (70). Although YP Face IT may improve appearance-related distress (186), the intervention has not been subjected to a RCT and there are concerns about whether adolescents have sufficient motivation to start and complete the full self-help program (72).

Recently, YP Face IT was translated to Dutch. To assess the acceptability and feasibility of the Dutch version of YP Face IT (*Face IT voor jongeren*) in The Netherlands, we conducted a mixed-method study. Conducting this study was a vital step in order to reveal aspects of the intervention that may require adjustment (including cultural adaptations) prior to full evaluation of its effectiveness via a RCT (187). The current study aimed to establish via in-depth interviews 1) the acceptability of the Dutch version of YP Face IT to Dutch adolescents and 2) the feasibility of using a RCT design to assess its effectiveness. More specifically, objectives of the current study were to establish:

1. The acceptability of therapeutic content;
2. The structure and presentation of the intervention;
3. The usefulness of the intervention;
4. And the acceptability of this study and study procedures.

Objective 1 was determined by qualitative data and quantitative data on completion rates and adherence to the intervention. Objective 2 was determined by qualitative data and quantitative data on the preference of eHealth or face-to-face care. Objectives 3 and 4 were informed by qualitative data.

2. Methods

This study was performed according to the SRQR guidelines (188). This study was registered prospectively in the Netherlands Trial Register, registration number NL7138. Ethical approval was obtained from the medical ethics review committee in Rotterdam, MEC-2018-052.

2.1. Participants

Participants were eligible if they a) had a self-declared visible difference due to any injury or condition, b) were aged 12 to 18 years old, c) had access to an internet-enabled computer or tablet. Patients were excluded from the study if they had either a) a learning disability that would interfere with their ability to follow and comprehend the intervention content, b) a visual impairment which prevented the participant from viewing the intervention, or c) reading skills below the level of a 12-year old. Patients did not have to experience appearance-related distress,

as adolescents that are coping well were judged to be able to provide valuable information too.

If the adolescent was younger than 16 years old, informed consent was obtained from both legal parents/carers and assent was obtained from the adolescent. For adolescents aged 16 or older informed consent was obtained from the adolescent.

2.2. Interview

Semi-structured audio-recorded interviews were conducted by the first author (MvD) between May and June 2019. The interviewer was familiar to the participants, as she was the contact person during the entire study. The interview was based on an interview schedule used by the British YP Face IT study (189). The interview in this study was used to elicit opinions on the intervention and on the study procedures. More specifically, questions focussed on: the acceptability of therapeutic content, its reliability and usefulness and presentation of the intervention, including use of language, structure and ease of navigation tools, views around adult supervision whilst completing the intervention, possible improvements, recruitment strategies and quantitative data collection procedures.

Participants were free to choose the means of interviewing (through the phone, a video call, face to face in the hospital or at home) and whether they wanted a parent to be present. This potentially improves response rates and provides a means of interviewing that is comfortable to the participant (190). Interviews were scheduled to last around one hour.

The first author who conducted the interviews was a PhD student at a Dutch university. She has a master's degree in clinical child and adolescent psychology, with no prior training on qualitative research methods. She was supported by Dr. Okkerse who is a clinical psychologist and has 25 years of experience in treating children and adolescents with a visible difference and appearance-related distress. Dr. Williamson is a researcher with extensive experience in qualitative research methods and research into the well-being of people with a visible difference. Prof. dr. Utens is a clinical psychologist with considerable research experience in intervention studies aimed at reducing anxiety in children and adolescents. Other members of the research team all have different areas of expertise. Prof. dr. Pasmans is a dermatologist with experience with adolescents with a visible skin difference, Mrs. Aendekerk is a clinical psychologist, Prof. dr. Mathijssen is a plastic surgeon with expertise in treating craniofacial disorders, Dr. Koudstaal is a maxillofacial surgeon specialised in children with craniofacial disorders including cleft lip and/or palate. Both Prof. dr. Mathijssen and Dr. Koudstaal are a member of multidisciplinary teams treating adolescents with a visible difference. Prof. dr. Hillegers is a child psychiatrist

and head of the department of Child and Adolescent Psychiatry/Psychology. None of the members of the research team have a visible difference themselves.

2.3. Questionnaires

The questionnaires are described in more detail in one of our previous papers (185). The following questionnaires were completed by participants at baseline and post-intervention:

1. The Social Anxiety Scale for Adolescents (SAS-A; 191) was used to measure social anxiety. The SAS-A contains 22 statements that are rated on a 5-point Likert scale.
2. The 'appearance' subscale from the Body Esteem Scale For Adolescents and Adults (BESAA; 192) was used to assess participants attitudes and feelings about their appearance. This subscale consists of 10 items rated on a 5-point Likert scale.
3. To assess aspects of self-worth, the Dutch version of the Self-Perception Profiles for Adolescents (SPPA; 193), the Competentiebelevingsschaal voor Adolescenten (CBSA; 194) was used. The CBSA consists of 35 items, each consisting of two contrasting statements. The participant is asked to choose one and define whether this statement is "sort of true for me" or "really true for me".
4. The Perceived Stigmatization Questionnaire (PSQ; 32) was used to assess stigmatisation behaviours commonly experienced by adolescents with a visible difference. The PSQ consists of 21 items containing examples of stigmatising behaviours. Adolescents are asked to rate on a 5-point Likert scale how often they experience each behaviour.
5. The EuroQol-5D-5L (EQ-5D-5L; 195) was used to assess health-related quality of life. The EQ-5D-5L consists of five statements and a visual analogue scale assessing global health.
6. The Body Image Life Disengagement Questionnaire (BILD-Q; 196) was used to measure the extent that worries relating to appearance stop a person from engaging in life activities or going to social events. The scale consists of 10 statements that are rated on a 4-point Likert scale.
7. The Child Depression Inventory – 2 (CDI-2; 197) was used to assess depressive symptoms. The questionnaire consists of 28 items with three answer options (e.g., I am sad sometimes, I am often sad, I am always sad).
8. The Mirror, Mirror.. questionnaire (Spiegeltje, spiegeltje..; 198) was used to assess appearance-related distress. This questionnaire consists of 58 statements about appearance (e.g. my appearance makes me insecure), rated on a 5-point Likert scale ranging from "never" to "always".

2.4. Procedure

This study used a pragmatic mixed-method design to assess adolescents' opinions on the study and the intervention.

Participants were recruited via purposive sampling through the Erasmus MC, The Netherlands and through Dutch patient organisations. Recruitment lasted 16 weeks. Participants recruited via hospital were first informed about the study by their treating clinician. A member of the research team was present in the waiting room to elaborate on the study and to provide an information package containing information letters and consent forms. When recruitment proceeded via patient organisations, patients were informed about the study by the patient organisation through social media, e-mail, magazine or the organisation's website. Interested parties received further information and consent forms after contacting the research team.

Fourteen days after receiving the information package, the research team phoned the adolescent or one of their parents to answer questions. After the research team received the signed informed consent forms, an online link to the questionnaires was sent. Adolescents were given two weeks to complete the questionnaires.

After completing the questionnaires, adolescents received the login details for YP Face IT. Participants were asked to complete seven weekly sessions. An additional booster session was completed after six weeks.

Upon completion of the intervention, participants once again received an online link to the questionnaires. Participants were given two weeks to complete the questionnaires. An interview was scheduled.

2.5. Intervention

YP Face IT is an online intervention developed for young people with a visible difference and experiencing appearance-related distress (70). The intervention combines social skills training with cognitive behavioural therapeutic techniques. There are eight sessions; seven weekly sessions and one booster session six weeks after session 7. Each session uses text, videos, tasks and different interactive activities to encourage young people to develop new skills. In between sessions participants complete short homework assignments.

YP Face IT is an easy-to-access self-help program, but progress is monitored in the background by psychologists to ensure progress and check for psychological issues that may need referral to face-to-face care. Adolescents can use the program in their own time and are encouraged to apply the learned techniques in everyday life. Contrary to other versions of YP Face IT, the Dutch version of YP Face IT does

not contain audio-recordings of the sessions. The content of the intervention is shown in Table 1.

To help facilitate making a session each week, the participants can set reminders. The system will then send an automatic e-mail when a session is due. Reminders were also sent by the research team via WhatsApp if a next session was not started 10 days after the prior session.

To ensure the safety of all data on the website, a two-factor authentication was installed on the website. After logging in, participants received an e-mail with a pin code containing 4 digits.

2.6. Data analysis

Interviews were audio-recorded and transcribed verbatim. Selected quotes for this article were translated from Dutch to English and edited for readability.

Inductive thematic analysis at a semantic level was used to analyse the qualitative data (199). We used the six steps as described by Braun and Clarke (199) to analyse and code the interviews. These steps include: familiarising yourself with the data, generating initial codes, searching for themes, reviewing themes, defining and naming themes and producing the report.

To ensure consistency in coding, two researchers (MvD and JO) independently coded the first interview. They then discussed this interview to identify relevant themes and to achieve consensus on how to score the other interviews. The first author (MvD) then coded all other interviews and generated the themes. Data analysis was conducted using MAXQDA 2018 software for qualitative data analysis (200).

The questionnaires were used primarily to elicit opinions about the study design. This design could then be adjusted for a future RCT. Also, the sample size was small. Hence, questionnaires were not analysed in detail.

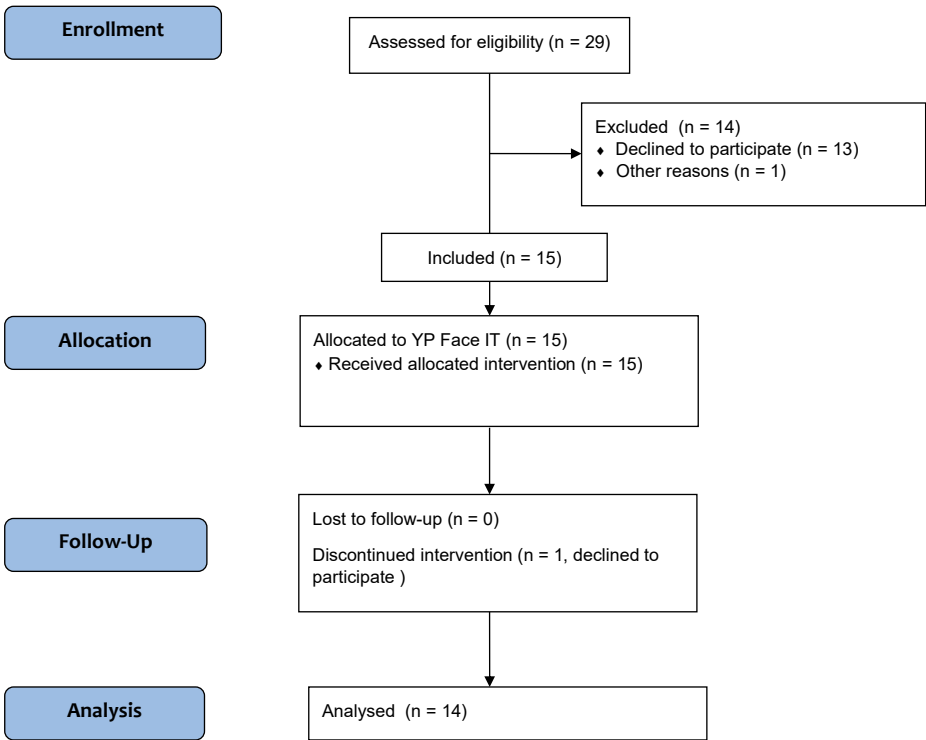
Descriptive statistics were calculated for therapeutic adherence and ratings adolescents gave YP Face IT during the interview.

Table 1. Content of the YP Face IT intervention

Session	Content	Type	Week
1. Common problems	Common problems experienced by adolescents with a visible difference; bystander responses, teasing, bullying.	SST	1
2. Improve your social skills	Body language, verbal and non-verbal skills and building positive social interaction skills.	SST	2
3. Don't be SCARED, REACH OUT	Effect of own behaviour on other people. <i>REACHOUT</i> toolbox of techniques to cope with difficult social situations (Reassurance, Effort and Enthusiasm, Assertiveness, Courage, Humour, Over there, Understanding, and Try again).	SST	3
4. Think, Feel, Do	Relationship between thoughts, feelings and behaviours. Identifying negative thoughts and using a positive voice to challenges these thoughts. Different coping strategies for negative thoughts.	CBT	4
5. SMART goals	Using SMART goals to help achieve goals, dividing the end goal into sub goals. Dealing with concerns around romantic relationships.	CBT	5
6. Beating anxiety	Relaxation techniques. Exposure therapy in the form of a fear ladder.	CBT	6
7. Looking at your progress	Summary session of key learnings from previous sessions.	SST/CBT	7
8. Booster quiz	Quiz with 16 questions on all taught techniques.	SST/CBT	13

Note: SST = Social Skills Training; CBT = Cognitive Behavioural Therapy

Figure 1. Flow-chart based on CONSORT statement



3. Results

As shown in Figure 1, 29 adolescents were assessed for eligibility. Five of those contacted the research team after hearing about the study from a patient organisation. Others were contacted by the research team during their appointment in the hospital. Thirteen adolescents declined to participate, and one was lost in contact by the research team. A total of 15 adolescents were included in the study. One person declined further participation after one session, considering YP Face IT irrelevant because she did not have any psychosocial problems. Overall 14 adolescents participated ($M_{age} = 15.35$, $SD = 1.73$, 71.4% male). This was deemed an appropriate number of participants to identify important themes and achieve data saturation (201). Interviews lasted a mean time of 49 minutes (range 32 – 82 minutes). Two interviews were conducted via telephone and 12 were face-to-face (six in the participant’s home and six at the hospital). Seven participants were diagnosed with a cleft lip and/or palate (CL/P), two with a congenital melanocytic nevi, one with Apert syndrome, two with craniofacial microsomia, one with Goldenhar syndrome and scaphocephaly and one with a port-wine stain. Details, with pseudonymised names are shown in Table 2.

Table 2. Demographics and condition characteristics

Name*	Medical diagnosis
Jack	Cleft lip/palate
Chloe	Congenital melanocytic nevi
Matt	Congenital melanocytic nevi
Samuel	Cleft lip/palate
Hannah	Cleft lip/palate
Daniel	Cleft lip/palate
Thomas	Cleft lip/palate
Emily	Apert Syndrome
Joshua	Craniofacial microsomia
Luke	Cleft lip/palate
Sophie	Cleft lip/palate
Oliver	Port-wine stain
Ben	Goldenhar syndrome & scaphocephaly
Ryan	Craniofacial microsomia

* All names were pseudonymised. To ensure anonymity of adolescents with a rare medical condition, age is not included in this table.

3.1. Acceptability of YP Face IT

Of the 15 adolescents that started on YP Face IT, 13 (86.67%) completed all eight sessions, one person (6.67%) completed seven sessions and one person (6.67%) dropped out after one session. The completers took an average of 12.77 weeks (median 13) to complete YP Face IT.

All adolescents indicated that they would recommend the program to other adolescents with a visible difference and experiencing appearance-related distress. On a scale of 1 (worst score) to 10 (best score) they evaluated the program with a median of 7.9 (IQR = 7.0 – 8.0).

3.1.1. Therapeutic content

Adolescents felt that the program was relatable and matched their experiences of living with a visible difference, although some adolescents commented that they had not experienced bullying or name-calling by a group of strangers.

Several adolescents also commented that they liked the techniques and thought the explanation of these techniques was clear: *“Everything was explained well, there were good ways to solve problems or things like that, nice activities and nice homework activities that you can do and apply.”* (Hannah, cleft lip/palate).

Some young people commented that learning about the think-feel-do technique was very helpful. This technique explains the relationship between thoughts, feelings and behaviour. The adolescents thought that YP Face IT did not miss any information, although one person mentioned that information on social media could be useful.

Opinions differed on which session was the best, but some adolescents commented on session 7 and 8: *"I liked that there was a sort of recap at the end. And also a quiz, so that you follow it better really."* (Daniel, cleft lip/palate).

The activities users were asked to complete during sessions and as homework helped embed key learnings: *"For me personally, you know if I write or type something myself, I will remember it better than when I read it and don't come back to it."* (Thomas, cleft lip/palate). The assignments did not take a lot of time, but the assignment in which a fear ladder was created was perceived as more strenuous: *"The one with the ladder, where you had to name different things. You have to think carefully, you have to name different steps, but if you only name three it's not enough for the entire ladder."* (Hannah, cleft lip/palate). Some adolescents skipped some of the homework assignments.

3.2. Structure and presentation of the intervention

3.2.1. Structure of YP Face IT

Overall, the adolescents appreciated the way YP Face IT was laid out with social skills training presented before cognitive behavioural therapy: *"With the social skills you learn how you come across and of course thoughts go along with this too, so how you come across gives you thoughts, so I liked the link between the two."* (Hannah, cleft lip/palate). No one wanted to change the order of the sessions. They appreciated the way YP Face IT looked and the way the information was set up. Several adolescents commented on the interactive features in the program. They liked the activities where you could select a response to see how others would react and the interactive videos playing out difficult social situations.

The length of the sessions was deemed appropriate and took the participants anywhere between 15 and 45 minutes. However, some participants commented that session 4 was very long: *"There were no sessions that were too short, but especially at [session] 4 the text was really long. So that was kind of annoying, because you thought, oh the text is almost done and then there was a lot more text."* (Sophie, cleft lip/palate)

Most adolescents indicated that they were able to complete the program by themselves. Some adolescents, especially the younger adolescents, asked their parents for help when they encountered words or things they did not fully

understand: *"They [the parents] did not help, because I did it all by myself. But if there was something I didn't really understand, I asked them."* (Luke, cleft lip/palate).

Some adolescents commented that there was repetition in the program, but there was no consensus on whether this was a good or a bad thing:

"No, it's not annoying, no, it's just, another repetition, because it's not like you can be a professional football player after playing keepie uppie just one time, you have to do it more often." (Oliver, port-wine stain)

"Everything is maybe, yes, sometimes explained three times. Then I think, yeah, after one time I also understand this." (Jack, cleft lip/palate)

3.2.2. Presentation of YP Face IT

The majority of adolescents thought the website was suited for adolescents aged 12-18. However, some adolescents older than 15 thought the website was tailored more towards the younger adolescents and thought some elements were childish. This was mostly due to the brighter colours used and the use of avatars. Other adolescents liked the colours and avatars: *"The website was actually quite attractive. The colours, the puppets, I liked how that was done."* (Sophie, cleft lip/palate).

The website was deemed as ordered and structured by most adolescents, although some commented that a register or search function could help them find information more easily: *"If you had, separate from the sessions, a sort of register that you can just quickly search in. that you can just, just find a word or something and see that belongs to this session."* (Samuel, cleft lip/palate).

The website contains a journal in which adolescents can document their progress or write about their day. Only a few adolescents used this function. Some suggested that it would be easier if the journal was always available, instead of at certain points in the session: *"I also think it would be handier if, when you want to use the journal, that it is already on the page."* (Oliver, port-wine stain).

The website contains a forum in which participants can talk to each other. This forum was not used by any of the adolescents in the current study. The majority of the adolescents indicated that a forum could be useful for some people, but not for them: *"It doesn't bother me, so I don't need it. But I think for people who are bothered by it.. They would like to talk about other people's experiences"* (Matt, congenital melanocytic nevi). Some said they did not use the forum, because it did not have any messages on there. Others felt that they would prefer talking to someone directly, or using chat groups such as on Facebook or WhatsApp.

When asked about things that they would change about YP Face IT, some adolescents commented on adding an audio-feature, because they preferred listening over reading: *"I personally like [audio fragments] better, that I can just put it in my ears, listen to it 2 or 3 times if necessary."* (Samuel, cleft lip/palate). Others commented on adding more videos and shortening some texts.

3.2.3. Preference for YP Face IT or face-to-face care

When asked about what type of care they would prefer, YP Face IT or face-to-face care, eight adolescents (57.14%) choose YP Face IT, four (28.57%) face-to-face care and two (14.29%) commented that it mattered on the type and severity of psychological issues they would experience. Advantages of YP Face IT were the anonymity it afforded, being able to schedule the session when it is most convenient, not having to disclose personal information to someone you do not know and ease of access to support with no need to travel:

"You can just do YP Face IT at home. That's just much easier than when you have to go somewhere or she comes to you and you have to make an appointment.. And there you can just, on YP Face IT, log in and just, done." (Matt, congenital melanocytic nevi)

Some identified that a limitation of YP Face IT is that it cannot be tailored to meet individual needs:

"I think with a psychologist you have to build trust before you are really able to tell them something, but the advantage is that if you are able to tell it, this person can adjust the advice directly to you. A program can too, but then it's less, it's just not personal." (Hannah, cleft lip/palate)

3.3. Usefulness of the intervention

3.3.1. Positive effects

Most adolescents reported learning something from completing YP Face IT. For most the changes were small: *"I learned things about body language. That you have to be open to other people and not slouching. You know, you always keep that in the back of your mind."* (Jack, cleft lip/palate). Others reported a better understanding of other people's thoughts and intentions: *"Sometimes it [the visible difference] still bothers me and this might help to make it [YP Face IT] more fun. For example, that I understand better why some people watch and how sometimes they laugh, while they are sometimes not laughing about me."* (Joshua, craniofacial microsomia)

One person in particular, reported a big change in her self-esteem. She had tried other programs and psychological counselling to improve her self-esteem, which had not really helped her. She said YP Face IT really helped her:

"I did do the exercises and I dare to ask a lot more questions now. [...] And I'm less afraid of walking up to strangers now. [...] In the past I would have thought, yeah, they don't like me anyway. But now I don't think like that anymore." (Sophie, cleft lip/palate)

3.3.2. Potential barriers and facilitating factors for completing YP Face IT

Despite using the 'set reminder' function, two participants reported that they did not read their e-mail and subsequently forgot about the session. Other participants reported simply forgetting about the sessions, until they received an automatic reminder or a reminder by the research team. Other barriers were a lack of time and motivation. As one person put it: *"I think I had the time, but I wasn't really feeling like it. [...] I would rather play games with my friends."* (Daniel, cleft lip/palate). Some participants also mentioned that the amount of text in the sessions was off-putting. Participants felt that sessions contained a lot of text, especially session 4.

In response to previous studies finding motivation problems amongst participants, we investigated whether it would be helpful to send an extra e-mail after session 4. This e-mail stated that they were halfway and that other sessions would be shorter. This helped increase motivation for most participants: *"It was kind of motivating. I thought, wow, I'm actually quite far."* (Jack, cleft lip/palate).

The adolescents thought that the two-factor authentication did not influence the amount of times they logged into the website, although some participants had some issues with receiving the code: *"Sometimes it worked and sometimes it didn't, and then I would get five passwords in a row and then I tried one and it wasn't correct, and I thought okay, I will do it in an hour."* (Emily, Apert syndrome). Some participants reported that it would be easier without the two-factor authentication, even though it didn't matter how often they would use the website. Others reported that it made them feel secure, knowing that other family members could not access their account: *"I think some people would actually like it. If you just know, if you do it on the family computer or something, that your entire family doesn't have access to it."* (Chloe, congenital melanocytic nevi).

When asked what they liked the least about the program, some adolescents commented that the website did not always function properly. For instance, the code for two-factor authentication was not always e-mailed right away. This was solved by sending the code to their mobile phone instead of to their e-mail.

3.4. Research and research procedures

3.4.1. Reasons for participation

Most adolescents cited helping others as a reason for participation. As one person put it: *"I just like participating in research. The more people participate, the better it is for other people in the end."* (Samuel, cleft lip/palate). One person participated for personal reasons: *"I was curious, because I have done several things for my self-esteem. So I really wanted to try it."* (Sophie, cleft lip/palate).

3.4.2. Research procedures

The adolescents informed about the study before their appointment in the hospital appreciated this personal approach: *"It was nice, to hear about it face-to-face so that you know what you are up for and can ask questions immediately."* (Ben, craniofacial condition).

Overall, most adolescents thought that information letters were clear, although some didn't read all the information: *"I don't really like reading. So it was a lot of reading, so I scanned through it, to see what the study involves."* (Daniel, cleft lip/palate).

Completing the questionnaires took participants approximately 15-45 minutes. One thought this was too long, but everyone else thought the length of the questionnaires was acceptable. Some reported that the questionnaires started a thought process: *"I liked doing the questionnaires. And then you tick boxes that you wouldn't expect. [...] I liked doing it, because you learn from it."* (Sophie, cleft lip/palate). Everyone completed the questionnaires at baseline. Nine people (81.82%) completed the questionnaires at follow-up.

Everyone appreciated the contact with and reminders by the research team: *"I like to be reminded sometimes, you know. It was quite good. And WhatsApp is of course very convenient, because, yeah.. everyone uses it. It's just fast."* (Chloe, congenital melanocytic nevi).

3.4.3. Recruiting adolescents into a new study

When asked what we could do to improve recruitment processes, adolescents indicated that we should address the potential participant directly: *"Talk to people about it, what awaits them, so that people know what they are up for. And tell it in a nice way, I think."* (Ben, craniofacial condition);

Make a promo video or use social media: *"It is helpful to, for example, put in on platforms such as Instagram or Twitter."* (Oliver, port-wine stain);

Or give some kind of reward: *“For example, if you give some kind of reward. [...] It could be anything. Like a gift card. But it could also be a fun day. It could also be a day here in the hospital.”* (Jack, cleft lip/palate).

Some adolescents commented that we should retain the current procedures.

4. Discussion

This study investigated the acceptability and feasibility of the Dutch YP Face IT program. Interviews with 14 adolescents with a wide range of visible differences were conducted. The data suggests that YP Face IT is acceptable and feasible to Dutch adolescents. Everyone recommended the intervention for adolescents experiencing appearance-related distress and most adolescents reported learning something from the intervention. YP Face IT has incorporated reminders to increase motivation. This was appreciated by the adolescents.

This study also showed that not all adolescents preferred eHealth. So, despite the current generation being seen as digital natives with 93.5% of adolescents using the internet (almost) every day (202), it is important to keep in mind that an eHealth intervention might not suit everyone. So, if YP Face IT were to become part of a stepped-care framework (see 203) in which the intensity of care provided is determined by psychological aspects, factors that determine who should use eHealth and who receives face-to-face care should be examined.

Concerning our research procedures, evidence suggests that procedures can be retained, with the addition of using social media to aid recruitment and rewarding participation.

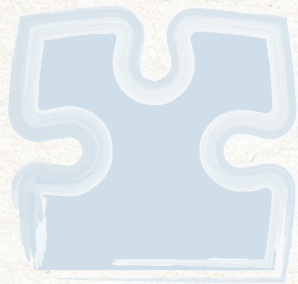
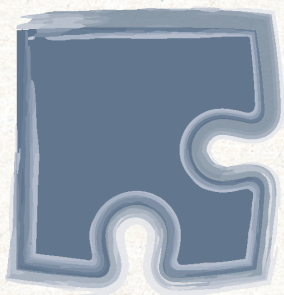
Our results are in line with previous research showing that YP Face IT is acceptable to British adolescents (186). Contrary to other studies reporting high attrition rates for American adolescents completing YP Face IT (72), retention was high with 13 (86.67%) adolescents completing YP Face IT and nine (81.82%) completing outcome measures. However, the study by Riobueno-Naylor, Williamson (72) did not use the automated reminder system. This might have also contributed to a higher attrition rate in comparison to our study, where adolescents received automated reminders and reminders by the research team. Second, Riobueno-Naylor, Williamson (72) only included adolescents with burns, an acquired condition. Our study only included adolescents with congenital visible differences.

The current study has a number of strengths and limitations. A strength is the high number of adolescents that completed the entire program ($n = 13$, 86.67%). Also, most adolescents completed YP Face IT within the 13-week timeframe. This improves the generalisability of current results to future clinical use. Furthermore, YP Face IT is an innovative, online psychological intervention. This is the first eHealth intervention specifically for adolescents with a visible difference living in The Netherlands.

A first limitation of this study is that all the visible differences were congenital and were present from birth. Despite contacting some adolescents with an acquired visible difference, none of them finished the study. One dropped out after one session and we were unable to reach another after sending the information package. Hence, we were unable to study adolescents with an acquired visible difference. The influence of this on our results remains unclear. To our knowledge, there are no studies that compare people with a congenital condition to those with an acquired condition. Previous research has shown that the subjective experience of the visibility of the condition is more important in predicting psychological adjustment than the objectively rated visibility (14). Whether adolescents with an acquired visible difference would report similar results is unknown.

A second limitation is that the first author was involved in both the recruitment, data collection and conducting the interviews. This could have led to a social desirability bias (204), where adolescents could be prone to respond more positively to questions asked during the interview. However, participants shared numerous critical points during the interviews, we think the extent of this bias is limited.

As results show that the Dutch version of YP Face IT is acceptable and feasible to Dutch adolescents, a RCT should be conducted to assess the effectiveness of the intervention. A RCT is currently being conducted in The Netherlands (184). Should the results of this study be positive, YP Face IT could be implemented in hospitals across The Netherlands.



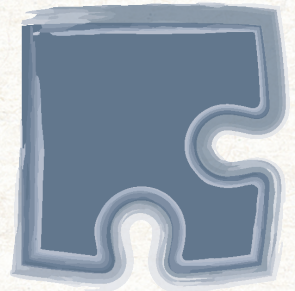


CHAPTER 5

Investigating online psychological treatment
for adolescents with a visible difference in
the Dutch YP Face IT study: protocol of a
randomised controlled trial

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Abstract

Introduction: This paper outlines the study protocol for the Dutch YP Face IT study. Adolescents with a visible difference (i.e. disfigurement) often experience challenging social situations such as being stared at, receiving unwanted questions or being teased. As a consequence, some of these adolescents experience adverse psychosocial outcomes and appearance-related distress. To address this appearance-related distress, an online psychotherapeutic intervention, YP Face IT, has been developed. YP Face IT uses Social Skills Interaction Training and Cognitive Behavioural Therapy. The Dutch YP Face IT study tests whether this intervention is effective in reducing social anxiety and improving body esteem. **Methods and analysis:** Participants are adolescents aged 12-18 with a visible difference and experiencing appearance-related distress. In this two-armed Randomised Controlled Trial, 224 adolescents will be randomised to care as usual or YP Face IT. Adolescents will complete questionnaires at baseline, at 13 weeks and at 25 weeks. Primary outcomes are differences in social anxiety and body esteem between YP Face IT and care as usual. Secondary outcomes are differences in aspects of self-worth, perceived stigmatisation, health-related quality of life, life engagement, appearance-related distress and depressive symptoms between the two groups. **Ethics and dissemination:** Research ethics approval was obtained from the Medical Ethics review Committee Rotterdam (reference number MEC-2018-052/NL63955.078.18). Findings will be disseminated through academic peer-reviewed publications, conferences and in newsletters to patient associations and participants of the study. **Trial registration:** This trial was registered in The Netherlands trial register, NL7626, Registered 26th March 2019, <https://www.trialregister.nl/trial/7626>.

Keywords: Visible difference; appearance-related distress; adolescents; anxiety; body-esteem

1. Introduction

Having a visible difference can have a substantial impact on one's life. People with a visible difference commonly encounter difficult social situations, such as being stared at, receiving unwanted questions and feeling isolated. A visible difference (i.e. disfigurement) to the face or body occurs in 1 in 44 people, a visible difference solely to the facial area in 1 in 111(1). A visible difference can be either congenital (e.g. cleft lip and palate, craniofacial conditions), result from a skin condition (e.g. vitiligo, psoriasis and acne), trauma (e.g. burns, scars), disease (e.g. cancer, meningitis and alopecia areata) or medical treatment (e.g. surgery or radiotherapy). Whether someone identifies as having a visible difference is a subjective experience. A clear definition of what a visible difference is can thus not be given.

Some studies show that adolescents with a visible difference experience no additional psychosocial problems(48, 87) and even perceive their friendship, social acceptance, appearance and emotional distress in a more positive way than unaffected peers(30). However, reviews show that a significant amount of adolescents with a visible difference do experience adverse psychosocial outcomes(180-182). More specifically, they experience higher levels of minor psychological disturbance, self-consciousness in public situations, neuroticism(183), internalising symptoms(62, 182) and anxiety, depression and difficulties with social functioning(86). Furthermore, parents perceive their children as being more shy and inhibited(205).

Available interventions for adolescents or adults with a visible difference are scarce and lack evidence-base(65-68). Research often lacks a solid design and overall methodological quality, and yields small effect sizes. However, there is some support for models involving Social Skills Training (SST), Cognitive Behavioural Therapy (CBT; 65, 67, 68) and self-help for managing anxiety(66).

YP (Young People) Face IT was developed in the UK, in collaboration with adolescents and the charity Changing Faces(70). YP Face IT was derived from the adult intervention Face IT which was found to be effective at reducing anxiety, depression and appearance concerns whilst increasing positive adjustment(71). In an acceptability and feasibility study concerning YP Face IT, the intervention was found to be acceptable, with most of the adolescents thinking it would help them improve their confidence and self-acceptance and help them develop new skills in dealing with difficult social situations(70).

1.1. Aims

In sum, interventions aimed at adolescents with a visible difference are scarce and have limited evidence to support them. The available evidence, however, does point to SST and CBT as being potentially effective methods for managing psychosocial difficulties amongst people with a visible difference. In an attempt to provide adolescents coping with a visible difference with an effective intervention focussing on improving emotional resilience, the Dutch YP Face IT study aims to test an online psychotherapeutic intervention combining Social Interaction Skills Training (SIST) and CBT. More specifically, the aims of the current study are to test the effectiveness of the Dutch version of YP Face IT in reducing anxiety and improving body-esteem amongst Dutch adolescents with a visible difference.

2. Methods

To assess the effectiveness of the Dutch version of YP Face IT, a randomised controlled trial (RCT) will be conducted. This trial was registered prospectively in the Netherlands Trial Register (NL7626).

2.1. Participants

This study will be conducted in a Dutch academic hospital. The target group for this study is Dutch adolescents aged 12-18 with a visible difference and experiencing appearance-related distress. Recruitment will take place throughout The Netherlands.

Adolescents will be eligible for participation if they are aged between 12 and 18, have a visible difference, access to a computer with internet and experience appearance-related distress. The appearance-related distress is operationalised as an elevated score on either social anxiety or depression, or a lower score on body esteem, as assessed by self-reports.

Exclusion criteria are a mental disability, reading ability below 12 years of age, visual impairments preventing comprehension of the online intervention, a clinical diagnosis of depression, psychosis, body dysmorphic disorder or an eating disorder, and insufficient proficiency of Dutch. Furthermore, adolescents who receive face-to-face care by a psychologist will be excluded from participation.

2.2. Intervention

YP Face IT (Dutch: *Face IT voor jongeren*) is an online psychotherapeutic intervention(70) specifically designed for adolescents and developed in cooperation with adolescents and the British charity Changing Faces. The intervention is aimed at helping adolescents cope with some key concerns people with a visible difference

may have, such as anxiety, depression, low self-esteem and appearance-related distress.

YP Face IT combines SIST with CBT. The intervention consists of seven weekly sessions and an additional booster session after six weeks, helping the adolescent recall what was learned during the weekly sessions. The first three sessions focus on SIST, sessions 4-6 focus on CBT and session 7 is a summary of all learned techniques. Session 8 is a booster quiz, six weeks after session 7. The content of each session is displayed in Table 1. Each session has different exercises and activities and takes 45-60 minutes to complete. In addition to the weekly sessions, participants will also be asked to complete small homework assignments between sessions. Participants will have access to an online journal in which they can write about their experiences and enter the answers to the homework assignments. Participants will have the opportunity to contact the research team if they are struggling with the homework activities. A reminder e-mail is sent if the participant has not entered data relating to the homework activity in their journal within five days following their last session.

YP Face IT is designed as a self-help intervention, without any active guidance by a psychologist. Adolescents work through the sessions on their own. Parents receive a short description of each session and will receive the reminders, but are not involved in the sessions themselves.

Monitoring will take place to assess whether adolescents complete the homework assignments and whether they are struggling in any way with the intervention or their mental health. Monitoring will be done by an experienced clinical psychologist and a master's student. Should we find that adolescents experience severe psychological symptoms, they are referred to other care that may better suit their needs.

2.2.1. Care As Usual (CAU)

CAU will consist of regular medical care. The type of the care may differ depending on the condition (e.g. skin care for eczema, orthodontics for cleft palate). Psychological care is not part of CAU. However, medical personnel will monitor the adolescents' well-being as part of CAU. They may refer the adolescents to a psychologist in case of suspicions of psychological problems. Adolescents that receive psychological care during participation in the study will not be allowed further participation.

Table 1. Content of the YP Face IT intervention

Session	Content	Type	Week
1. Common problems	Common problems experienced by adolescents with a visible difference; bystander responses, teasing, bullying.	SIST	1
2. Improve your social skills	Body language, verbal and non-verbal skills and building positive social skills.	SIST	2
3. Don't be SCARED, REACH OUT	Effect of own behavior on other people. Toolbox of techniques to cope with difficult social situations.	SIST	3
4. Think, Feel, Do	Relationship between thoughts, feelings and behaviours. Identifying negative thoughts and using a positive voice to challenges these thoughts. Different coping strategies for negative thoughts.	CBT	4
5. SMART goals	Using SMART goals to help achieve goals, dividing the end goal into sub goals. Dealing with concerns in romantic relationships.	CBT	5
6. Beating anxiety	Exposure therapy in the form of a fear ladder. Relaxation techniques.	CBT	6
7. Looking at your progress	Summary session, with summary of all previous sessions.	SIST/CBT	7
8. Booster quiz	Quiz with 16 questions on all taught techniques.	SIST/CBT	13

Note: SIST = Social Interaction Skills Training; CBT = Cognitive Behavioural Therapy

2.3. Materials

All outcome measures are completed at all three time points.

2.3.1. Primary outcomes

Social anxiety. The Social Anxiety Scale for Adolescents (SAS-A; 191) will be used to assess social anxiety. The SAS-A contains 22 statements that are rated on a 5-point Likert scale (e.g. I worry about what others say about me; I get nervous when I meet new people). A high score indicates high levels of social anxiety. The SAS-A contains three subscales, namely Fear of Negative Evaluation (FNE), social avoidance and distress in new situations (SAD – new), and social avoidance and distress in general (SAD-general). Cronbach's alphas are satisfactory for the subscales, being $\alpha = 0.91$, 0.83 and 0.76 respectively (191). Further research also yielded satisfactory Cronbach's alpha's of $\alpha = 0.89$, 0.80 and 0.70 for FNE, SAD-new and SAD-general respectively (206).

Body esteem. The subscale 'appearance' from the Body Esteem Scale For Adolescents and Adults (BESAA; 192) is used to assess participants attitudes and feelings about their appearance. A higher score indicates more satisfaction with one's appearance. This subscale consists of 10 statements, such as "I like how I look in photos". The items are rated on a 5-point Likert scale ranging from "never" to "always". The subscale demonstrates excellent internal consistency in a sample of American girls ($\alpha = 0.92$) and boys ($\alpha = 0.90$; 207) and in a sample of Dutch university students ($\alpha = 0.90$; 208).

2.3.2. Secondary outcomes

Aspects of self-worth. The Dutch version of the Self-Perception Profiles for Adolescents (SPPA; 193), the Competentiebelevingsschaal voor Adolescenten (CBSA; 194), will be used to assess different aspects of self-worth. The CBSA consists of eight specific domains and a global self-worth subscale. The specific domains are: scholastic competence, social competence, athletic competence, physical appearance, job competence, romantic appeal, behavioral conduct and close friendship. The CBSA consists of 35 items, each consisting of two contrasting statements (e.g. some teenagers are *not* happy with the way they look BUT other teenagers *are* happy with the way they look). The adolescent is asked to pick the statement that is most representative of them and choose whether the statement is 'sort of true for me' or 'really true for me'. All domains demonstrate good to excellent internal reliabilities, ranging from $\alpha = 0.74$ to $\alpha = 0.93$. The global self-worth subscale also demonstrates excellent reliability, with $\alpha = 0.80$ - 0.89 (193).

Perceived stigmatisation. The Perceived Stigmatization Questionnaire (PSQ; 32) will be used to measure stigmatisation behaviours commonly experienced by people with a visible difference. The PSQ is divided into three subscales, namely: absence

of friendly behaviour, confused/staring behaviour and hostile behaviour. These subscales amount to a total of 21 items concerning stigmatising behaviours, such as “people avoid looking at me” and “people call me names”. Participants are asked to rate how often they experience certain behaviour on a 5-point Likert scale. A high score reflects high perceived stigmatisation. The three subscales have been established(33) and the PSQ has adequate reliability in a sample of children and adolescents with a visible difference ($\alpha = 0.81$; 37).

Health-related quality of life. The EuroQol-5D-5L (EQ-5D-5L; 195) is used to assess health-related quality of life. The scale has five dimensions, namely: Mobility, Self-Care, Usual Activities, Pain/Discomfort and Anxiety/Depression. Each dimension can be assessed on five levels, which range from no problems to extreme problems. The EQ-5D-5L has good absolute and relative discriminatory power and good convergent validity(209).

Life Engagement. The Life Engagement Scale(210) will be used to measure the extent that worries or feeling bad about the way you look stop you from engaging in life activities such as going to a social event or doing sports. The scale consists of ten questions on which the adolescent can rate how much their worries or feeling bad about the way they look stopped them from doing activities on a 4-point scale. A high score indicates less life engagement. This instrument was purposively constructed for adolescents with a visible difference. The scale has good internal consistency, with $\alpha = 0.93$ for girls and $\alpha = 0.96$ for boys(210).

Appearance-related distress. The Mirror, Mirror.. (Spiegeltje, spiegeltje..; 198) questionnaire will be used to assess appearance-related distress. This questionnaire consists of 58 statements about appearance (e.g. my appearance makes me insecure), with a 5-point Likert scale ranging from “never” to “always”. The questionnaire also contains a section with 38 body-parts where adolescents have to indicate on a 5-point Likert scale how happy they are with said body part (e.g. skin colour, mouth). A high score indicates more dissatisfaction with appearance. As this questionnaire is new and unpublished, it has not been validated. We aim to validate this questionnaire using the data obtained in this study.

Depressive symptoms. The Child Depression Inventory – 2 (CDI-2; 197) will be used to assess depressive symptoms. The questionnaire consists of 28 items with three answer options (e.g., I am sad sometimes, I am often sad, I am always sad). The scale consists of the subscales emotional problems, divided into negative mood/physical symptoms and negative self-esteem, and functional problems divided into ineffectiveness and interpersonal problems. A high score indicates more depressive symptoms. The questionnaire has demonstrated excellent internal reliability both

for 13-16 year olds ($\alpha = 0.89$), and for 17-21 year olds ($\alpha = 0.85$; 197). The scale has good test-retest reliability ($r = 0.60$; 197).

2.4. Recruitment

Participants are recruited through several channels. The first is through patient organisations. Patient organisations will be approached and asked if they are willing to advertise the Dutch YP Face IT study on their website and in their newsletters. If an adolescent is willing to participate, he/she is encouraged to send an e-mail to the research team, providing his/her contact details. The adolescent will then receive an information package containing a patient information letter, an informed consent form and a response card. The second channel is through our website (www.faceitvoorjongeren.nl). On our website, adolescents can read information about YP Face IT and contact the research team. If they do so, they will receive an information package. The third channel is through the Erasmus MC – Sophia Children's hospital. Subjects will be drawn from the department of Child and Adolescent Psychiatry/Psychology, the department of Plastic and Reconstructive Surgery, the department of Oral and Maxillofacial Surgery and Special Dental Care, and the department of Dermatology. Subjects will be informed about the study by their treating doctor/clinician. It will be explicitly stated that participation is voluntary and that they can withdraw from the study at any time should they wish to do so. After informing the potential participant, they will receive an information package. If a potential participant does not have regular appointments at the Erasmus MC – Sophia children's hospital, we will send an information package to their home address.

A response card will be included in the information package. On this response card, adolescents can indicate whether they give permission to be contacted by the research team. If the response card has not been returned within two weeks, the research team will contact the adolescent.

If participants are willing to participate, they are asked to fill in a consent form. For participants younger than 16 years, both parents are required to sign the informed consent form. After receiving the informed consent form, the researchers will include the participant in the trial and send out the first set of online questionnaires.

Participants will receive a gift card worth €10,- after completing the entire study. If a participant decides to withdraw from the study prematurely, the adolescent will not receive a gift card.

2.5. Study design

A flow chart of the RCT is depicted in Figure 1. Prior to baseline, the in- and exclusion criteria as mentioned before (with the exception of appearance-related distress) are queried in a telephone call with the parent or adolescent. Appearance-related

distress is measured based on the questionnaires completed at T1 (baseline). Adolescents will receive an e-mail with a link to all questionnaires, with the exception of the CBSA. They will receive this questionnaire by post. This procedure is the same for T2 (13 weeks, direct follow-up) and T3 (25 weeks, three months follow-up).

After completing the questionnaires, screening for appearance-related distress will take place by the research team. The scores on the SAS-A, BESAA and CDI-2 are considered. For the SAS-A and the BESAA adolescents that score 0.5-2.0 standard deviations above average will be included in the study. For the CDI-2 we will include adolescents scoring in the 70th to 90th percentile, as the manual states that this corresponds to subclinical symptoms of depression(197). Adolescents that score within the defined range for one or more of the questionnaires will be randomised into the study. Adolescents that score below this range will be excluded from participation. Adolescents that score above this range will be contacted by the research team to assess whether there are clinical psychological symptoms. A phone call is made to both the adolescent and one of his/her parents. During this phone call, the DSM criteria for depressive disorder, social anxiety disorder or another suspected diagnosis will be asked. If suspicions of clinical psychological symptoms arise, the adolescents is referred to the appropriate psychological care. If no clinical symptoms are present, the adolescent is randomised into the study.

Adolescents with subclinical symptoms will be randomised to either Care As Usual (CAU) or YP Face IT. Adolescents in the CAU group will receive CAU and will complete T2 at 13 weeks and T2 at 25 weeks. The CAU group will have the opportunity to complete YP Face IT after their participation in the study. Adolescents in the YP Face IT group will receive CAU and YP Face IT, and will complete questionnaires immediately after completing YP Face IT (T2; 13 weeks) and three months after completing YP Face IT (T3; 25 weeks).

2.6. Randomisation and blinding

Participants will be randomised to either the CAU or the YP Face IT group in a 1:1 ratio. Randomisation will be stratified by age (12-13, 14-15 or 16-17 years old). Randomisation will be done using a list with a random sequence, generated using a computer program. With the stratification, six different types of blocks can be formed. Each block will independently vary between four and eight randomisation pairs. The adolescents are informed of the group they are randomised to through e-mail. The researcher analysing the data will be blind to the randomisation and will not be involved in monitoring the adolescents in the intervention. This researcher also supervises data collection by students, who are not blinded. The participants, the clinical psychologist and students monitoring the adolescents in the intervention will not be blind to the treatment conditions. When contacting the research team,

the adolescents are explicitly instructed not to talk about the group they were allocated to.

If, through monitoring, the research team suspects that a participant experiences clinically significant symptoms, unblinding may take place. The participant will be excluded from the study and will be transferred to more appropriate care.

Participants that drop out after randomisation will be asked if they are willing to complete the questionnaires at T2 and T3. They are in no way obliged to do so.

2.7. Sample size

For the sample size calculation we applied a mixed model ANOVA procedure, with a power of 0.80, a two-sided alpha of $\alpha=0.025$ (Bonferroni corrected for two primary outcome measures), a correlation between the repeated measurements of $r=0.70$ and three repeated linearly decreasing measurements. Bessell and colleagues(71) reported effect sizes of $d = 0.83$ for appearance and $d = 0.80$ for anxiety in a study on Face IT. However, as we are not certain that we will obtain such a large effect, we will consider a medium effect of $d = 0.50$. To detect a medium effect, 56 participants are needed in both groups. As drop-out is typically high in eHealth interventions (see 211, 212), we anticipated a drop-out of 50%. Therefore, 224 participants are needed in total.

2.8. Statistical analysis

The data will be analysed using multilevel linear regression analyses. There will be two levels in the models. The participants constitute the upper level, their repeated measures the lower level. For each outcome variable a model will be postulated using treatment group, time and interaction with treatment group as fixed effects. Time will be entered in two ways: categorical and continuous. First, for categorical we will postulate a model with T2 (direct follow-up) and T3 (three month follow-up) using T1(baseline) as reference group. Second, for continuous we will apply the logarithm of time, as generally treatments have the largest effect at start and the level of functioning stabilizes on the long run. The deviance statistic using restricted maximum likelihood will be applied to determine the covariance structure. The deviance test will be used to determine whether the more parsimonious (log) model is a too rigorous oversimplification (213). Effect sizes will be calculated from dividing differences between the primary time-point (i.e. three months) estimations and baseline by the estimated baseline standard deviation. Analyses are done on an intention-to-treat base.

Participants who do not experience subclinical symptoms at T1, and are thus not randomised, will not be included in the analyses.

2.9. Monitoring

As the risks associated with this study are minimal, monitoring will take place once a year. An independent investigator will randomly check study documents, participant selection and participant safety. As minimal risks are involved, no interim analyses will be done.

Auditing may be done by the Erasmus MC – Sophia Children's hospital.

2.10. Patient and public involvement (PPI)

The original YP Face it intervention was developed in collaboration with adolescents and the charity Changing Faces(70). For the Dutch translation, 6 adolescents and their parents have read and reviewed the translations. Prior to this RCT an acceptability and feasibility study was conducted. In this study 14 adolescents completed YP Face IT and participated in an interview. Feedback was asked on the intervention, as well as on the general study procedures (i.e. information packages, questionnaires and contact with the research team). Patient associations will be invited to help develop our dissemination strategy.

2.11. Trial status

The trial described in this paper has started in September 2019. Recruitment of participants will be until November 2020. Data collection will be until May 2021, after which the data will be analysed.

3. Ethics and Dissemination

3.1. Ethics, consent and permission

This study will be conducted in accordance to the Declaration of Helsinki.

Research ethics approval was obtained from the Medical Ethics review Committee (MERC) Rotterdam (reference number MEC-2018-052/NL63955.078.18). Any amendments to the study protocol and (serious) adverse events will be reported to this committee.

3.2. Data management and confidentiality

To ensure anonymous processing of the data, every participant will receive a study number. All research data will be processed using only this study number. The handling of data will comply with the European General Data Protection Regulation (GDPR). The study master file and all research data will be saved for 15 years, unless participants or their parents/guardians do not give consent for saving their data.

All data will be stored in locked cabinets, or password-protected documents. The data, including the final dataset, can be accessed only by members of the research team.

3.3. Dissemination of research findings

Results of this study will be presented on national and international conferences and in peer-reviewed scientific journals, within the scope of the target groups. The results will also be relayed to patients through patient organisations. Participants are also given the option to sign up for a brief study report after the results are finalised. If deemed effective, YP Face IT will be implemented in hospitals in The Netherlands.

5

4. Discussion

The Dutch YP Face IT study aims to test the Dutch version of YP Face IT. With this RCT we aim to retrieve data on the effectiveness of the intervention.

4.1. Strengths and limitations

A particular strength of this study is that it follows a stage model of behavioural therapies research(214) and has excellent methodological quality. Previous research has lacked methodological rigor, due to small sample sizes, not including a control group or not blinding personnel or participants(68). Due to the nature of this study, blinding of participants is not possible. However, this study does include an adequate sample size, includes a control group and blinding of relevant personnel. With this methodological quality, we hope to be able to provide evidence-base for YP Face IT and thus provide one of the first evidence-based treatments for adolescents with a visible difference(68). Furthermore, by recruiting our participants through several channels, we will be able to obtain a sample that is representative for Dutch adolescents in general rather than solely Rotterdam, where the research team is located. Because the intervention is available online, participants throughout the entire country are able to participate without adding extra burden to participating.

In addition to strengths, this study also has some limitations. First, the intervention is available for a range of conditions causing a visible difference. The overall group results might not be generalisable to one specific group. Second, participants are not blind to the treatment condition. Participants are informed about the randomisation groups. They are also informed that, if randomised to the CAU group, they will have the possibility to access YP Face IT after the study. This is a more ethical option than not offering treatment after the study and this knowledge may help keep attrition low. However, waiting list designs may lead to an overestimate of the treatment effect(215). Furthermore, this study includes only self-report measures. Diagnostic

interviews or parent-reports could provide more enriched data. However, due to time and financial constraints these data will not be collected.

Declarations

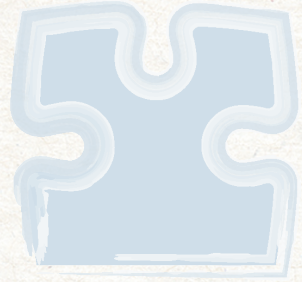
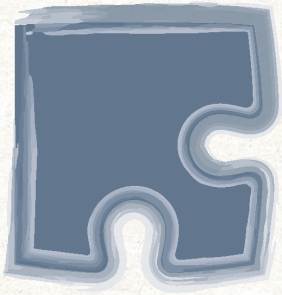
Author statement. JMEO, HW and EMWJU developed the study design. RT made the statistical analysis plan for the study. JMEO initiated the study and obtained funding. SGMAP, EWCA, IMJM, MJK, RT, MHJH and EMWJU reviewed and supported the funding application. JMEO and EMWJU supervise the study and data collection. MvD conducts the data collection, along with psychology and medical students. MvD wrote the first draft of the manuscript. All authors read and approved the final manuscript.

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Availability of data and material. Data sharing is not applicable to this article as no new data were created or analysed in this manuscript.

Competing interests. None declared.

Acknowledgements. Not applicable.



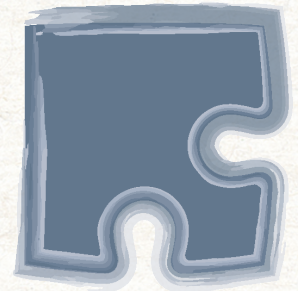


CHAPTER 6

A randomised control trial (RCT) of Young Person's Face IT: A web-based psychosocial intervention for adolescents distressed by a visible difference

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Abstract

A visible difference to the face or body may challenge adolescents' adjustment and engagement in life activities, and some adolescents therefore need psychosocial support. However, there is limited support for whether existing interventions aimed specifically for this group of adolescents reduce social or appearance-related distress. We therefore conducted a parallel group, randomised control trial (RCT) to evaluate the effectiveness of Young Person's Face IT (YPF), a web-based psychosocial intervention developed for adolescents with a visible difference that experience appearance-related distress. Adolescents ($N = 189$, aged 11-18) from two countries (Norway and The Netherlands), were randomly allocated to an intervention group or care as usual (CAU). Outcomes were body esteem, social anxiety, perceived stigmatisation, and life disengagement. Compared with CAU, participants who engaged with YPF showed reductions in social anxiety symptoms ($\eta^2_p = 0.03$) and specifically fear of negative evaluation ($\eta^2_p = 0.05$) post-intervention. No significant improvements were found for body esteem, perceived stigmatisation, or life disengagement. This study endorses the effectiveness of web-based psychosocial support in reducing social anxiety symptoms in adolescents distressed by a visible difference. Future studies are needed to further confirm the effectiveness of YPF and the intervention's potential to reduce social anxiety, including potential long-term intervention effects.

Keywords: eHealth; intervention; randomised control trial; visible difference; body esteem; social anxiety

1. Introduction

1.1. Living with a visible difference

Having a sense of normality and belonging is central to the psychological well-being of all individuals, and is especially important during adolescence. Therefore, a visible difference due to a congenital or an acquired condition can have a profound psychological impact (79, 135). Approximately one in 44 people live with a visible facial or bodily difference that deviates from the norm and is considered socially undesirable (1). A visible difference can be congenital or acquired, and include a range of different conditions (181). Congenital differences include for example craniofacial conditions (e.g. cleft lip and palate or craniosynostoses) and skin conditions (e.g. epidermolysis bullosa or ichthyosis). Acquired visible differences can result from accidental traumas (e.g. burn scars or injuries from traffic accidents), disease (e.g. meningitis), or medical interventions (e.g. hair loss from chemotherapy or scars).

While some adolescents manage to cope by acknowledging and accepting their situation (11), others adjust to the consequences of being visibly different by for example employing techniques to conceal their difference (216). Previous studies suggest that the presence of a visible difference tends to have a negative impact on adolescents' well-being compared with unaffected peers (8, 184, 217). For instance, stigmatising experiences or intrusive behaviours (e.g. teasing, bullying, stares, or unwanted questioning and attention from others) have been linked to reduced psychological adjustment and health-related quality of life (37), and have been associated with negative body image (36). Having a visible difference may also increase the risk of low self-esteem (217), make adolescents particularly susceptible to developing symptoms of anxiety (184), and increase concerns regarding the chances of being involved in romantic relationships (8). Adolescents who are worried or dissatisfied with their appearance may also experience challenges in peer relationships (218), fear of negative evaluations (8), and reduce their engagement in different life activities, such as school attendance, sports, and socialising with friends (196). Evidence-based interventions and support alternatives that could help adolescents develop effective coping strategies and strengthen psychological well-being may therefore be of central importance in the process of adjusting to their visible difference. However, evidence for the short- and long-term effectiveness of existing interventions for adolescent populations are scarce and therefore needed (68).

1.2. Interventions and support

Research suggest that there is limited evidence for the effectiveness of existing interventions aimed at improving psychological and psychosocial outcomes in adolescents experiencing appearance-related distress (68). Several methodological

issues also need to be taken into account, such as small sample sizes and lack of experimental designs (68). Moreover, existing interventions have mainly included adult samples when testing effectiveness (67).

Some of the psychosocial and educational approaches for adolescents with visible differences that have been evaluated, include the impact of residential social camps (219) and workshops aimed at coping with negative social experiences by increasing social and communication skills (220). Interventional techniques that show promise are Social Skills Training (SST) (221, 222) and Cognitive Behavioural Therapy (CBT), which puts emphasis on altering unhelpful cognitive schemas (109, 223). More specifically, studies using CBT-based interventions have reported psychological gains, such as reductions of anxiety (223) and increased levels of social engagement when using SST (221). CBT-based interventions have also shown potential in treating appearance-related anxiety due to a visible difference both in adolescents (68) and adults (109). Thus, interventions employing CBT and/or SST techniques may assist adolescents in recognising and changing negative thoughts and feelings directed at their own appearance, and strengthen coping mechanisms when dealing with social challenges.

1.3. Web-based psychosocial support

Despite research showing the potential psychological benefit of CBT and SST-based programmes for adolescents with a visible difference, the general availability of psychological treatment and interventions is limited (10). In Norway, geographic and demographic characteristics contribute to make specialised psychological treatment difficult to reach, and in both participating countries, there are few psychologists with clinical expertise in appearance psychology related to living with a visible difference in the local health care system. Given the variation in accessibility of appearance-related care, research needs to address the potential benefits of alternative ways of delivering interventions and reaching adolescents in need for support. Increasing evidence points to Internet-delivered Cognitive Behaviour Therapy (ICBT) as being potentially effective (224, 225). For instance, a recent review and meta-analysis (226), has suggested that guided ICBT in many instances is equally effective as standard face-to-face CBT in treating psychological difficulties such as social anxiety and depression in adults. ICBT has also shown promise in adolescent community samples in reducing symptoms of anxiety (227), depression (228), and negative body image (229, 230).

Little is currently known about the effectiveness of ICBT-interventions specifically developed for individuals with a condition affecting their appearance. Previous studies have indicated that adolescents may find it difficult to raise appearance concerns face-to-face with healthcare professionals (216), and may prefer more easily accessible support that offers a greater degree of anonymity and

confidentiality when discussing appearance issues (8). One web-based intervention, Face IT, developed for adults with a visible difference and integrating SST and CBT approaches, was evaluated via a RCT, and demonstrated that standard face-to-face intervention and Face IT equally reduced anxiety, fear of negative evaluations, depressive symptoms, and appearance-related distress (71).

1.4. The Young Person's Face IT (YPF) intervention

Based on evidence of Face IT's effectiveness in reducing depressive symptoms, anxiety, and appearance concerns in adults with a visible difference (67, 71), a similar intervention programme for adolescents, Young Person's Face IT (YPF) was developed by researchers at the Centre for Appearance Research at the University of the West of England, Bristol, UK, in close collaboration with adolescents with visible differences, their parents, and clinical experts and health professionals (189). The therapeutic content of YP Face IT is based on the adult version, Face IT (71), and consists of seven weekly sessions and one booster session completed six weeks later to maintain therapeutic effect (189). Each session takes around 30-40 minutes to complete and participants are encouraged to work through YPF independently, although they may also ask for advice and guidance from others (e.g. parents) if needed. Each session provides advice and guidance in written, audio, and video formats, and focuses on teaching and encouraging adolescents to practice strategies such as managing staring, bullying, and anxiety, through interactive and homework activities (189). A detailed description of the intervention content is published elsewhere (189). In addition, participants can record their own reflections and experiences in their YPF diary. Audio recordings for all written text are available on the English and Norway YPF intervention website, and will probably also be implemented in the Dutch version of YPF in the future (231), as this is expected to support participants who may struggle with reading.

The feasibility and acceptability of YPF has been explored in several studies across the world {van Dalen, 2021 #949, 2017; Gee et al., 2018; Williamson et al., 2019; Riobueno-Naylor et al., 2019; 2021), and the programme therefore exists in English (<https://www.ypfaceit.co.uk>), Norwegian (<https://ungfaceit.no/>) and Dutch (<https://faceitvoorjongeren.nl/>). The British study by Williamson, Hamlet (186), including adolescents with a wide range of appearance-affecting conditions, found YPF to be a safe and acceptable programme, and demonstrated preliminary results indicating that the intervention could improve body esteem and reduce social anxiety (186). The study by Riobueno-Naylor et al. (72, 232) included adolescents with burns and aimed to explore the feasibility of incorporating YPF into routine outpatient pediatric burn care in the United States. Although adolescents expressed interest in using YPF, few engaged actively with the programme, and the authors concluded that more knowledge is needed on how adolescents' engagement with the intervention can be supported (72).

In summary, YPF may potentially provide a cost-effective alternative to traditional face-to-face psychological treatment for adolescents that experience appearance-related distress as a result of their visible difference, and be easily accessed by adolescents in need of relevant support, irrespective of their geographical location (70). Several studies also suggest that the intervention is a safe, relevant, and acceptable tool (72, 186, 231). However, no previous large-scale randomised control trial has evaluated the effectiveness of YPF in order to determine the intervention's effectiveness.

1.5. Aim

Considering the need for more research providing evidence for the usefulness of existing psychosocial interventions for adolescents with a visible difference (68), the aim of the current study was to evaluate the effectiveness of YPF in improving psychological well-being in this adolescent group. Specifically, we aimed to examine whether YPF (1) improve body esteem and/or reduce social anxiety in adolescents with a visible difference (primary outcomes), (2) reduce perceived stigmatisation and/or life disengagement (secondary outcomes), and (3) examine whether age, gender, centre, time spent on YPF, and/or type of visible difference, predict an improvement in body esteem, social anxiety, perceived stigmatisation, and life disengagement.

2. Method

2.1. Trial design

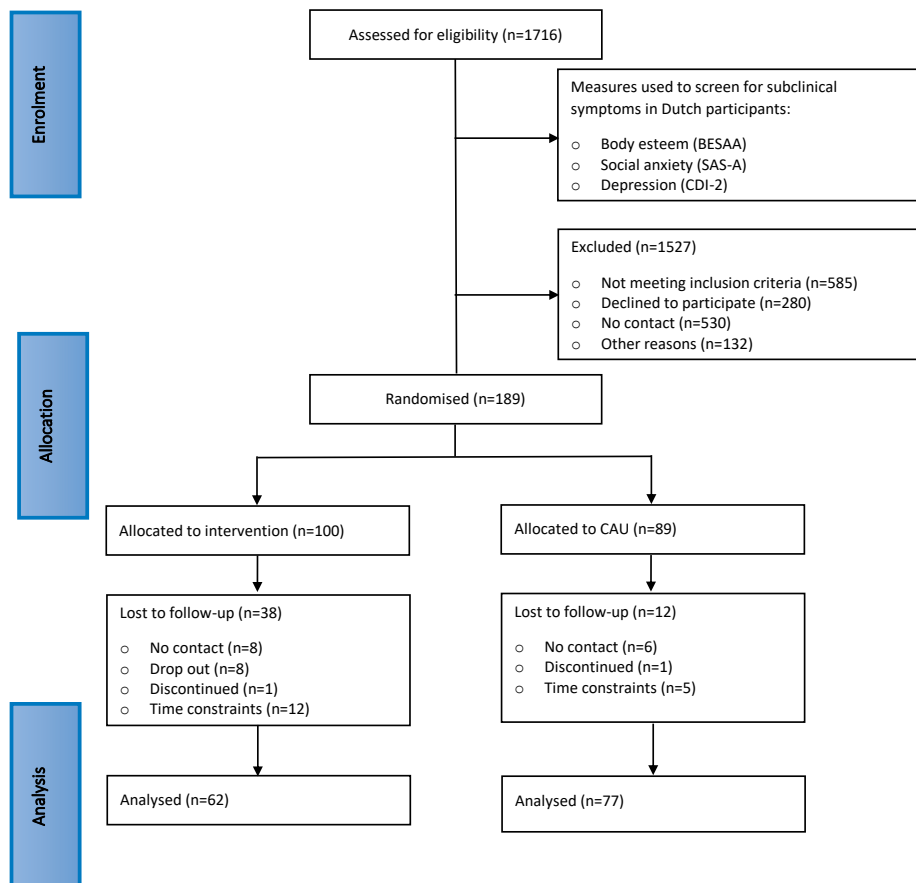
The study was a parallel-group, randomised control trial (RCT), including two centres, each from a separate country (Norway and The Netherlands). Participants were allocated to either an intervention group (YPF) or a control group receiving care as usual (CAU). All participants completed outcome measures prior to randomisation (baseline assessment) and thirteen weeks later (post-intervention assessment). The Norwegian study was reviewed by the Regional Committee for Medical Research Ethics ([Health Region], reference number [Number]) and accepted by the Data Protection Office based at Oslo University Hospital. For the Dutch study, approval was obtained from the Medical Ethics Committee in Rotterdam, The Netherlands (Reference number: MEC-2018-052). This trial followed the CONSORT 2010 guidelines (233).

2.2. Recruitment and procedure

In Norway, participants were recruited nationwide from University Hospitals, specialist treatment units, local healthcare services, patient organisations, and through social media. In The Netherlands, participants were recruited from a University/City hospital and nationwide through patient organisations.

Participants and/or participants' parents/primary caregivers contacted the research team by telephone or email if they wished to participate in the study. Following initial contact, all participants (and/or parents if adolescent < 16 years) were contacted via telephone by the research team, and answered questions in order to confirm eligibility. Inclusion criteria were: 1) age between 12-17 years with a visible difference and self-identified appearance-related distress, teasing or bullying; 2) access to the internet and a home computer or tablet; reading level > 12 years of age; 4) normal or corrected-to-normal vision. Exclusion criteria were: 1) a diagnosis of clinical depression, psychosis, eating disorder (see details below for differences in assessment procedures between the two participating countries), and post-traumatic stress disorder (PTSD), or within 12 months of traumatic injury; 2) learning disabilities that would impede understanding of the intervention content; 3) currently receiving a psychological face-to-face intervention. Informed consents were then obtained from eligible participants. For participants < 16, consents were also obtained from both parents/primary caregivers, and only from the participants if they were 16 years or older. After consent forms were obtained, baseline outcome measures were administered through secure online data collection platforms, accepted by the University Hospitals in Norway and The Netherlands. Participants also provided demographic information (e.g. birth date, gender, type of visible difference, and parental occupation/education) either during the screening conversations and/or as part of the baseline assessment. Consecutively, participants were randomised to either the intervention group or CAU in a 1:1 ratio, and were informed about their group allocation either by telephone or email.

There were some differences in procedures between the two study sites: a) In Norway, a single randomisation procedure was performed and neither participants nor research team members were blinded to the randomisation. In The Netherlands, randomisation was performed using a computer generated list with a random sequence and was stratified by age (12-13, 14-15 or 16-17 years); b) [Country B] participants were screened for subclinical symptoms of low body esteem, social anxiety, and depression using questionnaires at baseline (see Fig. 1), and only randomised accordingly; c) In Norway, a waiting list CAU group was used, and participants randomised to this group were given access to the intervention three months into the study. In The Netherlands, participants randomised to CAU were offered access to the intervention after participation in the study (after final completion of outcome measures at six months); d) In [Country A], progress with YPF for participants randomised to the intervention group was followed-up by a research team member; e) All participants were offered incentives for completing outcome measures. Participants living in Norway received a gift card for completion of the post-intervention measure (in total €30). Participants living in The Netherlands received a €10 gift card after study completion.

Figure 1. Flow chart of study procedures

2.3. Participants

A total of 1716 participants were assessed for eligibility. After screening (see recruitment and procedures for more details), 1527 were excluded (see Fig. 1 for details). The final study sample consisted of 189 participants randomised to the intervention group ($n = 100$) or CAU ($n = 89$). An a priori sample size calculation revealed that 62 participants were needed per group to achieve at least 80% for detecting any treatment effects. Therefore, this study was sufficiently powered to detect statistically significant results.

2.4. Intervention (YPF)

Participants randomised to the intervention group received a username and password to access YPF and completed the intervention on a computer or tablet at home or another self-selected location. Participants were asked to work through

each session independently, although encouraged to ask for advice and guidance if necessary (from the research team or from their parents/primary caregivers).

2.5. CAU

All participants received CAU, with those in the intervention arm also receiving YPF. None of the two participating countries offer standardised psychosocial or psychological treatment for this patient group, and CAU will therefore vary according to needs, resources, and expertise within local health care services. Participants receiving face-to-face interventions were excluded.

2.6. Assessment

Outcome measures that did not exist in Norwegian were translated and back-translated, following recommended procedures (234). Only one outcome measure had to be translated to Dutch; BILD-Q. Back-translation was not performed for this measure in neither language.

2.6.1. Primary outcomes

Body esteem. To assess body esteem, the appearance esteem subscale (BE-Appearance) of the Body Esteem Scale for Adolescents and Adults (BESAA) (192) was used. This subscale contains ten items rated on a five-point Likert scale from 0 (*never*) to 4 (*always*). Statements include “I worry about the way I look” and “I like what I see when I look in the mirror”. After negatively worded items have been reversed, higher mean values indicate greater appearance satisfaction (192). Good internal consistency of the BE-Appearance subscale has been demonstrated in a community sample of adolescents (235), as well as for all three subscale of the BESAA with adolescents with a visible difference (236). In this study, Cronbach's alpha was $\alpha=.91$ for the total sample.

Social anxiety. The Social Anxiety Scale for Adolescents (SAS-A) (191) was used to assess subjective experiences of social anxiety. SAS-A contains 18 descriptive self-statements divided into three subscales, with items rated on a five-point scale ranging from 1 (*never*) to 5 (*always*). All subscales were used in the present study. The first subscale, fear of negative evaluation (FNE), contains eight items (e.g. “I worry about what other kids think about me”). The second subscale, social avoidance and distress specific to new situations or unfamiliar peers (SAD-New), includes six items (e.g. “I get nervous when I meet new kids”). The third subscale, social avoidance and distress in general (SAD-General), contains four items (e.g. “I feel shy even with kids I know well”). Higher scores indicate higher levels of social anxiety (191). Good psychometric properties of the SAS-A have been demonstrated in a Finnish adolescent community sample (237). In this study, Cronbach's alpha was high for all subscales (FNE, $\alpha = .91$; SAD-New, $\alpha = .86$; SAD-General, $\alpha = .78$) and high for the overall scale ($\alpha = .93$).

2.6.2. Secondary outcomes

Perceived stigmatisation. The Perceived Stigmatization Questionnaire (PSQ) (32) was used to evaluate participants' perceptions of stigmatisation behaviours. PSQ consists of 21 items, divided into three subscales, that are rated on a five-point Likert scale from 1 (*never*) to 5 (*always*). All subscales were used in the present study. The subscales evaluate the absence of friendly behaviour (AFB), experiences of confused and staring behaviours from others (CSB), and the extent to which respondents encounter hostile behaviour (HB). Example of items include, "People are relaxed around me", "People avoid looking at me", and "People call me names". After reversing positively worded items, higher scores indicate higher levels of perceived stigmatisation (238). Acceptable psychometric properties have been demonstrated for the PSQ with children and adolescents with a visible difference (33). The PSQ has also previously been translated and used with Dutch adults with burn injuries (239). In this study, Cronbach's alpha was acceptable for two of the subscales (AFB, $\alpha = .79$; CSB, $\alpha = .75$, and good for the third subscale (HB, $\alpha = .90$) and the overall scale ($\alpha = .88$).

Life disengagement. The Body Image Life Disengagement Questionnaire (BILD-Q) (196, 240) was used to measure the extent to which appearance-related worries impact engagement or intention to engage in different life activities (e.g. "going to a social event" and "giving an opinion"). BILD-Q consists of ten items rated on a four-point Likert scale from 1 (*Hasn't stopped me at all*) to 4 (*Stopped me all the time*). Higher scores reflect greater life disengagement. Acceptable psychometric properties of the BILD-Q have been demonstrated in an adolescent community sample (196). In this study, Cronbach's alpha was good ($\alpha = .82$).

2.7. Statistical analysis

Data were analysed using the IBM Statistical Package for the Social Sciences Software (SPSS, version 26). Due to human error, one item in the PSQ (i.e. "People are nice to me") was omitted in the [Nationality A] version. This error was taken into account when calculating the AFB subscale and total scale. First, data were screened for outliers, normality, and for violations of assumptions of one-way analyses of covariance (ANCOVA) and multiple regression. No outliers were found that could impede analyses and data were considered normally distributed. Additionally, all assumptions for the main analyses were satisfied. An independent samples t-test was used to assess differences in age between the intervention group and CAU. Chi-square analyses were used to assess differences in type of visible difference and gender between the intervention group and CAU.

To test research questions 1 and 2, (i.e. whether YPF improves body esteem, and reduces social anxiety, perceived stigmatisation, and life disengagement), we conducted a series of ANCOVA's for each outcome. Group allocation (i.e. intervention

or CAU) was used as the independent variable and baseline scores on the outcome measures and centre (defined as Norway or The Netherlands) were used as covariates. Effect sizes (partial eta squared; η_p^2) were interpreted using Cohen's (241) guidelines for small ($\eta_p^2 = .01$), moderate ($\eta_p^2 = .06$), and large ($\eta_p^2 = .14$) effects. To test the third research question, (i.e. whether gender, age, centre, time spent on YPF, and/or type of visible difference, predict post-intervention body esteem, social anxiety, perceived stigmatisation and/or life disengagement), four separate hierarchical multiple regressions were conducted. Post-intervention outcome scores were used as dependent variables. In Step 1, we entered baseline scores of the respective outcomes. In Step 2, we entered gender, age, centre, time spent on YPF, and type of visible difference. The hierarchical multiple regression models were evaluated using R^2 , adjusted R^2 (R^2), and R^2 change (R^2).

An alpha level of $\alpha = .05$ (two-tailed) was used for all statistical tests. To avoid issues with multiple comparisons, a correction (i.e. the Benjamini-Hochberg adjustment) (156) was applied to the main analyses including participants from both the intervention group and CAU (i.e. the ANCOVA's) to reduce the risk of Type 1 errors.

3. Results

3.1. Sample characteristics

Participants were 189 adolescents ($M = 14.35$ years, $SD = 1.82$, range: 11-18), and there were more girls ($n = 114$, 60%, $M = 14.43$ years, $SD = 1.82$) than boys ($n = 75$, 40%, $M = 14.24$ years, $SD = 1.82$). Approximately half of the participants had a craniofacial condition ($n = 100$, 53%), almost a fifth had a skin condition ($n = 42$, 22%), or conditions affecting body form such as missing limbs or fused fingers/toes ($n = 36$, 19%). The remaining participants had a scarring condition resulting from for example surgery or burns ($n = 11$, 6%). Approximately two thirds of the participants' parents had completed primary, secondary, and/or high school ($n = 112$ fathers, 59% and $n = 111$ mothers, 59%). The remaining parents had a university degree (i.e. Bachelor's; $n = 21$ fathers, 11% and $n = 39$ mothers, 21%), or had an advanced degree (i.e. Master's and/or PhD; $n = 24$ fathers, 13% and $n = 20$ mothers, 11%).

Table 1. Mean levels of body esteem, social anxiety, perceived stigmatisation, and life disengagement among boys and girls by group and time.

Variable	Gender	Intervention Group		CAU	
		Baseline M (SD)	Post-intervention M (SD)	Baseline M (SD)	Post-intervention M (SD)
Body Esteem					
	Boys	2.53 (0.68)	2.84 (0.79)	2.68 (0.74)	2.73 (0.70)
	Girls	2.10 (0.93)	2.27 (0.74)	2.13 (0.84)	2.28 (0.82)
Social Anxiety					
FNE	Boys	18.98 (7.39)	15.26 (4.77)	18.30 (6.93)	16.93 (6.18)
	Girls	22.22 (8.79)	19.57 (6.95)	23.00 (6.65)	22.00 (6.90)
SAD-New	Boys	15.79 (5.52)	14.00 (4.24)	15.30 (5.24)	14.21 (5.27)
	Girls	18.34 (5.51)	17.03 (4.95)	18.11 (5.09)	18.41 (5.51)
SAD-General	Boys	8.38 (2.97)	7.52 (2.49)	8.61 (3.39)	8.82 (3.58)
	Girls	8.88 (3.73)	8.89 (3.08)	9.14 (3.62)	9.92 (3.74)
Total scale score	Boys	43.14 (13.57)	36.78 (8.75)	42.21 (13.96)	39.96 (13.17)
	Girls	49.45 (15.86)	45.49 (13.06)	50.25 (12.24)	50.33 (13.25)
Perceived Stigmatisation					
AFB	Boys	2.32 (0.50)	2.07 (0.45)	2.29 (0.59)	2.06 (0.55)
	Girls	2.15 (0.55)	2.18 (0.62)	2.16 (0.56)	2.16 (0.51)
CSB	Boys	2.13 (0.65)	1.93 (0.67)	2.06 (0.67)	1.93 (0.59)
	Girls	2.13 (0.66)	1.89 (0.61)	2.23 (0.70)	2.19 (0.68)
HB	Boys	1.83 (0.72)	1.72 (0.57)	1.90 (0.85)	1.81 (0.86)
	Girls	1.68 (0.80)	1.60 (0.76)	1.77 (0.83)	1.69 (0.73)

Table 1. Mean levels of body esteem, social anxiety, perceived stigmatisation, and life disengagement among boys and girls by group and time.

Variable	Gender	Intervention Group		CAU	
		Baseline M (SD)	Post-intervention M (SD)	Baseline M (SD)	Post-intervention M (SD)
Total scale score	Boys	2.13 (0.45)	1.93 (0.40)	2.11 (0.54)	1.95 (0.50)
	Girls	2.03 (0.54)	1.93 (0.52)	2.10 (0.53)	2.06 (0.53)
Life Disengagement					
	Boys	1.40 (0.47)	1.16 (0.20)	1.47 (0.48)	1.39 (0.39)
	Girls	1.57 (0.53)	1.51 (0.48)	1.59 (0.48)	1.59 (0.44)

Note. Body Esteem = BE-Appearance subscale; FNE = Fear of negative evaluation; SAD-New = Social avoidance and distress specific to new situations or unfamiliar peers; SAD-General = Social avoidance and distress in general; Total scale score = Social Anxiety Scale for Adolescents total scale; AFB = Absence of friendly behaviour; CSB = Confused and staring behaviours from others; HB = Hostile behaviour; life Disengagement = Body Image Life Disengagement Questionnaire; CAU = Care as usual.

Table 2. Bivariate correlations between all outcome variables across each group at baseline.

Variable	Intervention Group				CAU			
	1	2	3	4	1	2	3	4
1. Body Esteem	-				-			
2. Social Anxiety	-.64**	-			-.46**	-		
3. Perceived Stigmatisation	-.50**	.58**	-		-.29**	.54**	-	
4. Life Disengagement	-.53**	.56**	.49**	-	-.29**	.44**	.43**	-

Note. Body Esteem (n = 189) = BE-Appearance subscale; Social Anxiety (n = 189) = Social Anxiety Scale for Adolescents total scale; Perceived Stigmatisation (n = 186) = Perceived Stigmatization Questionnaire total scale; Life Disengagement (n = 187) = Body Image Life Disengagement Questionnaire; CAU = Care as usual.
** p < .01.

3.2. Preliminary analyses

Baseline and post-intervention means, and bivariate correlations for all outcome variables, are presented in Table 1 and Table 2. As randomisation was stratified by age only for participants living in The Netherlands, the relationship between age and group allocation for participants living in Norway was explored. For participants living in Norway, an independent samples t-test showed that age did not significantly vary between participants in CAU and the intervention group, $t(85) = 1.17, p = .48$. The relationship between gender, type of visible difference, and group allocation, was also explored for the total sample. Neither gender ($X^2(1, N = 189) = 0.48, p = .49$), nor type of visible difference ($X^2(3, N = 187) = 3.37, p = .34$), differed significantly between the intervention group and CAU.

3.3. The effectiveness of YPF in improving primary and secondary outcomes

To explore differences between the intervention group and CAU, ANCOVA analyses were performed, using baseline primary and secondary outcome scores and centre (i.e. country of residence) as covariates (see Table 3).

Table 3. Mean between-group difference at post-intervention for all outcome variables, as well as standard errors, and confidence intervals. One-way analysis of covariance (ANCOVA).

Variable	Between-group difference			
	<i>b</i>	<i>SE</i>	95% CI	n_p^2
Body Esteem	-0.07	0.02	-0.26, 0.12	0.004
Social Anxiety				
<i>FNE</i>	2.10	0.78	0.56, 3.64	0.05
<i>SAD-New</i>	1.14	0.57	0.01, 2.26	0.03
<i>SAD-General</i>	1.01	0.48	0.06, 1.96	0.03
<i>Total</i>	4.16	1.48	1.24, 7.08	0.06
Perceived Stigmatisation				
<i>AFB</i>	-0.01	0.07	-0.15, 0.12	0.00
<i>CSB</i>	0.07	0.08	-0.09, 0.24	0.006
<i>HB</i>	0.04	0.07	-0.11, 0.18	0.002
<i>Total</i>	0.03	0.06	-0.08, 0.14	0.002
Life Disengagement	0.10	0.06	-0.01, 0.21	0.02

Note. *b* = mean between-group difference; Body Esteem ($n = 139$) = BE-Appearance subscale; FNE ($n = 139$) = Fear of negative evaluation; SAD-New ($n = 139$) = Social avoidance and distress specific to new situations or unfamiliar peers; SAD-General ($n = 139$) = Social avoidance and distress in general; Total ($n = 139$) = Social Anxiety Scale for Adolescents total scale; AFB ($n = 132$) = Absence of friendly behaviour; CSB ($n = 132$) = Confused and staring behaviours from others; HB ($n = 132$) = Hostile behaviour; Life Disengagement ($n = 133$) = Body Image Life Disengagement Questionnaire. Baseline scores and centre (i.e. [Country A] or [Country B]) served as covariates in each analysis.

3.3.1. Body esteem and social anxiety

For body esteem, there was no statistically significant main effect of group post-intervention, $F(1, 135) = 0.57, p = .45, \eta^2_p = 0.004$; corrected $p = .64$.

For the social anxiety total scale, there was a significant main effect of group post-intervention, with a moderate effect size, $F(1, 135) = 7.94, p = .006, \eta^2_p = 0.06$. After applying the Benjamini-Hochberg correction, the significant main effect of group was still maintained ($p = .04$). The adjusted post-intervention mean for the intervention group ($M = 42.08, SE = 1.10$) was lower compared with CAU ($M = 46.24, SE = 0.99$), indicating that social anxiety was reduced in the intervention group ($b = 4.16$). For fear of negative evaluation, there was a statistically significant main effect of group post-intervention, with a moderate effect size, $F(1, 135) = 7.26, p = .008, \eta^2_p = 0.05$. After applying the Benjamini-Hochberg correction, the significant main effect of group was still maintained ($p = .04$). The adjusted post-intervention mean for the intervention group ($M = 17.89, SE = 0.58$) was lower than for CAU ($M = 19.99, SE = 0.52$), indicating that fear of negative evaluation had been reduced in the intervention group ($b = 2.10, SE = 0.78$). For social avoidance specific to new situations or unfamiliar peers, there was a statistically significant main effect of group post-intervention with a small effect size, $F(1, 135) = 3.99, p = .048, \eta^2_p = 0.03$. After applying the Benjamini-Hochberg correction, the significant main effect of group was no longer maintained ($p = .12$). For social avoidance and distress in general, there was a statistically significant main effect for group post-intervention with a small effect size, $F(1, 135) = 4.43, p = .04, \eta^2_p = 0.03$. After applying the Benjamini-Hochberg correction, the significant main effect of group was no longer maintained ($p = .12$).

3.3.2. Perceived stigmatisation and life disengagement

There were no statistically significant main effect post-intervention for the perceived stigmatisation total scale score ($F(1, 128) = 0.22, p = .64, \eta^2_p = 0.002$; corrected $p = .71$), absence of friendly behaviour ($F(1, 128) = 0.04, p = .84, \eta^2_p < .001$; corrected $p = .84$), confused/staring behaviour ($F(1, 128) = 0.79, p = .38, \eta^2_p = 0.006$; corrected $p = .62$), or hostile behaviour ($F(1, 128) = 0.27, p = .60, \eta^2_p = 0.002$; corrected $p = .71$). Centre was significantly related to the hostile behaviour subscale at post-intervention ($F(1, 128) = 6.51, p = .01$), indicating that participants in The Netherlands had higher perceptions of hostile behaviour compared with participants living in Norway.

For life disengagement, there was a non-significant main effect for group post-intervention ($F(1, 129) = 3.23, p = .08, \eta^2_p = 0.02$; corrected $p = .15$).

Table 4. Hierarchical multiple regressions predicting post-intervention body esteem, social anxiety, perceived stigmatisation, and life disengagement.

Step	Variable	Body Esteem					
		B (SE)	β	B 95% CI	R ²	R ² _{adj}	ΔF
Step 1	Baseline body esteem	0.65 (0.09)	0.70***	0.47, 0.83	0.49	0.48	49.86***
Step 2	Baseline body esteem	0.63 (0.10)	0.68***	0.43, 0.83	0.57	0.50	1.34
	Gender	-0.33 (0.17)	-0.21	-0.68, 0.01			
	Age	0.01 (0.05)	0.03	-0.08, 0.11			
	Centre	-0.34 (0.17)	-0.21	-0.68, 0.01			
	Time spent on YPF	0.01 (0.01)	0.08	-0.02, 0.03			
	Skin condition	-0.21 (0.25)	-0.12	-0.71, 0.28			
	Craniofacial condition	0.07 (0.21)	0.04	-0.35, 0.49			
	Scarring condition	0.02 (0.46)	0.00	-0.91, 0.95			
Step	Variable	Social Anxiety					
	B (SE)	β	B 95% CI	R ²	R ² _{adj}	ΔF	
Step 1	Baseline social anxiety	0.59 (0.07)	0.76***	0.45, 0.73	0.58	0.57	72.97***
Step 2	Baseline social anxiety	0.56 (0.07)	0.71***	0.41, 0.70	0.70	0.65	2.60*
	Gender	5.41 (2.21)	0.22	0.96, 9.87			
	Age	0.31 (0.60)	0.04	-0.90, 1.52			
	Centre	4.49 (2.29)	0.18	-0.11, 9.09			
	Time spent on YPF	-0.15 (0.15)	-0.09	-0.46, 0.15			
	Skin condition	3.43 (3.15)	0.12	-2.91, 9.76			
	Craniofacial condition	-2.65 (2.73)	-0.11	-8.13, 2.84			
	Scarring condition	-7.67 (5.96)	-0.12	-19.67, 4.33			

Table 4. Continued.

Step	Variable	Perceived Stigmatisation					
		B (SE)	β	B 95% CI	R ²	R ² _{adj}	ΔF
Step 1	Baseline perceived stigmatisation	0.65 (0.08)	0.74***	0.48, 0.81	0.55	0.54	62.73***
Step 2	Baseline perceived stigmatisation	0.64 (0.09)	0.74***	0.47, 0.82	0.62	0.55	1.18
	Gender	0.09 (0.09)	0.10	-0.10, 0.28			
	Age	0.02 (0.03)	0.07	-0.03, 0.07			
	Centre	0.15 (0.09)	0.16	-0.04, 0.33			
	Time spent on YPF	-0.01 (0.01)	-0.09	-0.02, 0.01			
	Skin condition	-0.08 (0.13)	-0.07	-0.34, 0.19			
	Craniofacial condition	-0.16 (0.12)	-0.17	-0.39, 0.08	-0.17		
	Scarring condition	-0.42 (0.25)	-0.17	-0.93, 0.09			

Table 4. Continued.

Life Disengagement		B (SE)	β	B 95% CI	R ²	R^2_{adj}	ΔR^2	ΔF
Step	Variable							
Step 1	Baseline life disengagement	0.54 (0.08)	0.68***	0.38, 0.71	0.46	0.45	0.46	43.69***
Step 2	Baseline life disengagement	0.46 (0.08)	0.58***	0.30, 0.63	0.60	0.53	0.14	2.25*
	Gender	0.25 (0.09)	0.29	0.07, 0.43				
	Age	0.02 (0.02)	0.08	-0.03, 0.07				
	Centre	0.05 (0.09)	0.06	-0.14, 0.23				
	Time spent on YPF	0.00 (0.01)	0.06	-0.01, 0.02				
	Skin condition	0.20 (0.13)	0.20	-0.06, 0.45				
	Craniofacial condition	-0.02 (0.11)	-0.03	-0.24, 0.19				
	Scarring condition	0.04 (0.24)	0.02	-0.44, 0.52				

Note. Body Esteem ($n = 55$) = BE-Appearance subscale; Social Anxiety ($n = 55$) = Social Anxiety Scale for Adolescents; Perceived Stigmatisation ($n = 54$) = Perceived Stigmatization Questionnaire; Life Disengagement ($n = 53$) = Body Image Life Disengagement Questionnaire.

* $p < .05$, *** $p < .001$

3.4. Underlying predictors related to potential intervention improvements

To test for associations between predictors (baseline outcome scores, age, gender, type of visible difference and time spent on YPF) and primary and secondary outcome scores within the intervention group, hierarchical multiple regressions were conducted (see Table 4).

3.4.1. Predictors of primary outcomes

Body esteem. In Step 1, baseline scores significantly accounted for 48.5% of the variance in body esteem post-intervention, $F(1, 53) = 49.86, p < .001$. In Step 2, entering age, gender, centre, time spent on YPF, and type of visible difference did not significantly improve the model.

Social anxiety. In Step 1, baseline scores significantly accounted for 57.9% of the variance in social anxiety post intervention, $F(1, 53) = 72.97, p < .001$. In Step 2, an additional 11.9% of the variance was significantly accounted for after introducing age, gender, centre, time spent on YPF, and type of visible difference, into the model, $F(8, 46) = 13.31, p < .001$. Gender emerged as a statistically significant predictor of overall levels of social anxiety post-intervention ($p = .018$), such that girls had higher levels of social anxiety compared with boys.

3.4.2. Predictors of secondary outcomes

Perceived stigmatisation. In Step 1, baseline scores significantly accounted for 54.7% of the variance in perceived stigmatisation post-intervention, $F(1, 52) = 62.73, p < .001$. In Step 2, entering age, gender, centre, time spent on YPF, and type of visible difference did not significantly improve the model.

Life disengagement. In Step 1, baseline scores significantly accounted for 46.1% of the variance in life disengagement post-intervention, $F(1, 51) = 43.69, p < .001$. In Step 2, and additional 14.2% of the variance was significantly accounted for after entering age, gender, centre, time spent on YPF, and type of visible difference, into the model, $F(8, 44) = 8.37, p < .001$. Gender emerged as a significant predictor of life disengagement post-intervention ($p = .009$), where girls had greater life disengagement compared with boys.

4. Discussion

The current study is the first large-scale trial to evaluate the effectiveness of YPF in improving body esteem, and/or reducing social anxiety, perceived stigmatisation, and life disengagement in adolescents with a visible difference. In general, results indicated that YPF reduced overall levels of social anxiety and fear of negative evaluation more specifically. However, there was no intervention effect on body

esteem, perceived stigmatisation, or life disengagement. Key findings and issues are further discussed below.

4.1. Web-based psychosocial support to reduce social anxiety

Research on adolescent samples with a visible difference has demonstrated higher levels of social anxiety and fear of negative evaluations in this population (8, 184). Therefore, the results of the present study, indicating that YPF reduces levels of social anxiety, and fear of negative evaluations in particular, are interesting and promising. This findings is in line with Williamson et al. (186), who also reported statistical significance for the remaining two other subscales of the SAS-A (i.e. Social avoidance in new and unfamiliar situations, and distress in general), subscales who were found to be non-significant in the present study, when corrections had been applied. Reduced levels of social anxiety and fear of negative evaluation in particular, may indicate that participants who completed YPF learned new social skills over the course of the programme that contributed to decrease their anxiety during interactions with others, and provided them with techniques to manage their anxiety. For instance, sessions in YPF specifically include advice and guidance on how adolescents can practice skills to handle teasing and bullying, and encourage adolescents to be mindful of how they deal with unwanted attention (186). Participants therefore get the opportunity to learn and actively engage with new social interaction skills that they can test in real-life situations. YPF also includes CBT-based sessions that focus specifically on teaching adolescents how to change existing negative thoughts and feelings, how to set realistic goals to overcome self-imposed limitations, and how to overcome social anxiety using management skills (186).

Research has shown that adolescents can adjust more positively to their visible difference by increasing the range of their social skills repertoire, and as a result be perceived as more confident, interesting, social, friendly, and attractive, by their peers without a visible difference (221, 222). Additionally, CBT-based interventions, delivered face-to-face to adolescents with a visible difference (223) or delivered online to adolescent community samples (227), have previously shown to be effective in reducing anxiety. The reduction in social anxiety among the participants that completed YPF is therefore consistent with the design and content of the programme. Social skills and anxiety management techniques can be considered key contributors to how adolescents cope with their visible difference, and YPF may aid adolescents in overcoming personal obstacles related to for example social interactions and in altering unhelpful thought patterns.

4.2. Measuring body esteem, perceived stigma, and life disengagement in adolescents with a visible difference

Second, our results suggest that YPF did not improve body esteem, or reduce perceived stigmatisation and life disengagement, relative to CAU, in contrast to Williamson et al. (186), who found positive changes for body esteem post-intervention. However, it should be noted that results from Williamson et al. (186) are based on a small sample size compared with the present study, and results may therefore reflect the potential impact of this methodological difference. Although our study suggests that the YPF intervention is not effective in improving body esteem, or in reducing perceived stigmatisation and life disengagement, alternative explanations are also possible.

Although this study included acknowledged, reliable, and valid measures, chosen measures may still not be sensitive enough to identify challenges specific to adolescents living with a visible difference. For instance, the presence of a visible difference is well-known to be a cause of appearance-related distress in adolescents (8, 184), irrespective of variations in size and location of the visible difference (14). This overall finding from general appearance research on the psychology of visible differences was confirmed in the present study by no significant findings related to types of included conditions or diagnoses. The appearance subscale of the BESAA (192) that was included in our study is primarily aimed at assessing adolescents' general appearance satisfaction, without specifically addressing concerns related to the presence and nature of a visible difference. A generic measure was chosen, since the large variation in included types of visible differences impeded the use of condition-specific measures. A general challenge within appearance-related research is the lack of validated psychometric cross-condition instruments that assess appearance concerns specifically in adolescents with a visible difference (242). It might therefore be the case that existing measures were not sensitive enough to capture variations in individuals' experiences of living with a visible difference and some measures therefore missed potential interventional benefits. Nonetheless, body esteem levels are generally found to be higher in adolescent community samples (243) compared to the current study sample. This could indicate that the appearance subscale of the BESAA did capture some dissatisfaction with body esteem in our sample of adolescents with visible differences.

Another explanation to the non-significant results could also be related to participants' engagement with YPF. In the study by Williamson et al. (186), engagement with YPF (defined as number of YPF sessions completed) was significantly related to positive changes in body esteem and fear of negative evaluation post-intervention. In the present study, a slightly different measurement of engagement was included, that is, how many weeks participants spent completing YPF, irrespective of whether they completed all sessions or not. Both variables

may indicate participants' engagement and motivation, but can unfortunately not be directly compared. Engagement with the programme presumably includes additional aspects, such as the adolescent's own motivation, and should possibly be explored in future research by a closer investigation of the number of sessions completed, amount of time spent on each session, and whether participants were prompted to complete the programme by the research team and/or by caregivers.

4.3. Predictors related to intervention improvements

In order to explore the impact of underlying factors that could potentially be related to post-intervention improvements in the intervention group, hierarchical multiple regressions were conducted. Overall, results did not provide support for age, centre (i.e. country of residence), time spent on YPF, nor type of visible difference, in predicting improvements due to engagement with YPF. Gender, however, significantly predicted social anxiety and life disengagement post-intervention, after accounting for baseline levels. Although social anxiety and life disengagement decreased from baseline to post-intervention for both boys and girls, the hierarchical multiple regressions showed that gender differences in levels of social anxiety and life disengagement that were present at baseline (where girls reported more social anxiety and life disengagement than boys), were further increased after completing YPF. These results might indicate that YPF is more effective in reducing social anxiety and life disengagement among boys than girls. Further investigation on gender differences and how and/or why they relate to the effectiveness of YPF in reducing social anxiety and life disengagement is therefore warranted.

4.4. Clinical implications and future research

Taken together, our study demonstrates that web-based psychosocial support, using and including SST and CBT techniques, might be successful in reducing levels of social anxiety, and fear of negative evaluation in particular, in adolescents with a visible difference, while the intervention's effect on body esteem, perceived stigmatisation, and life disengagement may be questioned. Still, our results suggest that YPF may benefit adolescents who struggle with the common social challenges related to living with a visible difference. Research and clinical experience indicate that many adolescents have limited access to specialised, evidence-based, and tailored interventions (186), highlighting the usefulness of easy accessible treatment offers such as YPF for those who experience appearance-related anxiety. Nonetheless, more studies are needed to investigate the potential short-term and long-term effectiveness of YPF in improving body esteem and reducing social anxiety, perceived stigmatisation, and life disengagement. Consecutively, future studies should seek to explore how YPF may be implemented in for example primary care settings and/or outpatient clinics, and ultimately offered to adolescents in need of support (72). Future research should also consider investigating whether YPF could also be offered as an early intervention to pre-adolescents who are at risk

of developing symptoms of social anxiety and/or dissatisfaction with appearance due to a visible difference, and who may benefit from increasing their range of social skills and challenges negative cognitive subjective appearance schemas. Since YPF may constitute an available alternative to traditional face-to-face treatment, we encourage further investigation on the cost-effectiveness of implementing the intervention. Potential challenges with implementation, financing, and intake of patients, should also be further explored and addressed (244).

4.5. Strengths and limitations

The main strength of the current study was the RCT-design, which made it possible to eliminate potential confounders and thus improve internal validity. The study was also a result of an international collaboration and included participants from two countries, which strengthens the generalisability of results to a broader population. Additionally, we managed to include a large enough sample size to reach sufficient power to detect statistically significant changes in outcomes, which is often a general challenge within the visible difference research field (186, 245) and in intervention studies (246).

Despite the study strengths, several limitations need to be considered. First, our study only included two points of assessment. Including several time-points would have provided an estimate of participants' outcome levels in the longer term, and determine the course and stability of intervention effects. Future research should therefore test the potential long-term effect of YPF and evaluate whether adolescents differ in their improvement levels over time.

Second, although we used validated outcome instruments, included measures were not constructed specifically for a population consisting of adolescents with visible differences, and were therefore possibly not sensitive enough to capture changes in the adolescents' adjustment to their visible difference following completion of the intervention. However, there are currently no cross-condition measures that possibly would assess such changes. We therefore encourage future studies to investigate which existing measures could capture changes in adolescents with a visible difference across conditions, and/or consider developing new instruments specifically tailored to examine appearance concerns, perceived stigmatisation behaviours, and life disengagement, in mixed groups such as in the present study.

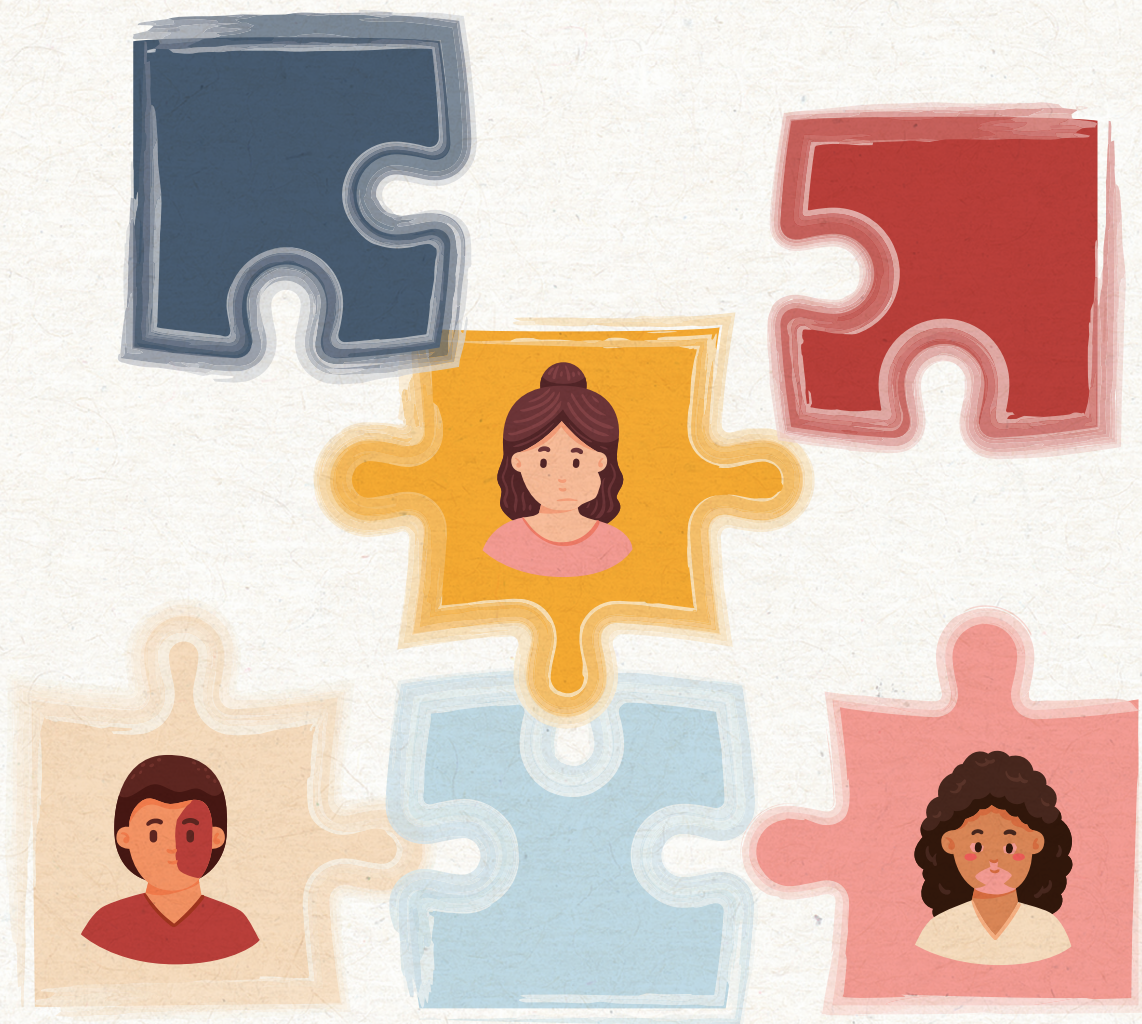
Third, there were some methodological differences between the two study centres that could have impacted on the results. The waiting-list control group in [Country A] could have prompted expectations that might have influenced outcome scores. On the other hand, this solution was chosen in order to secure recruitment, since the pilot study (186) indicated that participants and parents had ethical concerns regarding a traditional control group where YPF would not be offered to participants.

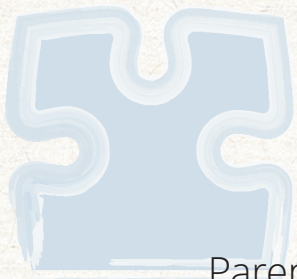
Moreover, no screening for subclinical symptoms was done in the study centre in [Country A] and participants were therefore included irrespective of levels of body esteem, social skills, and/or symptoms of depression. However, the randomisation procedure and ANCOVA models should account for systematic baseline differences between participants and no differences were found for gender or type of visible difference between the two experimental groups. Nonetheless, variations in baseline outcome levels between the two study sites could mean that participants had different experiences of appearance-related distress and support needs, which may in turn have affected intervention effects.

Finally, the lockdown that ensued in both participating countries from the COVID-19 pandemic might have negatively impacted participants' psychological well-being and influenced results, and therefore have inserted an additional factor that was not controlled for in the present analyses. Since YPF teaches social skills which are meant to be practiced in real-life situations, participants who completed the programme during the pandemic may not have had the same opportunity to apply new social skills as adolescents completing YPF before the pandemic. Considering the impact that the COVID-19 lockdown may have had on the frequency of adolescents' body image (247), future studies should investigate how the pandemic might have affected the psychological well-being of adolescents with a visible difference.

5. Conclusion

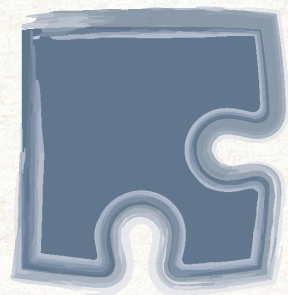
This is the first study to experimentally test the effectiveness of YPF, a web-based psychosocial intervention developed for adolescents experiencing appearance-related distress and social challenges as a result of having a visible difference. Our results indicated that engagement in YPF reduced social anxiety symptoms, and fear of negative evaluation in particular, whereas we found no intervention effect on body esteem, perceived stigmatisation, or life disengagement. To conclude, our study supports the notion of a web-based intervention such as YPF having the potential to provide adolescents with knowledge and skills to manage the many social consequences of having a visible difference. Future studies are encouraged to further explore the effectiveness of YPF and its potential in reducing social anxiety, as well as investigating its long-term effects.

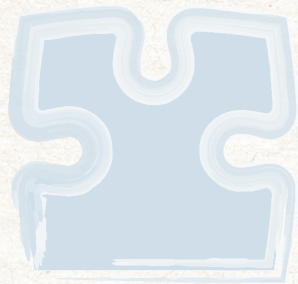
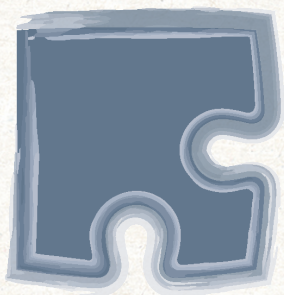


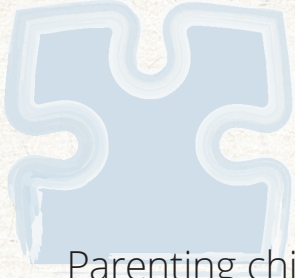


PART III

Parenting a child with a visible difference





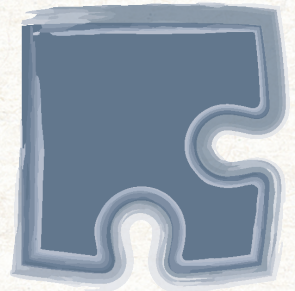


CHAPTER 7

Parenting children with a cleft lip with or without
cleft palate or a visible infantile haemangioma:
a cross-sectional study of distress and
parenting stress

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Abstract

Objective: Parents of children with a medical condition and a visible difference can experience challenging situations. We evaluated distress and parenting stress in parents of children with a cleft lip with or without cleft palate (CL±P) or a visible infantile haemangioma (IH). **Setting:** This cross-sectional study took place in an academic medical hospital in Rotterdam, The Netherlands. **Participants:** 309 parents ($M_{age} = 40.30$, 56.00% mothers) of children with CL±P and 91 parents ($M_{age} = 36.40$, 58.24% mothers) of children with IH. **Main outcome measures:** The Dutch version of the Parenting Stress Index – Short Form and the subscales Anxiety, Depression and Hostility of the Symptom Checklist – 90. **Results:** One sample *t*-tests and mixed linear modelling were used. On average, parents of children with CL±P and of children with IH showed significantly lower parenting stress compared to normative data. Anxiety was significantly lower in parents of children with CL±P than in the norm group. Visibility of the condition was not related to distress or parenting stress. Child behaviour problems were positively related to parenting stress, depression and hostility. **Conclusions:** Parents of children with CL±P and IH report less distress and parenting stress compared to the norm. On average, these parents seem well-adjusted. A practical implication is to monitor parents of children with behavioural problems.

Keywords: Psychological stress; parents; cleft lip; infantile haemangioma.

1. Introduction

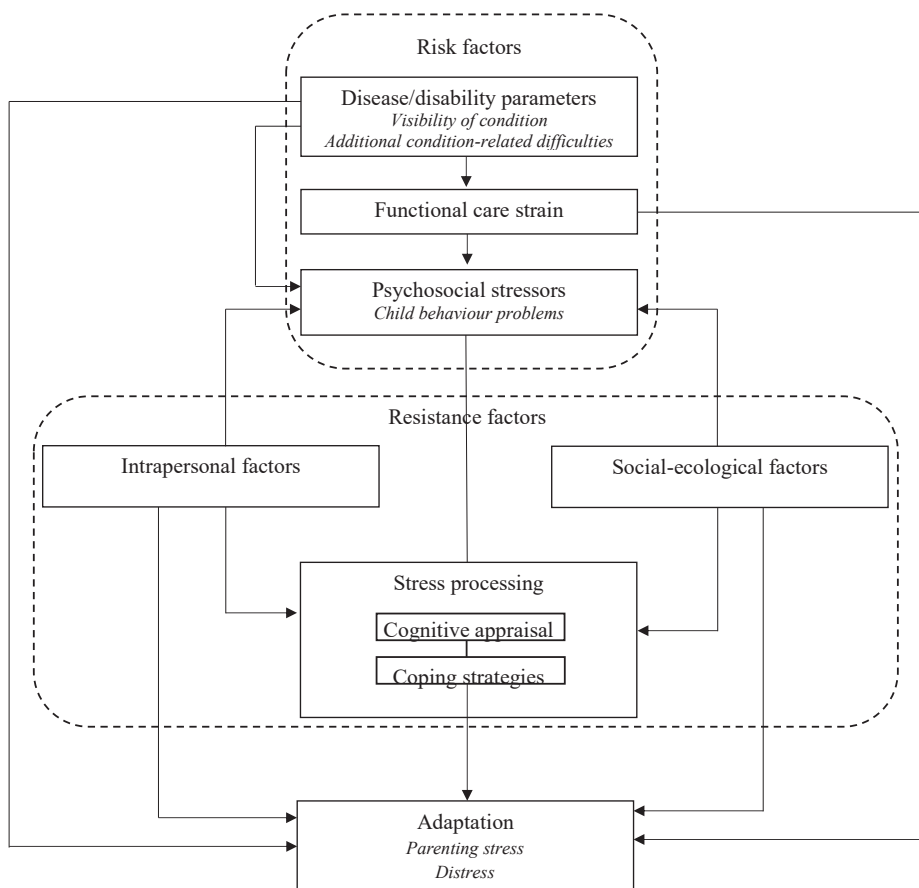
Parenting children with a medical condition, such as a cleft lip with or without cleft palate (CL±P) or an infantile haemangioma (IH) can present significant challenges. Apart from having to face medical treatment and possible hospitalisations, the visibility of these conditions means that these parents may have to cope with negative social feedback related to the child's appearance (77, 78). Hence, raising a child with a visible difference due to a medical condition can have an impact on parental psychological adaptation.

In an attempt to explain how parents adapt to having a child with a chronic condition and/or illness, Wallander et al. (248) posited a model of risk and resistance factors that have a direct impact on parental adaptation. An adaptation of this model is shown in Figure 1 along with the constructs tested in the current study. Furthermore, risk factors have an indirect influence on parental adaptation through stress processing (i.e., cognitive appraisal and coping strategies). The current study focuses on the direct impact of risk factors on parental adaptation, conceptualised as distress and parenting stress, in parents of children with CL±P or IH. Both conditions are present from birth or very shortly afterwards and may involve frequent hospital visits. In addition, these conditions become less visible over time, either due to surgery (CL±P) or due to the natural course of the condition itself (IH). Both conditions may also leave permanent marks on the face. In CL±P a scar may be visible (249). IHs regress over time, with the majority of the regression occurring before four years of age (250) and 50% to 70% of IHs eventually resolve. However, residual skin changes such as scars or redundant skin can be present (250).

Parenting stress has been defined as “a set of processes that lead to aversive psychological and physiological reactions arising from attempts to adapt to the demands of parenthood” (251). Parenting distress has been defined as “the extent to which the parent perceives stress in his/her role as a parent” (252). While specific measures exist for measuring parenting stress (e.g., the Parenting Stress Index (PSI); 253), parenting distress is most often conceptualised as parental depression or anxiety (254). When looking at parents of children with a chronic illness in general, recent meta-analyses (81, 82) showed that parents of children with a chronic physical illness experience more parenting stress, anxiety and depression compared to parents of healthy children or normative data. For parents of children with craniofacial conditions or CL±P no significant differences were found on parenting stress, parental anxiety and parental depression compared to normative data or a control group (81, 82). Parents of children with IH were not included in these meta-analyses. Although visibility was not investigated across diagnoses, moderate elevations of parental anxiety and depression were reported for skin diseases, which are often visible. A recent review and meta-analysis has shown that adolescents with

a visible difference experience more anxiety than unaffected peers (184). Rumsey et al. (5) showed that 47% of adults with a visible difference have subclinical or clinical symptoms of anxiety. However, less is known about the impact of the visible difference on parents. Qualitative studies showed parents have to manage other people's questions and reactions to their child's altered appearance (80). Hoornweg et al. (130) reported that parents' quality of life is not associated with the visibility of the child's haemangioma. However, to date, no literature exists that quantitatively examines the impact of the visible difference on parents' stress and distress.

Figure 1. Model posited by Wallander et al. (1989). Constructs measured in the current study in italics.



Literature on distress and parenting stress in CL±P, reflecting parental adaptation, is scarce. In a study by Hasanazadeh et al. (85), 55 mothers of children aged 8-18 with CL±P participated. Of these mothers, 38.2% experienced psychological distress and 23.6% showed signs of serious psychological problems, such as depression and anxiety. A recent study by Stock et al. (256) among 1163 parents of children with cleft lip and/or palate (CL/P) showed that mothers of newborn children with CL/P score higher on anxiety and depression when compared to normative data. Fathers scored lower on anxiety but higher on depression when compared to normative data. Nevertheless, small effect sizes were reported for all findings in this study and visible clefts were not reported separately from the nonvisible clefts. Another study found no significant differences on parenting stress between parents of children with CL±P and controls (257). There is also literature showing that parents of children with CL±P experience low levels of distress and a high degree of positive adjustment (258). Literature on IH is less common. Cazeau et al. (259) reported that 70% of parents are psychologically impacted by the child's IH, for instance through the gaze of others and experiencing anxiety, and that only 10% were offered psychological support.

This study quantitatively investigated distress and parenting stress in parents of children with CL±P or IH. This is important, as previous literature has shown that parenting stress can lead to child behaviour problems (76). Furthermore, parents' distress and stress can be transferred to the child through emotional contagion (260). We sought to answer two research questions: 1) Do parents of children with CL±P or IH report higher levels of distress and parenting stress than parents from the general population? 2) How are parent-perceived visibility and other parent-reported factors related to distress and parenting stress in parents of children with CL±P or IH? We examined the roles of parent-perceived visibility, medical problems related to the condition, child behavioural problems, parent age, child age and child gender in parental adjustment. As earlier research has shown that subjective visibility (i.e., the visibility as experienced by the child or parents) of the condition is a much stronger predictor of adjustment in the person with a visible difference than "objective" visibility (i.e., the visibility as judged by a physician; 14), we focused only on subjective visibility as experienced by parents. Following others (85, 256, 259), we hypothesised that parents of children with CL±P or IH would experience more distress and parenting stress than other parents, as they face many different challenges. As there is minimal literature specifically assessing the influence of subjective visibility on distress and parenting stress, we did not have any prior hypotheses concerning research question 2.

2. Methods

2.1. Sample and procedure

This study was part of a larger project assessing parental well-being and behaviour of parents with children with CL±P or IH. The study was conducted in accordance to the Declaration of Helsinki (148).

Recruitment took place in the Centre of Paediatric Dermatology of the Department of Dermatology and the Department of Oral and Maxillofacial surgery of the Erasmus MC – Sophia Children’s Hospital in Rotterdam, The Netherlands. Recruitment took place from 2008 until 2011 and data was later analysed and reported in 2019 and 2020 by a PhD student. Inclusion criteria were: 1) sufficient knowledge of the Dutch language by parents and 2) having a child with a visible CL±P or IH, aged between 0 and 12 years old. This age range was chosen as, in The Netherlands, children often make the transition to secondary education at age 12. For many parents and their children this is seen as the end of childhood and the start of adolescence. Children with an isolated cleft palate or cleft alveolus were not eligible for this study, due to the non-visible nature of these conditions. Each eligible family received an informed consent letter, two sets of questionnaires and a prepaid envelope. Parents were asked to fill out the questionnaires separately and independently from their partner. As an incentive, parents received a small gift for their child, worth approximately €1,-. Reminders were sent approximately one month later and again after 3 months.

2.2. Medical care at the Erasmus MC – Sophia Children’s Hospital, The Netherlands

Cleft care was provided at the Erasmus MC – Sophia Children’s Hospital, the Netherlands by multidisciplinary teams with average cleft lip surgery at the age of three months and cleft palate closure at the average age of 12 months. The alveolar cleft is closed around 9-12 years of age. Access to speech therapy is guaranteed through the treating hospital. Patients are followed up regularly by the multidisciplinary team until age 22.

Medical care for patients with an IH was provided at the Centre for Congenital Vascular Anomalies of the Erasmus MC. Treatment was administered (such as propranolol topical/systemic, prednisone, system/intralesional, surgery) to children with IH. All treated IHs were either potentially (life-)threatening or had functional risk, local discomfort or cosmetic consequences. In case of treatment, follow-up is until the end of systemic treatment. If cosmetic surgery is a suspected possibility, the IHs or its residuals are re-evaluated at age 3.

2.3. Instruments

Parent and child characteristics. Demographic and participant characteristics were obtained using questionnaires, and included age and ethnicity of children and parents and parental educational level as a proxy measure of socio-economic status. Parental education was divided into low, middle and high, based on the International Standard Classification of Education (ISCED) guidelines (150). These guidelines provide an international classification for organising education programs by education levels. It consists of nine education levels (261). Parents with primary or lower secondary education were coded as low. Parents with upper secondary, post-secondary non-tertiary or short cycle tertiary education were classified as average. Examples of these programs include vocational certifications and Associate's Degrees. Parents with a bachelor's degree or higher were classified as high.

Parenting stress. The NOSI-K (262) is the Dutch, shortened version of the Parenting Stress Index (PSI; 253). The NOSI-K is designed to measure parenting stress in parents of children aged 2-13 years old; however, the NOSI-K has also been

used in studies of infants younger than age 2 (e.g., 263, 264). Participant results must be interpreted with caution given the context of the younger age range in the IH group from the norm groups. The scale consists of 25 items rated on a 6-point scale ranging from 1 (*totally disagree*) to 6 (*totally agree*). A total parenting stress score is obtained by summing the ratings across items, with high scores reflecting high levels of parenting stress. The normative data of the NOSI-K consists of 161 mothers and 84 fathers (262). Scores can be classified into seven categories, ranging from extremely low to extremely high.

The NOSI-K discriminates well between clinical and non-clinical samples (262) and has acceptable internal consistency in other studies (263, 265). In the present study, Cronbach's alpha was $\alpha = .94$ for the CL±P group and $\alpha = .95$ for the IH group.

Distress. Distress experienced by parents was operationalised by symptoms of depression, anxiety and hostility as measured by the corresponding subscales of the Dutch translation of the Symptom Checklist-90 (SCL-90; 266). Depression and anxiety capture internalising problems, while hostility captures externalising problems such as feelings of anger and aggression. Hostility was included as clinical practice learns that parents may experience resentment or angry feelings following their child's diagnosis (267). The SCL-90 is a 90-item multidimensional questionnaire designed to screen for a broad range of psychological problems. The 16-item Depression (e.g., feeling lonely), 10-item Anxiety (e.g., suddenly scared for no reason) and 6-item Hostility (e.g., having urges to beat, injure, or harm someone) subscales were used. They are rated on a 5-point Likert scale, ranging from 1 (*not at all*) to 5 (*very much*).

Scale scores are calculated by summing the item scores with higher scores reflecting higher levels of depressive feelings, anxiety and feelings of hostility.

Adequate psychometric properties have been found in a sample of 2366 adults from the general population (266). In the present study, Cronbach's alpha for measures of parenting distress ranged between $\alpha = .76$ and $\alpha = .92$. The subscale hostility for IH ($\alpha = .76$) was the only subscale below $\alpha = .80$.

Child behaviour problems. The Child Behavior Checklist: Ages 1½-5 (CBCL 1½-5; 146) and the Child Behavior Checklist: Ages 6-18 (CBCL 6-18; 56) are widely-used parent-reported measures of childhood behavioural problems and competencies. The CBCL 1½-5 consists of 100 items, the CBCL 6-18 contains 120 items. Both are scored on a 3-point scale ranging from 0 (*not true*) to 2 (*very true or often true*). The Total Problems scale is obtained by summing the item scores, with high scores reflecting higher levels of behavioural problems. Because the two CBCL age versions differ in number in items, a 120-item equivalent of CBCL 1½-5 total scores was computed. As with the NOSI-K, some participants in the IH group were younger than the CBCL 1½-5 was developed to measure; however, total raw scores rather than norm comparisons were used in interpreting the CBCL results. In the present study, Cronbach's alpha ranged between $\alpha = .93$ and $\alpha = .97$.

Visibility. To assess subjective visibility of the condition, parents were asked two questions, both rated on a 5-point Likert scale: (1) "To what extent do you think your child's condition is visible?" and (2) "To what extent do you feel that bystanders look at your child's visible difference?" (both ranging from *not at all* to *very much*). The two items were summed to derive a total visibility score. The items correlated significantly ($r = .59, p < .001$).

Additional condition-related difficulties. Additional questions were posed for potential medical or adjustment problems ("Does your child have feeding problems?", "Does your child have speech problems?", "Does your child have learning difficulties?" and "Does your child have psychological problems? [e.g., is your child aggressive, is your child depressed?]"). All questions were rated on a 5-point Likert scale and summed to derive a total score.

2.4. Statistical analysis

The means and standard deviations of all variables were calculated. In preliminary analyses, the demographic variables of the CL±P versus IH group were compared using Chi-squared tests for categorical variables and independent samples *t*-tests for continuous variables. The Levene's test was used to assess equal variances for both groups in the independent samples *t*-tests. If this test is significant, SPSS automatically corrects the degrees of freedom.

For the first research question, one sample *t*-tests were used to compare scores on the NOSI-K and SCL-90 with the normative mean scores. Cohen's *d* was calculated as a measure of effect size. Following Cohen (241), *d* = 0.20 was considered a small effect, *d* = 0.50 medium and *d* = 0.80 large.

The second research question was tested using linear mixed models to compare distress and stress measures (NOSI-K, SCL-90 anxiety, depression and hostility) amongst the CL±P and IH groups. This analysis accounts for clustering in the data (i.e., mothers and fathers reporting on the same child). Separate analyses were conducted for each outcome measure of distress or stress. Parent and child age, parent and child gender, child behaviour problems, visibility of the condition, parent education and other difficulties related to the condition were used as covariates. To assess whether cleft type influenced distress and parenting stress, secondary analyses were run. Mixed linear models were computed as described previously, however, instead of type of condition (CL±P and IH) type of cleft (cleft lip or cleft lip and palate) was included.

To account for multiple testing, *p*-values were corrected using Bonferroni correction. All *p*-values were two-tailed. Statistical analyses were performed using IBM SPSS Statistics for Windows, version 25.0 (268).

3. Results

A total of 337 families with children with CL±P and 111 families with children with IH were eligible for the study, amounting to a total of 448 families. After invitation, 4 parents of children with CL±P and 9 parents of children with IH indicated they did not have sufficient knowledge of the Dutch language. These parents were excluded from participation.

Of the families with a child with CL±P, 173 mothers and 136 fathers returned completed questionnaires (46.3%). In the IH group, the response rate was 41.6% (53 mothers, 38 fathers). One mother in the CL±P group had completed the questionnaires twice, so one duplicate record was removed prior to data analysis. A total of 400 parents (227 mothers, 173 fathers) from 237 families completed the questionnaires.

3.1. Preliminary analysis

A non-response analysis did not reveal significant differences in age of the children with CL±P between the participants and the non-responders. However, on average, the children of non-responders in the IH group were older ($M = 4.55$, $SE = .58$), than the children in the included IH sample ($M = 3.59$, $SE = .38$, $t(142) = -1.47$, $p < .05$).

Of the 181 children with CL±P, 66% of children had a cleft lip and palate and 34% had an isolated cleft lip. Of the 55 children with an IH, 90.1% of the children had an IH in the head and neck region. The other 8.9% had an IH on another location of the body. Prior to the main analysis, group differences in sociodemographic characteristics were tested. On average, parents of children with IH were younger than those of children with CL±P, $t(160.46) = 5.57, p < .001$, and children with IH were younger than children with CL±P, $t(121.24) = 7.93, p < .001$. Furthermore, there were more girls in the group of children with IH than in the CL±P group, $\chi^2(1) = 41.45, p < .001$. Table 1 shows the families' sociodemographic characteristics.

Table 1. Sociodemographic characteristics of the sample

	CL±P (N=309)	IH (N=91)	P value
Parent gender, N (%)			
Male	136 (44.00)	38 (41.76)	.703
Female	173 (56.00)	53 (58.24)	
Parent age (years), mean (SD)	40.30 (6.31)	36.40 (5.73)	< .001
Parent age (years), range	25.58 – 71.42	24.00 – 49.92	
Child gender, N (%)			
Male	118 (65.19)	13 (23.21)	< .001
Female	63 (34.81)	43 (76.79)	
Child age (years), mean (SD)	7.23 (2.71)	4.30 (3.64)	< .001
Child age (years), range	2.42 – 12.50	.08 – 11.67	
Nationality, N (%)			
Dutch	301 (97.40)	86 (94.51)	.181
Other/unknown	8 (2.60)	5 (5.49)	
Education, N (%)			
Low	34 (11.07)	9 (9.89)	.945
Average	146 (47.56)	44 (48.35)	
High	122 (39.74)	37 (40.66)	
Other/unknown	5 (1.62)	1 (1.10)	

Note: CL±P = Cleft Lip with or without a cleft Palate, IH = Infantile Haemangioma

Parents rated the child's condition as more visible for children with IH than children with CL±P, $t(112.68) = -7.40, p < .001$. Parents of children with CL±P rated their children as having more additional difficulties, $t(269.73) = 8.90, p < .001$ and as having more behavioural problems $t(81.77) = 3.17, p = .002$ than parents of children with IH.

3.2. Distress and parenting stress compared to normative data

As shown in Table 2, both mothers and fathers in the CL±P and IH group had significantly less parenting stress than the normative population, with large effect sizes ($d = -.79$ - $d = -1.53$). Furthermore, all parent groups scored significantly below the normative mean range, indicating low levels of parenting stress in parents of children with CL±P or IH.

Both mothers and fathers of children with CL±P reported less anxiety than the normative population, with small to medium effect sizes. For IH, only mothers reported significantly less anxiety ($M = 11.91$, $SD = 3.33$, $p = .002$, $d = -.46$). Fathers of children with IH scored within the normal range, with a negligible effect size. On measures of depression and hostility, none of the parent groups differed significantly from the normative population.

Table 2. One-sample T-test for observed and normative mean scores of distress and parenting stress

			Sample		Norm group			
Instrument	Condition	N	Mean (SD)	Mean (SD)	Mean range	P value	Cohen's <i>d</i>	
Fathers								
Parenting stress ¹	CL±P	134	35.82 (15.41)	48.5 (16.4)	39-53	< .001*	-.82	
	IH	37	34.38 (17.97)	48.5 (16.4)	39-53	< .001*	-.79	
Anxiety ²	CL±P	134	11.39 (2.47)	12.23 (3.80)	12-14	< .001*	-.34	
	IH	38	12.16 (4.55)	12.23 (3.80)	12-14	.923	-.02	
Depression ³	CL±P	134	19.57 (6.30)	20.58 (6.76)	20-23	.067	-.16	
	IH	38	20.90 (9.37)	20.58 (6.76)	20-23	.834	.03	
Hostility ⁴	CL±P	134	7.19 (2.11)	7.22 (2.11)	7-8	.855	-.02	
	IH	37	7.58 (2.97)	7.22 (2.11)	7-8	.462	.12	
Mothers								
Parenting stress ¹	CL±P	171	37.33 (17.33)	54.4 (19.3)	43-61	< .001*	-.99	
	IH	53	33.76 (13.50)	54.4 (19.3)	43-61	< .001*	-1.53	
Anxiety ²	CL±P	170	12.04 (3.63)	13.43 (4.91)	12-14	< .001*	-.38	
	IH	53	11.91 (3.33)	13.43 (4.91)	12-14	.002*	-.46	
Depression ³	CL±P	169	21.33 (7.11)	22.89 (8.24)	20-23	.005	-.22	
	IH	53	21.09 (5.78)	22.89 (8.24)	20-23	.028	-.31	
Hostility ⁴	CL±P	169	7.19 (1.91)	7.33 (2.11)	7-8	.334	-.07	
	IH	53	7.11 (1.87)	7.33 (2.11)	7-8	.402	-.12	

* Significant at a Bonferroni-corrected level of $\alpha = .003$.

¹ As measured by the NOSI-K, using norms of children ages 2-13, ² As measured by the SCL-90 Anxiety subscale, ³ As measured by the SCL-90 Depression subscale, ⁴ As measured by the SCL-90 Hostility subscale.

Overall, when compared to the norm group, 3.49% of fathers and 3.08% of mothers were classified as scoring extremely high on parenting stress. Also, 4.05% of fathers and 2.20% of mothers scores were classified as high on parenting stress. For anxiety, 2.25% of parents scored extremely high and 9.25% parents scored above average/high. For depression, 4.25% of parents scored extremely high, while 11% scored high. For hostility, 5.25% of parents scored extremely high, while 8.75% parents scored high/above average. Detailed sample characteristics, split by parent gender and child condition are shown in Table 3.

Table 3. Clinical interpretation of scores of distress and parenting stress, N(%)

	Condition	N	Below average	Average	Above* average	High*	Extremely high
Fathers							
Parenting stress ¹	CL±P	133	98 (73.7)	22 (16.5)	3 (2.3)	6 (4.5)	4 (3.0)
	IH	37	29 (78.4)	3 (8.1)	3 (8.1)	2 (5.4)	3 (8.1)
Anxiety ²	CL±P	134	95 (70.9)	30 (22.4)		7 (5.2)	2 (1.5)
	IH	38	26 (68.4)	7 (18.4)		4 (10.5)	1 (2.6)
Depression ³	CL±P	134	96 (71.6)	21 (15.7)	4 (3.0)	9 (6.7)	4 (3.0)
	IH	37	23 (62.2)	8 (21.6)	3 (8.1)	1 (2.7)	2 (5.4)
Hostility ⁴	CL±P	134	61 (45.5)	55 (41.0)		12 (9.0)	6 (4.5)
	IH	38	19 (50.0)	11 (28.9)		3 (7.9)	5 (13.2)
Mothers							
Parenting stress ¹	CL±P	169	130(76.9)	25 (14.8)	3 (1.8)	5 (3.0)	6 (3.6)
	IH	53	42 (79.2)	8 (15.1)	2 (3.8)	0 (0)	1 (1.9)
Anxiety ²	CL±P	171	110(64.3)	37 (21.6)		19 (11.1)	5 (2.9)
	IH	53	38 (71.7)	7 (13.2)		6 (11.3)	2 (3.8)
Depression ³	CL±P	171	92 (53.8)	36 (21.1)	5 (2.9)	29 (17.0)	9 (5.3)
	IH	53	28 (52.8)	15 (28.3)	2 (3.8)	5 (9.4)	3 (5.7)
Hostility ⁴	CL±P	171	79 (46.2)	67 (39.2)		18 (10.5)	7 (4.1)
	IH	53	28 (52.8)	17 (32.1)		5 (9.4)	3 (5.7)

*For the anxiety and hostility scales, norm scores are reported in a combined category of above average and high scores in the manual.

¹. As measured by the NOSI-K, using norms of children ages 2-13, ². As measured by the SCL-90 Anxiety subscale, ³. As measured by the SCL-90 Depression subscale, ⁴. As measured by the SCL-90 Hostility subscale.

3.3. Distress and parenting stress in both parent groups

Linear mixed models were run to test our second research question. Results are shown in Table 4. All models had the lowest -2 log likelihood ratio, and thus the best fit, when including the covariates parent age, child age, child gender, child behaviour problems, visibility of the condition and other problems related to the condition.

Regarding parenting stress, parents of children with CL±P reported higher levels of parenting stress than parents in the IH group $F(233.22) = 5.20, p = .023$. As noted earlier, these stress levels were lower than the normative group. Child behaviour problems ($F(286.50) = 191.54, p < .001$), child diagnosis ($F(233.22) = 5.20, p = .023$) and other condition-related problems ($F(295.32) = 14.60, p < .001$) were positively related to parenting stress. Parents of children with more behaviour problems and other condition-related had higher levels of parenting stress. Parents of children with CL±P experienced more parenting stress than parents of children with an IH. Visibility of the condition was not related to parenting stress, nor was parent age, parent gender, child age or child gender.

Concerning feelings of anxiety, none of the independent variables reached significance. Feelings of anxiety were not related to the condition of the child (CL±P or IH) nor to any of the proposed covariates.

The model for parental depression showed no significant effect of condition or children's age. Child behaviour problems, $F(1,182.36) = 9.61, p = .002$, and additional problems related to the medical condition, $F(328) = 9.85, p = .020$ were significantly related to parenting symptoms of depression, with parents of children with more behavioural and additional problems reporting more depressive symptoms.

Concerning hostility, condition (CL±P or IH) did not significantly influence the model, but additional condition-related difficulties did, $F(254.82) = 8.73, p = .003$.

Overall, none of the covariates (i.e., parent age, parent gender, child age, child gender or visibility of the condition) were significantly related to either measures of distress and parenting stress.

Table 4. Mixed Linear Models for distress and parenting stress for total sample

	Visibility	Condition ⁵	Behaviour problems ⁶	Condition-related problems	Parent age	Parent gender	Child age	Child gender
Parenting stress¹								
B	.61	-4.84*	.52***	1.36***	.18	-1.69	.20	-.47
Std. Error	.42	2.08	.04	.37	.12	1.10	.29	1.50
95% CI								
Lower	-.20	-8.93	.45	.64	-.07	-3.87	-.38	-3.42
Upper	1.43	-.75	.59	2.08	.42	.49	.78	2.48
Anxiety²								
B	.10	-.43	.01	.19	<-.01	.36	.15	-.45
Std. Error	.11	.53	.01	.10	.03	.34	.08	.38
95% CI								
Lower	-.12	-1.48	<-.01	<-.01	-.06	-.32	<-.01	-1.20
Upper	.32	.62	.03	.38	.07	1.05	.30	.31
Depression³								
B	.30	-1.27	.06**	.49*	<-.01	.83	.29	-1.03
Std. Error	.23	1.09	.02	.20	.07	.74	.16	.78
95% CI								
Lower	-.15	-3.42	.02	.09	-.14	-.62	<-.01	-2.56
Upper	.75	.88	.10	.88	.13	2.28	.60	.50
Hostility⁴								
B	.05	-.10	<.01	.19**	-.02	-.15	<-.01	-.07
Std. Error	.07	.36	.01	.06	.02	.20	.05	.26
95% CI								
Lower	-.10	-.81	-.01	.06	-.06	-.55	-.10	-.58
Upper	.19	.61	.02	.31	.02	.25	.10	.44

Note. * $p < .05$. ** $p < .01$. *** $p < .001$.

¹ As measured by the NOSI-K, using norms of children ages 2-13 ² As measured by the SCL-90 Anxiety subscale;

³ As measured by the SCL-90 Depression subscale, ⁴ As measured by the SCL-90 Hostility subscale, ⁵ CL±P or LH,

⁶ As measured by the CBCL using measures developed for children ages 1½-5 and 6-18.

Table 5. Mixed Linear Models for distress and parenting stress for parents of a child with CL±P

	Visibility	Cleft type ⁵	Behaviour problems ⁶	Condition-related problems	Parent age	Parent gender	Child age	Child gender
Parenting stress¹								
B	.66	.65	.49***	1.30**	.15	-.92	.23	-.61
Std. Error	.51	1.93	.04	.40	.14	1.19	.34	1.71
95% CI	-.34	-3.16	.41	.51	-.11	-3.27	-.44	-3.99
Lower								
Upper	1.66	4.45	.57	2.09	.42	1.43	.89	2.78
Anxiety²								
B	.12	-.36	.01	.17	-.01	.57	.18*	-.57
Std. Error	.14	.49	.01	.11	.04	.38	.09	.42
95% CI	-.15	-1.34	-.01	-.04	-.08	-.19	.01	-1.43
Lower								
Upper	.39	.62	.04	.38	.06	1.33	.35	.29
Depression³								
B	.34	.59	.05*	.51*	-.04	1.32	.35	-.62
Std. Error	.28	1.01	.02	.22	.07	.74	.18	.88
95% CI	-.20	-1.41	<.01	.09	-.18	-.14	<-.01	-2.37
Lower								
Upper	.89	2.60	.09	.94	.11	2.79	.70	1.14
Hostility⁴								
B	.06	-.31	<.01	.15*	-.03	-.12	.04	-.11
Std. Error	.09	.33	.01	.07	.02	.22	.06	.29
95% CI	-.11	-.96	-.01	.02	-.08	-.56	-.08	-.69
Lower								
Upper	.24	.34	.02	.29	.01	.31	.15	.47

Note. * $p < .05$, ** $p < .01$, *** $p < .001$.¹ As measured by the NOSI-K, using norms of children ages 2-13. ² As measured by the SCL-90 Anxiety subscale.³ As measured by the SCL-90 Depression subscale. ⁴ As measured by the SCL-90 Hostility subscale, ⁵ Cleft lip or cleft lip + palate,⁶ As measured by the CBCL using measures developed for children ages 1½-5 and 6-18.

3.4. Secondary analyses for cleft type

To assess whether cleft type influenced the amount of distress and parenting stress, mixed linear models were run with cleft type as a covariate. Results are shown in Table 5. Cleft type did not significantly influence the amount of parenting stress, anxiety, depression or hostility in parents. Including cleft type in the models did not change the significance of predictors for parenting stress, depression and hostility in comparison to the main analysis. For anxiety, child age was significantly related to parental stress, $F(50.83) = 4.64$, $p = .036$. Parents of older children experienced more anxiety than parents of younger children. This effect was not found in the main analyses.

4. Discussion

The present study aimed to determine whether parents of children with CL±P or IH experience more distress and parenting stress than parents from the general population. Furthermore, we sought to understand how visibility and other parent-reported factors associated with the medical condition are related to distress and parenting stress. Our findings indicate that parents of children with a visible difference (CL±P or IH) report lower levels of parenting stress and less symptoms of anxiety than parents from the general population. They did not differ significantly from the general population in feelings of depression and hostility.

Current results are not consistent with our expectations, as we expected parents of children with CL±P and IH to report higher levels of distress and parenting stress. This expectation was primarily based on meta-analyses by Pinquart (81, 82, 255) reporting elevated levels of distress and parenting stress in parents of children with a medical condition. An explanation for the current findings may be post-traumatic growth or a response shift.

Historically, the majority of research has focused on the negative impact on parents of having a child with a medical condition, resulting in poor adjustment, parenting stress, depression or anxiety (269). However, there is a growing body of literature on stress-related growth and beneficial effects among parents of children with a medical condition (e.g., Li et al. (270)). This is termed post-traumatic growth and is very common. About 58 – 83% of people who have experienced a traumatic event report positive change in at least one life domain (271). The present study shows that the parents of children with CL±P or IH report less stress and equal levels of distress compared to adults in the general population. The current results can be seen in the light of post-traumatic growth, but more research is needed to study this phenomenon.

Another possibility is that a response shift occurs in parents of children with a medical condition. Response shift refers to changing internal standards, values and the conceptualisation of the target construct, such as quality of life (167, 272). For example, research has shown that caregivers of head and neck cancer patients experience fewer symptoms of depression and anxiety six months after diagnosis, compared to 0 or 3 months after diagnosis (273). Although longitudinal data is needed to detect a response shift, parents of children with CL±P or IH may undergo a process of adaptation to the demands of having a child with a visible difference. Similarly, as included in the Wallander, Varni (248) model, it may be that parents in this sample have developed strong coping skills that helped mitigate possible risk factors.

The second research question focused on factors related to levels of distress and parenting stress. We found that subjective visibility was not related to distress or parenting stress. On the other hand, child behaviour problems were significantly and positively related to parenting stress and parental depression. Furthermore, additional problems related to the medical condition were positively related to parenting stress, depression and hostility. Correspondingly, parents of children with CL±P reported more parenting stress than parents of children with an IH, possibly due to more additional condition-related problems. However, the type of cleft (cleft lip or cleft lip and palate) did not influence the amount of distress and parenting stress. Parent age, child age and child gender were not significantly related to distress and parenting stress. When comparing the results to the model by Wallander et al. (248), child behaviour problems and additional condition-related difficulties were risk factors for lower parental adaptation, while the parent-reported degree of visibility of the condition was not related to parental adaptation.

While the present study does support previous research showing that learning- and feeding difficulties (274), behavioural problems and disease complexity (81) are related to parental burden; however, several of our findings are inconsistent with those from previous studies. First, while the subjective visibility is generally seen as a consistent predictor of maladjustment for people with a visible difference (14), parental subjective visibility of the condition in their children was not related to any of the outcome variables in the present study. As this study concerns parents, who are not the direct focus of the onlookers' reactions, different effects might come into play. It may be that the subjective visibility of the condition is primarily limited to maladjustment in the person with the visible difference and not to maladjustment in family members.

Second, neither the children's age, nor their parents' age was significantly related to distress or parenting stress. This is in contrast with Pinquart (81, 255) who reported that parents of older children experience less parenting stress and anxiety than

parents of younger children. However, this may be explained by the fact that Pinquart (81) included all medical conditions for chronically ill children, while the current study only looked at CL±P and IH. In addition, the age of children in the sample skewed younger with a large group of infants with IH.

The result that child behavioural problems were associated with parenting stress and depressive symptoms is significant, as our sample primarily included children with few behavioural problems. The scores on the CBCL ranged from 0 to 111, with 75% scoring 30 or lower (275). This might imply that even with relatively few behavioural problems, parents may experience more stress and depressive symptoms. This finding is consistent with earlier literature indicating that child behavioural problems are related to parenting stress (75, 76). However, as previous literature has indicated a bidirectional relationship between child behaviour problems and parenting stress (76), the interplay between the two remains subject to debate.

This study also has some strengths and limitations. A particular strength of this study is the substantial number of parents ($N = 400$) participating in this study. Besides including 227 mothers, we were also able to include 173 fathers. As most studies often focus on mothers, we believe that this study makes an important contribution to current knowledge about fathers of children with CL±P and IH, which was similar to the results found for mothers. We also contributed to the scarce IH literature by reporting on distress and parenting stress in parents of children with IH. Despite these strengths the current study also has some limitations.

First, we used normative data with a large norm group representative of the population, which reduces bias. However, for the SCL-90 it is not clear how many people in this group are parents. This might hamper the comparison of our group of parents with the normative data. Second, the CBCL 1½-5 (146) and NOSI-K (262) are appropriate for children aged 1,5 and older and 2 and older, respectively. By including children under these ages in the IH group reflecting the key phase of their medical monitoring and treatment, our results should be interpreted with caution. Third, the cross-sectional design of the current study limits the strengths of our conclusions. A longitudinal design could be more informative, so that it is also possible to assess the development of distress and parenting stress over time. Fourth, this study only uses self-report measures. Assessing mental health in structured clinical interviews could contribute to assessing distress and parenting stress in a more detailed way.

We recommend that future research on distress and parenting stress assesses the influence of personal growth or positive adjustment on distress and parenting stress. More insight into these factors may offer a more practical approach for

clinicians in recognising parents experiencing a burden when caring for their child with a visible difference.

In conclusion, parents of children with CL±P or IH in this sample seem well-adjusted to having a child with a visible difference. As some parents were experiencing significant difficulties, careful screening is needed to identify parents in need of support. Further, as child behaviour problems are related to both parenting stress and anxiety, we recommend monitoring parents of children with behavioural problems and if indicated, providing appropriate psychological support.

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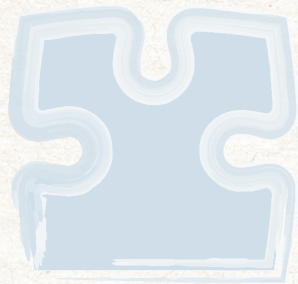
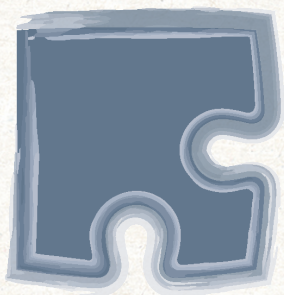
This work was supported by 'Stichting In Face' (no grant number).

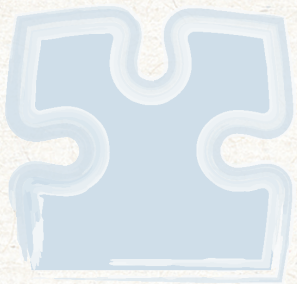
Conflicts of interest

No conflicts of interest to declare.

Data availability statement

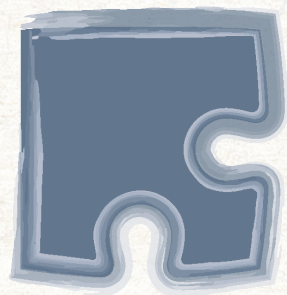
The data that support the findings of this study are available from the corresponding author, JO, upon reasonable request.





CHAPTER 8

General discussion



General discussion

The overall aim of this thesis was to study emotional and behavioural functioning in children and adolescents with a visible difference and their parents. Another aim was to study an innovative online psychological intervention, YP Face IT, aimed at improving psychological well-being of adolescents with a visible difference. To this purpose, this thesis was divided into three parts with three distinct aims: **part I** focused on studying psychosocial problems in children and adolescents with a visible difference; **part II** on improving psychological well-being of adolescents with a visible difference by the online intervention YP Face IT and **part III** on determining psychosocial adjustment of parents with a child with a visible difference. In this general discussion, findings will be elaborated on and discussed. The strengths and limitations, future directions for research and clinical implications resulting from the studies included in this thesis will also be discussed.

Part I. Psychosocial problems in children and adolescents with a visible difference

The aims were to study:

1. Whether children and adolescents with a visible difference experienced more psychosocial problems than unaffected children and adolescents;
2. What factors were related to these problems in children and adolescents with a visible difference.

Chapter 2 focused on symptoms of anxiety and depression in adolescents aged 12 to 18 years with a visible difference. To this end, meta-analyses were conducted. A total of 11 studies were included; nine focused on anxiety and nine focused on depression. All studies included a control group of unaffected peers. Analyses showed that adolescents with a visible difference experienced more anxiety than unaffected peers. They did not differ from unaffected peers on the amount of depressive symptoms they experienced.

This is striking, as anxiety and depression often present as comorbid conditions (104). However, the results are consistent with observations in clinical practice showing that referrals for social anxiety are more common than referrals for depression in children and adolescents (10). It appears that adolescents with a visible difference are at risk for experiencing symptoms of anxiety, but not depression.

A post-hoc power analysis showed that both the meta-analysis for symptoms of anxiety and for depression were underpowered. Furthermore, all included studies focused on general anxiety, rather than social anxiety. More research is needed to determine whether adolescents with a visible difference experience more anxiety

and depression than unaffected peers. Based on clinical observations, these studies should also assess symptoms of social anxiety specifically.

Subgroup analyses were conducted based on type of visible difference (e.g. skin conditions, congenital conditions, conditions due to trauma, conditions due to disease or conditions due to medical treatment). These analyses showed that adolescents with a skin condition did not differ from unaffected peers regarding the anxiety and depressive symptoms they experienced. Due to the limited number of studies included, subgroup analyses could not be conducted for other types of visible differences.

The reason that adolescents with a skin condition do not differ from unaffected peers could be due to the severity of skin conditions. Skin conditions often have a mild presentation and severe skin conditions are rarer. For instance, a severe presentation has been reported in 6.5% of adolescents with eczema (106) and in 15% to 20% of adolescents with acne (107). In one of the studies included in our meta-analysis, severe acne was found in only 2.1 % of adolescents with acne (19). It has been shown that adults with severe skin conditions are more likely to experience anxiety and depression than adults with mild conditions (276, 277). Hence, including studies with a sample consisting primarily of adolescents with a mild skin condition might have contributed to the nonsignificant findings. However, power problems might also have contributed towards the nonsignificant findings.

Chapter 3 presented the results of a cross-sectional study focusing on emotional and behavioural problems in children with a Cleft Lip with or without Palate (CL±P) or Infantile Haemangioma (IH). Parents reported less emotional and behavioural problems for these children when compared to normative data. Mothers of children with a CL±P or IH reported more internalising, externalising and total problems in their children than fathers. Children with more comorbid mental or medical conditions were rated as having more internalising, externalising and total problems than children with less comorbid conditions. Parents that experienced more negative affect often reported more internalising problems for their children. Interestingly, parent-reported visibility of the condition (CL±P or IH) was not related to child behaviour problems.

Results are not in line with previous studies reporting either no differences between children with a visible difference and normative data (37, 87, 127, 134, 278) or more emotional and behavioural problems in children with a visible difference (62, 159). When comparing these studies, it appears that studies that found more emotional and behavioural problems have a slightly older sample. Furthermore, these studies were conducted North-America, whereas the other studies were conducted in Europe. Our study concerned a young sample studied in Europe. This partly

accounts for the discrepant findings, but more research is needed to determine the extent of emotional and behavioural problems in children with a visible difference.

Several explanations for why parents report less emotional and behavioural problems than normative data come to mind. A first explanation is that emotional and behavioural problems in children with CL±P or IH don't become prevalent until adolescence, when body image start to play a more prominent role in well-being (163) and self-esteem (279). As mentioned in the introduction of this thesis, the majority of adolescents in the general population experience body dissatisfaction (43). As body dissatisfaction is a predictor for negative psychosocial outcomes, such as (social) anxiety (39, 40) and depressive symptoms (41, 42), it could play an important role in the aetiology of emotional and behavioural problems in adolescents. Also, romantic concerns are prevalent amongst adolescents a visible difference (6, 7). In short, body dissatisfaction and romantic concerns can explain why adolescents with a visible difference experience more anxiety than unaffected peers (**chapter 2**), while children with a visible difference do not experience emotional and behavioural problems (**chapter 3**).

A second explanation is a reporter bias. Studies in the general population showed that mothers with more internalising problems report more internalising problems in their children (280). As reported in **chapter 7**, parents included in our sample have adapted well and report little internalising problems. This might have resulted in parents underreporting emotional and behavioural problems in their children. On the other hand, a positive correlation exists between parents' mental health and children's mental health (281, 282). Following this line of reasoning, the children in our study have less emotional and behavioural problems than normative data due to their parents having less mental health problems than other parents.

In summary, results from **chapter 2** and **chapter 3** provided no evidence for emotional- and behavioural problems in children with a visible difference, but did show that adolescents with a visible difference experienced more anxiety than unaffected peers. Although these results are derived from two different studies and can therefore not be compared directly, these results could potentially indicate that adolescents with a visible difference do experience psychological problems, while children with a visible difference do not (yet) experience psychological problems to the same extent.

Part II. YP Face IT: an online psychosocial intervention for adolescents with a visible difference

The aims were to determine:

1. The acceptability and feasibility of the Dutch version of YP Face IT, a web-based intervention consisting of Social Skills Training (SST) and Cognitive Behavioural Therapy (CBT), to Dutch adolescents;
2. The effectiveness of YP Face IT in improving psychological outcomes in Dutch and Norwegian adolescents.

In **chapter 4** an acceptability and feasibility study was described. Acceptability and feasibility studies are needed to determine whether an intervention is culturally appropriate and whether aspects of the intervention need to be changed prior to conducting a RCT (187). Fourteen Dutch adolescents aged 12-18 completed the Dutch version of YP Face IT and participated in in-depth interviews. They completed questionnaires both prior to and directly after completing YP Face IT. Thematic analysis showed that the therapeutic content of the intervention was acceptable to Dutch adolescents and study methods were feasible for a future RCT. Not everyone preferred eHealth over face-to-face care, mainly due to the lack of flexibility in standardised eHealth interventions. Providers of eHealth interventions should take into account that, despite the current generation of adolescents being digital natives, a minority prefers face-to-face care. The results provided a first indication that YP Face IT could be effective at reducing appearance-related distress in adolescents with a visible difference.

These positive results are in line with previous research showing that YP Face IT is acceptable to British adolescents (186). Acceptability for adolescents with burns in the USA was lower, as only 19.4% of adolescents used YP Face IT (72). However, in contrast to our study, Riobueno-Naylor, Williamson (72) solely recruited adolescents with burns. Our feasibility study did not include adolescents with an acquired condition. This discrepancy may explain the contrasting findings.

The positive outcomes of our acceptability and feasibility study were the basis for initiating a RCT into the effectiveness of the Dutch version of YP Face IT. Feasibility studies concerning YP Face IT have been conducted in the UK (186), the USA (72) and The Netherlands (**chapter 4**), but the intervention has not been thoroughly tested in a RCT. **Chapter 5** describes this study protocol in detail.

In our RCT adolescents aged 12-18 with a visible difference and experiencing appearance-related distress were randomised to YP Face IT or CAU. Both groups completed questionnaires at baseline, after 13 weeks (or directly after completing YP Face IT) and after 25 weeks (or three months after completing YP Face IT). Mixed

linear models were used to assess whether YP Face IT was effective at reducing appearance-related distress. Primary outcome measures were body esteem and social anxiety.

For our RCT, the recruitment procedure was challenging. Many adolescents declined participation due to time constraints and parents often expressed concerns about raising appearance issues with their children. They feared this might negatively influence their child's mental health. Adolescents sometimes also refused to talk about appearance issues with their parents. As a result, a small sample size was obtained. To overcome power issues, data from our RCT were combined with data from a Norwegian RCT. **Chapter 6** included the results of this first study into the effectiveness of YP Face IT. In this study 87 Norwegian and 102 Dutch adolescents with a visible difference aged 12-18 were randomised to YP Face IT or a control group. Both groups completed questionnaires at baseline and after 13 weeks (or after completing YP Face IT). Results showed that adolescents who completed YP Face IT experienced less symptoms of social anxiety than adolescents in the control group. More specifically, they showed improvements in their fear of negative evaluation. No effects were found for body esteem, perceived stigmatisation or life disengagement. No differences were found between Dutch and Norwegian adolescents, so results hold for different countries.

The reason why no effects were found for body esteem, perceived stigmatisation or life disengagement could be related to the engagement participants have shown with the YP Face IT intervention. Previous research on YP Face IT found that engagement was related to positive changes in body esteem and fear of negative evaluation (186). In our study participants took a median of 9.4 weeks (mean 11) to complete YP Face IT, but the maximum time spent was 41 weeks for Norwegian adolescents and 34 weeks for Dutch adolescents. So, engagement differed amongst participants. Another measure of engagement is how often adolescents use the techniques taught in YP Face IT. Unfortunately, data during the direct follow-up we did not collect on how often participants used the techniques they were taught in YP Face IT. However, our study used several techniques to enhance adherence and engagement that were not used in prior studies concerning YP Face IT (72, 186). For instance, a motivating e-mail was sent after session 4, telling the participant that he/she was halfway and that sessions would become shorter. Also, WhatsApp messages were sent to remind participants that their session was due. These were mentioned as improving engagement in our previous study (**chapter 4**), but the exact impact remains unclear.

Consistent with results from the adult version of YP Face IT, we found no improvements on body esteem. In a study on adults completing Face IT, no improvements were found on body image (71). YP Face IT and Face IT focus on

appearance, but do not include techniques to directly improve body image. It appears that to facilitate an improvement in body image and body esteem, specific techniques to improve body image should be used. Examples of these techniques include changing negative body language and educating people on monitoring and restructuring cognitions (283). If we want to improve body esteem through YP Face IT, these techniques should be incorporated into the intervention.

Another explanation for our nonsignificant findings could be related to the choice of questionnaires. Questionnaires for adolescents with a visible difference are scant and most questionnaires are not designed with people with a visible difference in mind. Hence, these questionnaires may not be sensitive enough to detect differences in the population studied. Condition-specific questionnaires do exist (e.g. 284), but cannot be directly compared and can thus not be used in research across medical conditions.

In sum, results point to YP Face IT being acceptable, feasible and effective for Dutch adolescents. However, concerns remain about adolescents' engagement with the intervention. The current results provide enough evidence for YP Face IT to be implemented in hospitals across The Netherlands.

Part III. Parenting a child with a visible difference

As parents are impacted by the child's visible difference and face challenges, they themselves may be at risk for developing psychological complaints. Therefore, the aims were to establish:

1. Whether parents of children with a visible difference experienced more distress and parenting stress than other parents;
2. What factors were related to distress and parenting stress in parents of children with a visible difference.

In **chapter 7** the results of a study into distress and parenting stress in parents of children with a CL±P or IH were presented. A total of 226 mothers and 174 fathers completed questionnaires. Results showed that parents of a child with CL±P or IH reported less parenting stress when compared to normative data. Furthermore, mothers of children with CL±P or IH and fathers of children with CL±P reported less anxiety than normative data. No differences were found for symptoms of depression or hostility.

Parents reported more parenting stress and when their child had behaviour problems or comorbid medical or mental health problems. In addition, parents reported more hostility when their child had comorbid medical or mental health problems. None of the investigated factors were related to parental anxiety.

The finding that parents experience less distress and parenting stress than other parents is striking, as elevated levels of distress and parenting stress have been reported in meta-analyses of parents with a child with a chronic medical condition (81, 82, 255). The positive adjustment in our sample may be explained by post-traumatic growth or a response shift.

In post-traumatic growth, people experience personal growth following stressful situations. This has previously been reported in children with a medical condition (270) and could also have played a role in our findings. A response-shift means that internal standards and values have changed (167, 272), in this case due to the child's visible difference. It is possible that parents have adapted to the demands of having a child with a visible difference and have developed strong coping skills. However, we cannot firmly say that these effects have occurred in our sample. Longitudinal research is needed to establish whether this is indeed the case.

Another possible explanation for these findings is that a selection bias occurred (285). For parents of a child with CL±P 46.3% of eligible parents participated. For parents with a child with an IH this number was 41.6%. It is possible that parents with more distress and parenting stress were less willing to participate in our study. Parents with higher levels of distress and stress are possibly experiencing a higher burden of childcare and might perceive participating in a study as too strenuous. On the other hand, parents that are coping well might not see any urgency to participate in research focusing on their psychological well-being. So, despite our conclusion that parents seem to have adapted well to having a child with a visible difference, the effect sizes could have been biased.

Strengths and limitations

This thesis has some strengths and limitations. A first strength is that this thesis included an RCT studying the effect of the innovative eHealth intervention YP Face IT. This is the first RCT into YP Face IT and the first RCT to study a psychosocial intervention for adolescents with a visible difference in The Netherlands. By setting up an international collaboration with Norway, we have improved the power and overall strength of the conclusions of our RCT. Furthermore, for our feasibility study (**chapter 4**) and our RCT (**chapter 5**) recruitment has taken place across The Netherlands. This improves the generalisability of study findings to the entire population of adolescents with a visible difference in The Netherlands. Our studies and results advance psychosocial care for adolescents with a visible difference in The Netherlands and possibly in other countries too.

Another strength is that YP Face IT was assessed both qualitatively (**chapter 4**) and quantitatively (**chapter 5**). By doing so, we were able to not only assess the efficacy of YP Face IT, but also how YP Face IT was experienced by the end users. Studying

the acceptability and feasibility also gives indications of treatment adherence and whether changes to the intervention need to be made (187).

A final strength is that, in addition to child outcomes, distress and parental stress were also studied. It is important to recognise that having a visible difference impacts not only the person with the visible difference, but also their family (e.g., 77, 78). Furthermore, parental well-being can influence their children's well-being (75, 76, 281). Therefore, by studying the person with the visible difference and family members, we gain more insight into the full picture.

Despite these strengths, a number of limitations should also be considered. First, some of the work in this thesis was cross-sectional. Although these studies provide a useful insight into well-being of children with CL±P and IH (**chapter 3**) and their parents (**chapter 7**), longitudinal research is needed to determine well-being and fluctuation of well-being in these groups. For instance, as medical procedures may be especially stressful both to children (286, 287) and parents (288, 289), it might add valuable information to study well-being in periods with and without medical procedures. Furthermore, as this thesis found satisfactory well-being in children, but not in adolescents, studying a group of children into adolescence (and possibly longer) will provide useful information that can be used to assess in which phase of life people with a visible difference benefit most from psychosocial care.

Another limitation is that study groups in this thesis were too small to analyse different types of visible difference (e.g., congenital, skin conditions, traumatic injuries, due to disease or due to medical trauma) separately, with the exception of CL±P and IH. Hence, this thesis cannot provide insight into whether psychological well-being is equal across these types of conditions and whether YP Face IT is equally effective across these conditions.

Directions for future research

Despite the findings in our study, more research is needed to assess well-being and factors that influence well-being in people with a visible difference and their parents. For instance, due to the lack of relevant literature, the meta-analysis described in **chapter 2** included a mere total of 11 studies and was underpowered. Studies should focus on the aetiology and maintaining factors of anxiety in adolescents.

Studies on parents should focus on what factors influence distress and parenting stress. We found indications that parenting stress and distress was influenced by child behaviour problems, but we did not assess what behaviour problems were especially troublesome for parents. Furthermore, as a bidirectional relationship has been described between parenting stress and child behaviour problems (76), longitudinal studies should assess the interaction between parenting stress and

child behaviour problems. Efforts should be made to include parents with a broad range of distress, resilience and psychopathology.

Despite results in this thesis showing that parents of children with a visible difference experiences less parenting stress than other parents, some parents may be in need of psychological care. Recently, this need has been identified in qualitative work (290). Earlier research has provided indications that, for chronically ill children, parents with more parenting stress struggle to manage their child's disease effectively (291). Furthermore, parents with greater parenting stress have children with more internalising and externalising problems (81, 291). Future research should be conducted to determine how these parents can best be supported, especially as interventions aimed at parents can prevent psychological problems in their children. Efforts have been made to develop and test interventions for parents of a child with a chronic illness (e.g. 292), however none of the existing interventions address the challenges that arise for parents of children with a visible difference. Also, there is no information available on when these interventions should be provided to parents. However, it makes sense to study two time periods specifically. The first is around the period the child is born. Parents may be experience different emotional reactions to having a child with a visible difference, such as disbelief or fear (293, 294) and have to learn to cope with negative observer responses (77, 78). The second period is when appearance-related concerns start to develop in the child. During this period parents can be supported in ways to speak to their child and support the child with their concerns. However, it is not yet clear at what age appearance-related concerns develop (295).

Furthermore, as having a visible difference can impact the entire family (74), future studies should be undertaken to examine whether siblings of children and adolescents with a visible difference are in need of psychosocial care. Previous literature on siblings of children with a chronic illness found that these siblings are prone to experiencing issues in academic functioning (296) and experience internalising problems (297). Hence, future studies should focus on identifying whether siblings of children with a visible difference need psychosocial care. Studies should also examine how this care should be delivered.

Research on YP Face IT should focus on what parts of YP Face IT are effective. As YP Face IT consists of social skills training and cognitive behavioural therapy, it is insightful to know which of these parts or which combination of techniques ensures the effectiveness of the program. Currently, there is no knowledge about what parts of the program facilitate emotional and behavioural change and are the most effective.

Furthermore, YP Face IT is currently designed as a self-help program for adolescents with subclinical complaints. However, it also lends itself for use as a blended tool in which regular meetings with a psychologist take place. In adults, guided internet-delivered CBT (iCBT) is more effective than self-help iCBT for symptoms of anxiety and depression (298). Future research should determine whether this a guided delivery influences the effectiveness of YP Face IT. One should consider whether the benefits outweigh the costs of adding therapist support in adolescents with subclinical complaints. Another consideration is how the intervention should be guided. This can range from chat sessions with a therapist to face-to-face meetings. Future research should determine the most effective format for delivery, tailored to the needs of adolescents. Similarly, research should examine what formats of delivery are most practical for health professionals.

A last recommendation for future research on interventions for adolescents with a visible difference is to examine the effectiveness of Acceptance and Commitment Therapy (ACT). ACT has been argued to be an effective therapy for people with a visible difference (69) and user experiences of face-to-face ACT have been positive (299). However, there is no literature examining the effectiveness of ACT for people with a visible difference.

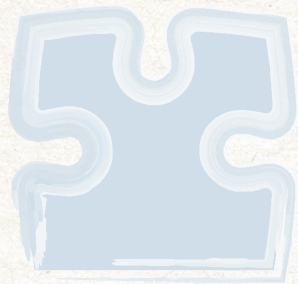
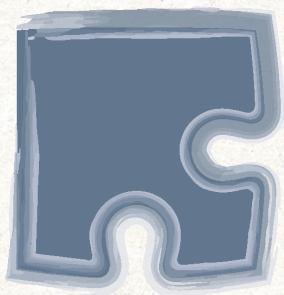
Clinical implications and recommendations

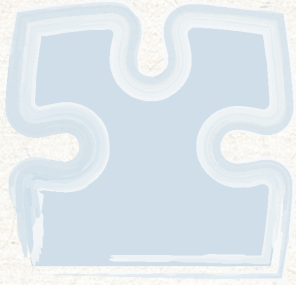
This thesis has provided results that point to several clinical implications and recommendations. These can be divided into recommendations towards screening for psychological problems and recommendations towards treating psychological problems.

Screening for psychological problems. Regular screening, also called Routine Outcome Monitoring (ROM), for psychological problems can help identify children and adolescents in need of additional psychological care (300). A lack of follow-up has previously been identified as a reason why children and adolescents with a visible difference do not always get the psychosocial care they need (301). Furthermore, research has shown that raising appearance-related issues with patients and parents is often perceived as difficult by medical professionals (301). ROM could help these professionals in raising appearance-related issues as they can use the responses on the questionnaires as a conversation starter to assess whether a patient is in need of additional psychosocial support. Based on the current literature it is unclear whether the ROM should include general or condition-specific questionnaires. General questionnaires are preferred when one wants to make comparisons across different medical conditions. Condition-specific questionnaires are preferred when the ROM is only used to screen patients in possible need of psychosocial support.

Following the results of this thesis, ROM may be more important in adolescents than in children as the former group experiences more issues with psychological well-being. However, ROM should be implemented in both age groups to identify everyone in need of care. For children under 8 the ROM can be completed by parents. Furthermore, ROM should also be implemented to focus on parents and special attention should be paid to parents when the child is showing behavioural problems.

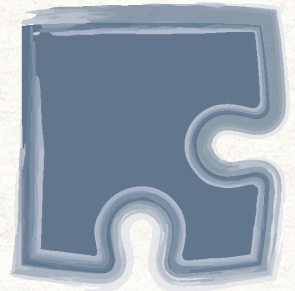
Treatment of psychological problems. Our RCT on YP Face IT showed that YP Face IT can be used to reduce social anxiety problems in adolescents with a visible difference. Based on these results, we recommend implementing YP Face IT into regular psychological care for adolescents with a visible difference experiencing subclinical symptoms of appearance-related distress. For adolescents with a social anxiety disorder face-to-face care might be indicated. However, YP Face IT can provide useful techniques and augment face-to-face care as a blended tool.





CHAPTER 9

Summary & Samenvatting



Summary

The main aim of this thesis was to examine and improve the psychological well-being of children and adolescents with a visible difference and their parents. The general introduction in **chapter 1** describes the background of the studies in this thesis. Approximately 1 in 44 people have a visible difference on their face or body and 1 in 111 people have a visible difference solely on the face. Causes of visible differences can be divided into congenital conditions (i.e., cleft lip or craniosynostosis), skin conditions (i.e., psoriasis or acne), visible differences due to trauma (i.e., burns or scars), disease (i.e. cancer or meningitis) or medical treatment (i.e., surgery or radiotherapy).

Due to negative observer responses, including stigmatisation, teasing and bullying, children and adolescents with a visible difference may be at risk for adverse psychosocial outcomes. These include low body image and body dissatisfaction, (social) anxiety, depression and externalising problems.

However, there is a paucity of interventions and none have undergone thorough testing yet. To reduce appearance-related distress in adolescents with a visible difference, YP Face IT (Dutch: *Face IT voor jongeren*) was developed by Dr. Heidi Williamson at the Centre for Appearance Research (University of the West of England). YP Face IT is a web-based intervention combining Social Skills Training (SST) and Cognitive Behavioural Therapy (SST). It has eight sessions which are completed independently by the adolescent. Sessions consist of text, videos and exercises to get acquainted with the taught techniques.

Lastly, research on parents is described. After all, children and adolescents grow up in a family context and parents and their children have a mutual influence on each other. These parents face challenges such as negative observer responses and having to manage their child's medical condition. Qualitative research shows that these parents may be distressed, but quantitative research has not been conclusive.

In **chapter 2** the results of a meta-analysis on anxiety and depression in adolescents with a visible difference are presented. Adolescents with a visible difference may be at risk for anxiety and depression due to negative observer responses, stigmatisation and a low body image. The aim therefore was to examine whether adolescents with a visible difference experienced more symptoms of anxiety and depression than unaffected peers. A total of 11 studies were included in the meta-analyses. Compared to unaffected peers, adolescents with a visible difference experience more symptoms of anxiety, but not depression. Adolescents with a skin condition did not differ from unaffected peers on the amount of anxiety or depressive symptoms they experienced. Subgroup analyses could not be done for

other types of visible differences compared to unaffected peers, as not enough studies were found to study this. Based on these results we recommend that adolescents with a visible difference should be screened for symptoms of anxiety.

Chapter 3 describes the results on a cross-sectional study of emotional and behavioural problems in children with a Cleft Lip with or without Palate (CL±P) or Infantile Haemangioma (IH). A first aim was to assess whether parents of these children reported more emotional and behavioural problems than parents of children in the norm group. A second aim was to study what factors were related to emotional and behavioural problems in these children. A total of 400 parents completed questionnaires on their children's emotional and behavioural problems, the visibility of the condition, additional condition-related difficulties and their own affect. Children were 1.5 to 12 years old. Results showed that parents reported fewer emotional and behavioural problems for their children than parents in the norm group. Looking at what factors predicted emotional and behavioural problems, we found that children with learning difficulties had more emotional and behavioural problems as reported by their parents. Mothers reported more emotional and behavioural problems than fathers. Lastly, we found that parents experiencing more negative affect themselves reported more internalising problems in their children.

These results are surprising, as previous studies found either no difference in emotional and behavioural problems between children with a visible difference and unaffected peers or more emotional and behavioural problems in children with a visible difference. Several explanations arise. A first explanation is that children with a visible difference may grow up in a protective environment and parents may have a protective parenting style. A second explanation is that emotional and behavioural problems in children with a visible difference become more prevalent during adolescence when appearance and body image start to play a central role in the child's self-esteem. A third explanation is that parents may experience a response shift, shifting their norms and values to different standards, and thus evaluate their child's emotional and behavioural problems in a milder way.

Chapter 4 describes the results of a mixed-method study on YP Face IT. The aims of this chapter were to assess opinions of adolescents with a visible difference on: 1) the acceptability of the therapeutic content of the intervention, 2) the structure and presentation of the intervention, 3) the usefulness of the intervention and 4) the acceptability of study procedures. Fourteen adolescents, aged 12-18 years old, completed YP Face IT and participated in an in-depth interview. They completed questionnaires at baseline and after completing YP Face IT.

Adolescents appreciated YP Face IT and would recommend it to adolescents with a visible difference distressed by their appearance. All adolescents reported personal

growth and having learned (inter)personal skills from YP Face IT. Motivation to complete one session each week was a problem for some adolescents, but the reminders by the website and the research team were perceived as helpful in overcoming motivation problems. Overall, results indicate that Dutch adolescents accept the therapeutic content of the intervention, rate the structure and presentation positively and view YP Face IT as a useful intervention. Research procedures were also rated positively.

In **chapter 5** the study protocol of a Randomised Controlled Trial (RCT) on YP Face IT is outlined. The aim of this RCT was to establish whether YP Face IT reduces social anxiety and improves body esteem. Adolescents aged 12-18 years old with a visible difference completed questionnaires on social anxiety, body esteem, aspects of self-worth, perceived stigmatisation, health-related quality of life, life disengagement, appearance-related distress and depressive symptoms. Those experiencing appearance-related distress, as indicated by higher scores on social anxiety, body esteem or depressive symptoms, were randomised to YP Face IT or Care As Usual (CAU). Questionnaires were completed again directly after YP Face IT (or after 13 weeks) and three months after completing YP Face IT (or after 25 weeks).

Chapter 6 describes the results of an international RCT, in which data from our RCT were combined with those from a similar Norwegian RCT into YP Face IT. The aims were to study the effectiveness of YP Face IT and to study what factors predicted an improvement in psychological problems. A total of 189 adolescents (102 Dutch, 87 Norwegian) aged 12-18 were randomised to YP Face IT or CAU. Questionnaires were completed at baseline and directly after completing all eight sessions of YP Face IT.

Adolescents that completed YP Face IT showed less symptoms of social anxiety at follow-up when compared to adolescents that did not complete YP Face IT. More specifically, the former group had less fear of negative evaluation. No differences were found for body esteem, perceived stigmatisation or life disengagement between adolescents that completed YP Face IT and adolescents that did not complete the intervention.

Chapter 7 presents the results of a cross-sectional study on distress and parenting stress in parents of children with a Cleft Lip with or without Palate (CL±P) or Infantile Haemangioma (IH). The aims were to assess whether these parents experienced more distress (i.e., anxiety, depression and hostility) and parenting stress than parents from the norm group and to assess what factors influenced their distress and parenting stress. A total of 400 parents completed questionnaires. Analyses showed that these parents reported experiencing less parenting stress compared to normative data. Mothers of children with CL±P experienced less anxiety than

normative data. Distress and parenting stress were significantly influenced by child behaviour problems.

Finally, **chapter 8** provided a general discussion, in which the main findings were presented alongside with conclusions and recommendations for future research and clinical practice. Results showed less emotional and behavioural problems in children with a visible difference compared to normative data, but did point towards anxiety problems in adolescents. It may be the case that children do not (yet) experience appearance-related distress. Evidence also suggested that YP Face IT is effective and can be used to alleviate appearance-related distress in adolescents with a visible difference, as it lowers social anxiety. We also found that parents of children with a visible difference seem to have adjusted well, as they reported less parenting stress compared to normative data. However, there is still a small group of parents that is in need of psychosocial support.

Strengths of this thesis are that it included the first Randomised Controlled Trial (RCT) on an intervention aimed at adolescents with a visible difference, that this intervention was studied both quantitatively and qualitatively and that research on parents was also included. Limitations included cross-sectional studies preventing causal conclusions and a small sample size preventing subgroup analyses into differential outcomes as to the type of visible difference (i.e., congenital, skin conditions, traumatic injuries, due to disease or due to medical trauma). It remains unclear how people with different types of visible differences compare to each other in terms of psychological well-being.

The discussion included several directions for future research. Research on YP Face IT should examine what techniques are most useful and whether YP Face IT should be offered as a blended therapy. Acceptance and Commitment Therapy (ACT) should also be examined as a possible therapy for adolescents with a visible difference. Studies on parents should focus on factors predicting distress and parenting stress. Future research should also determine what psychosocial support is most suitable for parents and if siblings are in need of psychosocial support.

Clinical implications can be divided into implications for screening for psychosocial problems and implications for treating psychosocial problems. Routine Outcome Monitoring (ROM) should be implemented for screening for psychosocial problems in children, adolescents and parents. Results can be used by healthcare professionals to initiate conversations on psychosocial problems and appearance-related issues. YP Face IT should be used to treat psychosocial problems in adolescents with a visible difference, possibly as a blended tool.

Samenvatting

Het hoofddoel van dit proefschrift was om het psychologische welbevinden van kinderen en adolescenten met een zichtbare aandoening en hun ouders te bestuderen en verbeteren. De algemene introductie in **hoofdstuk 1** omschrijft de achtergrond van de studies in dit proefschrift. Ongeveer 1 op de 44 mensen heeft een zichtbare aandoening ergens op het lichaam of in het gezicht en 1 op de 111 mensen heeft een zichtbare aandoening alleen in het gezicht. De oorzaken van een zichtbare aandoening kunnen onderverdeeld worden in aangeboren aandoeningen (bijv. schisis of craniosynostose), huidaandoeningen (bijv. psoriasis of acne), zichtbare aandoeningen door trauma (bijv. brandwonden of littekens), door ziekte (bijv. kanker of meningitis) of door medische behandeling (bijv. chirurgie of radiotherapie).

Door negatieve reacties van anderen, zoals stigmatisering, plagen en pesten, kunnen kinderen en adolescenten een verhoogd risico hebben op ongunstige psychosociale uitkomsten. Dit omvat onder anderen een negatief lichaamsbeeld, ontevredenheid over het lichaam, (sociale) angst, depressie en externaliserende problematiek.

Er zijn echter weinig interventies beschikbaar, die bovendien ook niet grondig getest zijn. Om uiterlijkgerelateerde stress in jongeren met een zichtbare aandoening te verminderen is Face IT voor jongeren (Engels: *YP Face IT*) ontwikkeld door Dr. Heidi Williamson, werkzaam bij het *Centre for Appearance Research (University of the West of England)*. Face IT voor jongeren is een online interventie die sociale vaardigheidstraining en Cognitieve Gedragstherapie (CGT) combineert. De interventie bestaat uit acht sessies die de jongere zelf doorloopt. De sessies bestaan uit tekst, video's en oefeningen om de geleerde technieken onder de knie te krijgen.

Tenslotte richtte dit proefschrift zich ook op ouders. Immers, kinderen en adolescenten groeien op in de context van een gezin opgroeien waarin ouders en kinderen elkaar wederzijds beïnvloeden. De ouders kunnen te maken krijgen met uitdagingen, zoals negatieve reacties van anderen op het uiterlijk van hun kind en het moeten omgaan met de medische aandoening van hun kind. Kwalitatief onderzoek laat zien dat deze ouders stress kunnen ervaren, maar kwantitatief onderzoek laat geen eenduidig resultaat zien.

In **hoofdstuk 2** worden de resultaten van een meta-analyse naar angst en depressie bij jongeren met een zichtbare aandoening gepresenteerd. Adolescenten met een zichtbare aandoening kunnen risico lopen op het ervaren van angst en depressie door negatieve reacties van anderen, stigmatisering en een laag lichaamsbeeld. Het doel was dan ook om te bestuderen of jongeren met een zichtbare aandoening meer symptomen van angst en depressie vertonen dan leeftijdsgenoten zonder een

zichtbare aandoening. In totaal zijn 11 studies meegenomen in de meta-analyses. Vergeleken met leeftijdsgenoten ervaren jongeren met een zichtbare aandoening meer symptomen van angst, maar niet meer depressieve symptomen. Adolescenten met een huidaandoening verschillen ten opzichte van leeftijdsgenoten niet in de hoeveelheid angst of depressie die zij ervaren. Er konden geen subgroepanalyses worden gedaan voor andere typen zichtbare aandoeningen ten opzichte van leeftijdsgenoten, omdat er niet genoeg studies waren gevonden om dit te onderzoeken. Gebaseerd op deze resultaten raden we aan dat jongeren met een zichtbare aandoening gescreend moeten worden op angstklachten.

Hoofdstuk 3 omschrijft de resultaten van een cross-sectioneel onderzoek naar emotionele- en gedragsproblemen bij kinderen met een schisis (lipspleet of lip- en gehemeltepleet) of infantiel hemangioom (IH). Het eerste doel van dit onderzoek was om na te gaan of ouders van deze kinderen meer emotionele- en gedragsproblemen rapporteerden dan ouders van kinderen in de normgroep. Een tweede doel was om te bestuderen welke factoren gerelateerd waren aan emotionele- en gedragsproblemen bij deze kinderen. In totaal hebben 400 ouders vragenlijsten ingevuld over emotionele- en gedragsproblemen bij hun kinderen, over de zichtbaarheid van de aandoening, over andere problemen gerelateerd aan de aandoening en over hun eigen affect. De kinderen waren 1,5 tot 12 jaar oud. De resultaten lieten zien dat ouders in dit onderzoek minder emotionele- en gedragsproblemen rapporteerden bij hun kinderen dan ouders van kinderen in de normgroep. Als we bekijken welke factoren emotionele- en gedragsproblemen voorspelden volgens de ouderrapportage, vonden we dat kinderen met leerproblemen meer emotionele- en gedragsproblemen hadden. Moeders rapporteerden meer emotionele- en gedragsproblemen dan vaders. Als laatste vonden we dat ouders die zelf meer negatief affect ervoeren meer internaliserende problemen rapporteerden in hun kinderen.

Deze resultaten zijn verrassend, omdat eerdere studies geen verschil in emotionele- en gedragsproblemen vonden tussen kinderen met een zichtbare aandoening en leeftijdsgenoten of juist meer emotionele- en gedragsproblemen vonden bij kinderen met een zichtbare aandoening. Er zijn verschillende verklaringen mogelijk voor deze bevinding. Een eerste verklaring is dat kinderen met een zichtbare aandoening mogelijk opgroeien in een beschermende omgeving en ouders mogelijk een beschermende opvoedstijl hanteren. Een tweede verklaring is dat emotionele- en gedragsproblemen bij kinderen pas ontstaan in de adolescentie als het uiterlijk en het lichaamsbeeld een centrale rol gaan spelen in het zelfvertrouwen. Een derde verklaring is dat ouders een *response shift* ervaren, waarbij hun normen en waarden verschuiven, en de emotionele- en gedragsproblemen van hun kind milder beoordelen.

Hoofdstuk 4 omschrijft de resultaten van een *mixed-method* onderzoek naar Face IT voor jongeren. De doelen van dit hoofdstuk waren om meningen van jongeren met een zichtbare aandoening te verkrijgen over: 1) de acceptatie van de therapeutische inhoud van de interventie, 2) de structuur en presentatie van de interventie, 3) de bruikbaarheid van de interventie en 4) de acceptatie van de onderzoeksprocedures. Veertien jongeren in de leeftijd van 12 tot 18 jaar volgden Face IT voor jongeren en namen deel aan een verdiepend interview. Ze vulden voor en na Face IT voor jongeren verschillende vragenlijsten in.

Jongeren waardeerden Face IT voor jongeren en zouden de interventie aanraden aan andere jongeren met een zichtbare aandoening die problemen met hun uiterlijk ervaren. Alle jongeren rapporteerden persoonlijke groei en hadden interpersoonlijke vaardigheden geleerd door Face IT voor jongeren. Motivatie om elke week een sessie te doen was voor sommige jongeren een probleem, maar de herinneringen die de website en het onderzoeksteam stuurden werden gezien als nuttig en fijn om met motivatieproblemen om te gaan. Over het geheel genomen laten resultaten zien dat Nederlandse jongeren de therapeutische inhoud van de interventie accepteren, de structuur en presentatie positief beoordelen en Face IT voor jongeren als een bruikbare interventie zien. Ook de onderzoeksprocedures positief beoordeeld.

In **hoofdstuk 5** wordt het onderzoeksprotocol van een gerandomiseerd gecontroleerd onderzoek (RCT) naar Face IT voor jongeren omschreven. Het doel van deze RCT was om te bepalen of Face IT voor jongeren sociale angst vermindert en lichaamsbeleving verbetert. Jongeren van 12 tot 18 jaar met een zichtbare aandoening vulden vragenlijsten in over sociale angst, lichaamsbeleving, competentiebeleving, stigmatisering, gezondheidsgerelateerde kwaliteit van leven, teruggetrokken leefstijl en depressieve klachten. Jongeren die uiterlijkgerelateerde stress ervaren, aangegeven door een verhoogde score op sociale angst, lichaamsbeleving of depressieve klachten, werden gerandomiseerd naar Face IT voor jongeren of een controlegroep (alleen medische zorg). De vragenlijsten werden nogmaals ingevuld direct na het afronden van Face IT voor jongeren (of na 13 weken) en drie maanden na het afronden van Face IT voor jongeren (of na 25 weken).

Hoofdstuk 6 omschrijft de resultaten van een internationale RCT waarin data van onze RCT gecombineerd zijn met data van een soortgelijke Noorse RCT naar Face IT voor jongeren. De doelen waren om de effectiviteit van Face IT voor jongeren te onderzoeken en te bestuderen welke factoren een verbetering van psychologische problemen voorspellen. Uiteindelijk zijn 189 jongeren (102 Nederlands, 87 Noors) van 12 tot 18 jaar oud gerandomiseerd naar Face IT voor jongeren of een controlegroep. De vragenlijsten zijn aan het begin van de studie en direct na het volgen van de acht sessies van Face IT voor jongeren ingevuld.

Jongeren die Face IT voor jongeren hadden gevolgd, hadden op de nameting minder symptomen van sociale angst dan jongeren die Face IT voor jongeren niet hadden gevolgd. Specifieker gezegd had de eerste groep jongeren minder angst voor negatieve beoordeling. Er werden geen verschillen gevonden voor lichaamsbeleving, stigmatisering of teruggetrokken leefstijl tussen jongeren die Face IT voor jongeren hadden gevolgd en jongeren die de interventie niet hadden gevolgd.

Hoofdstuk 7 presenteert de resultaten van een cross-sectioneel onderzoek naar ouderlijke stress, angst, depressie en vijandigheid bij ouders van kinderen met een schisis (lipspleet of lip- en gehemeltlespleet) of een infantiel hemangioom (IH). De doelen waren om te onderzoeken of deze ouders meer ouderlijke stress, angst, depressie en vijandigheid ervaarden dan ouders uit de normgroep en om te bekijken welke factoren dit beïnvloedden. In totaal hebben 400 ouders vragenlijsten ingevuld. De analyses lieten zien dat deze ouders minder ouderlijke stress ervaarden in vergelijking met normatieve data. Moeders van kinderen met een schisis ervaarden minder angst dan normatieve data. Ouderlijke stress, angst, depressie en vijandigheid werden significant beïnvloed door gedragsproblemen van het kind.

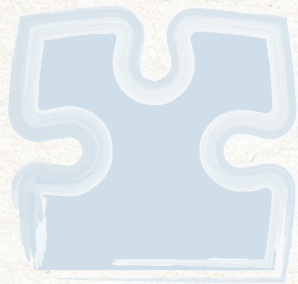
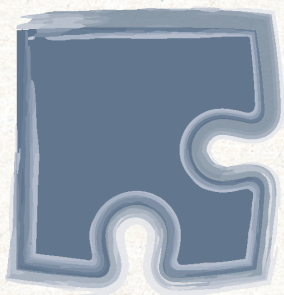
Tenslotte omvat **hoofdstuk 8** een algemene discussie, met hierin een bespreking van de hoofdbevindingen samen met conclusies en aanbevelingen voor toekomstig onderzoek en de praktijk. De resultaten van het huidige onderzoek toonden minder emotionele- en gedragsproblemen in kinderen met een zichtbare aandoening in vergelijking met een normgroep. Daarentegen waren er wel aanwijzingen voor angstproblemen bij jongeren. Het kan zo zijn dat kinderen (nog) geen uiterlijkgerelateerde stress ervaren. Er was ook bewijs dat Face IT voor jongeren effectief is en gebruikt kan worden om uiterlijkgerelateerde stress bij jongeren met een zichtbare aandoening te verminderen, aangezien Face IT voor jongeren sociale angst vermindert. We vonden ook dat ouders van kinderen met een zichtbare aandoening zich goed aangepast hebben, gezien zij minder ouderlijke stress rapporteerden dan een normgroep. Er is echter nog een kleine groep ouders die behoefte heeft aan psychosociale ondersteuning.

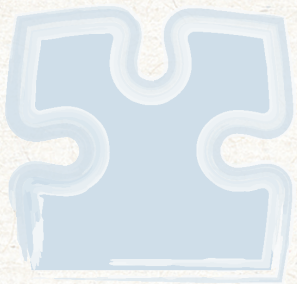
De sterke punten van dit proefschrift zijn dat het de eerste RCT bevat naar een interventie voor jongeren met een zichtbare aandoening, dat deze interventie zowel kwalitatief als kwantitatief onderzocht is en dat het proefschrift ook onderzoek naar ouders bevat. De beperkingen zijn dat er in de cross-sectionele onderzoeken geen causale conclusies getrokken kunnen worden en dat er door een beperkte steekproefgrootte geen uitspraken gedaan konden worden over psychosociale problemen bij verschillende typen zichtbare aandoeningen (i.e., aangeboren aandoeningen, huidaandoeningen, zichtbare aandoeningen door trauma, door ziekte of door medische behandeling). Het blijft nog onduidelijk in hoeverre mensen

met verschillende typen zichtbare aandoeningen zich tot elkaar verhouden als het gaat om psychologisch welbevinden.

De discussie bevat verschillende aanbevelingen voor toekomstig onderzoek. Onderzoek naar Face IT voor jongeren moet bekijken welke technieken het nuttigst zijn en of Face IT voor jongeren als een *blended* therapie gebruikt kan worden. *Acceptance and Commitment Therapy* (ACT) zou ook bekeken kunnen worden als mogelijke therapie voor jongeren met een zichtbare aandoening. Onderzoek moet zich richten op factoren die stress bij ouders voorspellen. Toekomstig onderzoek moet ook bepalen welke psychosociale steun het meest geschikt is voor ouders en of broers en zussen behoefte hebben aan psychosociale ondersteuning.

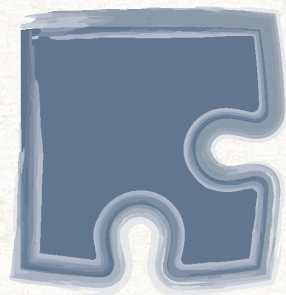
De klinische aanbevelingen kunnen verdeeld worden in implicaties voor het screenen op psychosociale problemen en implicaties voor het behandelen van psychosociale problemen. *Routine Outcome Monitoring* (ROM) moet geïmplementeerd worden om op psychosociale problemen te screenen bij kinderen, adolescenten en hun ouders. De resultaten hiervan kunnen door professionals in de gezondheidszorg gebruikt worden om het gesprek over psychosociale problemen en uiterlijkgerelateerde problematiek aan te gaan. Face IT voor jongeren moet gebruikt worden om psychosociale problemen bij jongeren met een zichtbare aandoening te behandelen, mogelijk als *blended* therapy.





APPENDICES

References
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References

1. Changing Faces. Prevalence of disfigurement 2010 [Available from: <http://admin.changingfaces.org.uk/downloads/FE%20Campaign,%20Epidemiology%202%20pages.pdf>].
2. Changing Faces. Disfigurement in the UK 2017 [Available from: <http://admin.changingfaces.org.uk/downloads/FE%20Campaign,%20Epidemiology%202%20pages.pdf>].
3. Sharratt ND, Jenkinson E, Moss T, Clarke A, Rumsey N. Experiences of living with visible difference: Individual and social reflections. *Health Psychology Update*. 2019;28(2).
4. Jewett LR, Gumuchian ST, Pepin M, Rice DB, Kolorz F, Harrison P, et al. Factors associated with negative observer responses towards individuals with visible differences: A scoping review. *Body Image*. 2018;25:103-32.
5. Rumsey N, Clarke A, White P, Wyn-Williams M, Garlick W. Altered body image: appearance-related concerns of people with visible disfigurement. *Journal of advanced nursing*. 2004;48(5):443-53.
6. Sharratt ND, Jenkinson E, Moss T, Clarke A, Rumsey N. Understandings and experiences of visible difference and romantic relationships: A qualitative exploration. *Body Image*. 2018;27:32-42.
7. Feragen KB, Stock NM, Sharratt ND, Kvaalem IL. Self-perceptions of romantic appeal in adolescents with a cleft lip and/or palate. *Body Image*. 2016;18:143-52.
8. Griffiths C, Williamson H, Rumsey N. The romantic experiences of adolescents with a visible difference: exploring concerns, protective factors and support needs. *Journal of Health Psychology*. 2012;17(7):1053-64.
9. Rumsey N, Harcourt D. Body image and disfigurement: issues and interventions. *Body image*. 2004;1(1):83-97.
10. Harcourt D, Hamlet C, Feragen KB, Garcia-Lopez LJ, Masnari O, Mendes J, et al. The provision of specialist psychosocial support for people with visible differences: A European survey. *Body Image*. 2018;25:35-9.
11. Egan K, Harcourt D, Rumsey N, Appearance Research C. A qualitative study of the experiences of people who identify themselves as having adjusted positively to a visible difference. *Journal of Health Psychology*. 2011;16(5):739-49.
12. Rankin M, Borah GL. Perceived functional impact of abnormal facial appearance. *Plastic and reconstructive surgery*. 2003;111(7):2140-6.
13. Masnari O, Schiestl C, Weibel L, Wuttke F, Landolt MA. How children with facial differences are perceived by non-affected children and adolescents: Perceiver effects on stereotypical attitudes. *Body Image*. 2013;10(4):515-23.
14. Moss TP. The relationships between objective and subjective ratings of disfigurement severity, and psychological adjustment. *Body Image*. 2005;2(2):151-9.
15. Gupta MA, Gupta AK. Psychiatric and psychological co-morbidity in patients with dermatologic disorders: epidemiology and management. *American Journal of Clinical Dermatology*. 2003;4(12):833-42.

16. Ong J, Clarke A, White P, Johnson M, Withey S, Butler PE. Does severity predict distress? The relationship between subjective and objective measures of appearance and psychological adjustment, during treatment for facial lipoatrophy. *Body Image*. 2007;4(3):239-48.
17. van den Elzen ME, Versnel SL, Hovius SE, Passchier J, Duivenvoorden HJ, Mathijssen IM. Adults with congenital or acquired facial disfigurement: impact of appearance on social functioning. *Journal of Craniomaxillofacial Surgery*. 2012;40(8):777-82.
18. Fu L, Bundy C, Sadiq SA. Psychological distress in people with disfigurement from facial palsy. *Eye (Lond)*. 2011;25(10):1322-6.
19. Aktan S, Özmen E, Şanlı B. Anxiety, depression, and nature of acne vulgaris in adolescents. *International journal of Dermatology*. 2000;39(5):354-7.
20. Dennis H, Rostill H, Reed J, Gill S. Factors promoting psychological adjustment to childhood atopic eczema. *J Child Health Care*. 2006;10(2):126-39.
21. Eyüboğlu M, Kalay I, Eyüboğlu D. Evaluation of Adolescents Diagnosed with Acne Vulgaris for Quality of Life and Psychosocial Challenges. *Indian J Dermatol*. 2018;63(2):131-5.
22. Feragen KB, Stock NM. A longitudinal study of 340 young people with or without a visible difference: The impact of teasing on self-perceptions of appearance and depressive symptoms. *Body Image*. 2016;16:133-42.
23. Luquetti DV, Brajcich MR, Stock NM, Heike CL, Johns AL. Healthcare and psychosocial experiences of individuals with craniofacial microsomia: Patient and caregivers perspectives. *Int J Pediatr Otorhinolaryngol*. 2018;107:164-75.
24. Rimmer RB, Foster KN, Bay CR, Floros J, Rutter C, Bosch J, et al. The reported effects of bullying on burn-surviving children. *Journal of Burn Care & Research*. 2007;28(3):484-9.
25. Hunt O, Burden D, Hepper P, Stevenson M, Johnston C. Self-reports of psychosocial functioning among children and young adults with cleft lip and palate. *Cleft Palate Craniofac J*. 2006;43(5):598-605.
26. Carroll P, Shute R. School peer victimization of young people with craniofacial conditions: A comparative study. *Psychology, health & medicine*. 2005;10(3):291-305.
27. Feragen KB, Stock NM. Risk and Protective Factors at Age 10: Psychological Adjustment in Children With a Cleft Lip and/or Palate. *Cleft Palate Craniofac J*. 2016;53(2):161-79.
28. Zimmer-Gembeck MJ, Webb HJ. Body image and peer relationships: Unique associations of adolescents' social status and competence with peer- and self-reported appearance victimization. *J Adolesc*. 2017;61:131-40.
29. Magins P, Adams J, Heading G, Pond W, Smith W. Experiences of appearance-related teasing and bullying in skin diseases and their psychological sequelae: results of a qualitative study. *Scandinavian Journal of Caring Sciences*. 2008;22(3):430-6.
30. Feragen KB, Kvaalem IL, Rumsey N, Borge AI. Adolescents with and without a facial difference: The role of friendships and social acceptance in perceptions of appearance and emotional resilience. *Body Image*. 2010;7(4):271-9.
31. Cambridge Dictionary. Stigmatization 2021 [Available from: <https://dictionary.cambridge.org/dictionary/english/stigmatization>].

32. Lawrence JW, Fauerbach JA, Heinberg LJ, Doctor M, Thombs BD. The reliability and validity of the Perceived Stigmatization Questionnaire (PSQ) and the Social Comfort Questionnaire (SCQ) among an adult burn survivor sample. *Psychological Assessment*. 2006;18(1):106-11.
33. Lawrence JW, Rosenberg L, Rimmer RB, Thombs BD, Fauerbach JA. Perceived stigmatization and social comfort: validating the constructs and their measurement among pediatric burn survivors. *Rehabilitation Psychology*. 2010;55(4):360-71.
34. Masnari O, Landolt MA, Roessler J, Weingaertner SK, Neuhaus K, Meuli M, et al. Self-and parent-perceived stigmatisation in children and adolescents with congenital or acquired facial differences. *Journal of Plastic, Reconstructive & Aesthetic Surgery*. 2012;65(12):1664-70.
35. Strauss RP, Ramsey BL, Edwards TC, Topolski TD, Kapp-Simon KA, Thomas CR, et al. Stigma experiences in youth with facial differences: a multi-site study of adolescents and their mothers. *Orthodontics & craniofacial research*. 2007;10(2):96-103.
36. Crerand CE, Rumsey N, Kazak A, Clarke A, Rausch J, Sarwer DB. Sex differences in perceived stigmatization, body image disturbance, and satisfaction with facial appearance and speech among adolescents with craniofacial conditions. *Body Image*. 2020;32:190-8.
37. Masnari O, Schiestl C, Rossler J, Gutlein SK, Neuhaus K, Weibel L, et al. Stigmatization predicts psychological adjustment and quality of life in children and adolescents with a facial difference. *Journal of Pediatric Psychology*. 2013;38(2):162-72.
38. Grogan S. *Body image : understanding body dissatisfaction in men, women and children*. London: Routledge/Taylor & Francis Group; 2017. Available from: <https://doi.org/10.4324/9781315681528>.
39. Vannucci A, Ohannessian CM. Body Image Dissatisfaction and Anxiety Trajectories During Adolescence. *Journal of Clinical Child and Adolescent Psychology*. 2017:1-11.
40. Fitzsimmons-Craft EE, Bardone-Cone AM. Examining Prospective Mediation Models of Body Surveillance, Trait Anxiety, and Body Dissatisfaction in African American and Caucasian College Women. *Sex Roles*. 2012;67(3):187-200.
41. Flores-Cornejo F, Kamego-Tome M, Zapata-Pachas MA, Alvarado GF. Association between body image dissatisfaction and depressive symptoms in adolescents. *Braz J Psychiatry*. 2017;39(4):316-22.
42. Murray K, Rieger E, Byrne D. Body image predictors of depressive symptoms in adolescence. *Journal of adolescence*. 2018;69:130-9.
43. Dion J, Blackburn M-E, Auclair J, Laberge L, Veillette S, Gaudreault M, et al. Development and aetiology of body dissatisfaction in adolescent boys and girls. *International Journal of Adolescence and Youth*. 2015;20(2):151-66.
44. Shpigelman C-N, HaGani N. The impact of disability type and visibility on self-concept and body image: Implications for mental health nursing. *J Psychiatr Ment Health Nurs*. 2019;26(3-4):77-86.
45. Crerand CE, Sarwer DB, Kazak AE, Clarke A, Rumsey N. Body Image and Quality of Life in Adolescents With Craniofacial Conditions. *Cleft Palate-Craniofacial Journal*. 2017;54(1):2-12.

46. Dalgard F, Gieler U, Holm JØ, Bjertness E, Hauser S. Self-esteem and body satisfaction among late adolescents with acne: Results from a population survey. *Journal of the American Academy of Dermatology*. 2008;59(5):746-51.
47. Bilgiç O, Bilgiç A, Bahalı K, Bahalı AG, Gürkan A, Yılmaz S. Psychiatric symptomatology and health-related quality of life in children and adolescents with alopecia areata. *Journal of the European Academy of Dermatology and Venereology*. 2014;28(11):1463-8.
48. Díaz-Atienza F, Gurpegui M. Environmental stress but not subjective distress in children or adolescents with alopecia areata. *Journal of Psychosomatic Research*. 2011;71(2):102-7.
49. Pasini A, Lo-Castro A, Di Carlo L, Pitzianti M, Siracusano M, Rosa C, et al. Detecting anxiety symptoms in children and youths with neurofibromatosis type I. *American Journal of Medical Genetics, Part B: Neuropsychiatric Genetics*. 2012;159 B(7):869-73.
50. Bilgiç O, Bilgiç A, Akiş HK, Eskioğlu F, Kiliç EZ. Depression, anxiety and health-related quality of life in children and adolescents with vitiligo. *Clinical and Experimental Dermatology*. 2011;36(4):360-5.
51. Hon KLE, Pong NH, Poon TCW, Chan DFY, Leung TF, Lai KYC, et al. Quality of life and psychosocial issues are important outcome measures in eczema treatment. *Journal of Dermatological Treatment*. 2015;26(1):83-9.
52. Sheerin D, MacLeod M, Kusumakar V. Psychosocial adjustment in children with port-wine stains and prominent ears. *J Am Acad Child Adolesc Psychiatry*. 1995;34(12):1637-47.
53. Pope AW, Ward J. Factors associated with peer social competence in preadolescents with craniofacial anomalies. *Journal of pediatric psychology*. 1997;22(4):455-69.
54. Rønnstad ATM, Halling-Overgaard A-S, Hamann CR, Skov L, Egeberg A, Thyssen JP. Association of atopic dermatitis with depression, anxiety, and suicidal ideation in children and adults: A systematic review and meta-analysis. *Journal of the American Academy of Dermatology*. 2018;79(3):448-56.e30.
55. Drosdzol A, Skrzypulec V, Plinta R. Quality of life, mental health and self-esteem in hirsute adolescent females. *Journal of Psychosomatic Obstetrics and Gynecology*. 2010;31(3):168-75.
56. Achenbach TM, Rescorla LA. *Manual for the ASEBA school-age forms & profiles: an integrated system of multi-informant assessment* Burlington, VT: University of Vermont. Burlington, VT: Research Center for Children, Youth, & Families; 2001.
57. Goodman R. The Strengths and Difficulties Questionnaire: a research note. *Journal of child psychology and psychiatry*. 1997;38(5):581-6.
58. Johns AL, Wallace ER, Collett BR, Kapp-Simon KA, Drake AF, Heike CL, et al. Behavioral Adjustment of Preschool Children With and Without Craniofacial Microsomia. *The Cleft Palate-Craniofacial Journal*. 2021;58(1):42-53.
59. Dufton LM, Speltz ML, Kelly JP, Leroux B, Collett BR, Werler MM. Psychosocial outcomes in children with hemifacial microsomia. *J Pediatr Psychol*. 2011;36(7):794-805.

60. Koot HM, Waard-van der Spek D, Peer CD, Mulder PGH, Oranje AP. Psychosocial sequelae in 29 children with giant congenital melanocytic naevi. *Clinical and experimental dermatology*. 2000;25(8):589-93.
61. Hergüner S, Kılıç G, Karakoç S, Tamay Z, Tüzün Ü, Güler N. Levels of depression, anxiety and behavioural problems and frequency of psychiatric disorders in children with chronic idiopathic urticaria. *British Journal of Dermatology*. 2011;164(6):1342-7.
62. Pope AW, Snyder HT. Psychosocial Adjustment in Children and Adolescents With a Craniofacial Anomaly: Age and Sex Patterns. *The Cleft Palate-Craniofacial Journal*. 2005;42(4):349-54.
63. Strobel L, Renner G. Quality of life and adjustment in children and adolescents with Moebius syndrome: Evidence for specific impairments in social functioning. *Research in developmental disabilities*. 2016;53:178-88.
64. Feragen KB, Stock NM, Kvaalem IL. Risk and Protective Factors at Age 16: Psychological Adjustment in Children With a Cleft Lip and/or Palate. *Cleft Palate Craniofac J*. 2015;52(5):555-73.
65. Bessell A, Moss TP. Evaluating the effectiveness of psychosocial interventions for individuals with visible differences: a systematic review of the empirical literature. *Body Image*. 2007;4(3):227-38.
66. Muftin Z, Thompson AR. A systematic review of self-help for disfigurement: effectiveness, usability, and acceptability. *Body Image*. 2013;10(4):442-50.
67. Norman A, Moss TP. Psychosocial interventions for adults with visible differences: a systematic review. *PeerJ*. 2015;3:e870.
68. Jenkinson E, Williamson H, Byron-Daniel J, Moss TP. Systematic Review: Psychosocial Interventions for Children and Young People With Visible Differences Resulting From Appearance Altering Conditions, Injury, or Treatment Effects. *Journal of Pediatric Psychology*. 2015;40(10):1017-33.
69. Zucchelli F, Donnelly O, Williamson H, Hooper N. Acceptance and Commitment Therapy for People Experiencing Appearance-Related Distress Associated With a Visible Difference: A Rationale and Review of Relevant Research 2018. 171-83 p.
70. Williamson H, Griffiths C, Harcourt D. Developing young person's Face IT: Online psychosocial support for adolescents struggling with conditions or injuries affecting their appearance. *Health Psychology Open*. 2015;2(2):1-12.
71. Bessell A, Brough V, Clarke A, Harcourt D, Moss TP, Rumsey N. Evaluation of the effectiveness of Face IT, a computer-based psychosocial intervention for disfigurement-related distress. *Psychology, Health & Medicine*. 2012;17(5):565-77.
72. Riobueno-Naylor A, Williamson H, Canenguez K, Kogosov A, Drexler A, Sadeq F, et al. Appearance Concerns, Psychosocial Outcomes, and the Feasibility of Implementing an Online Intervention for Adolescents Receiving Outpatient Burn Care. *Journal of Burn Care & Research*. 2020.
73. Zelihić D, Williamson H, Kling J, Feragen KB. "It's tough because I see that it's upsetting her...": A qualitative exploration of parents' perceptions of talking with their adolescents about having a visible difference. *Body Image*. 2021;38:306-16.

74. Alderfer MA, Rourke MT. Family psychology in the context of pediatric medical conditions. *The Wiley-Blackwell handbook of family psychology*: Wiley Blackwell; 2009. p. 527-38.
75. Buodo G, Moscardino U, Scrimin S, Altoè G, Palomba D. Parenting Stress and Externalizing Behavior Symptoms in Children: The Impact of Emotional Reactivity. *Child Psychiatry Hum Dev*. 2013;44(6):786-97.
76. Neece CL, Green SA, Baker BL. Parenting stress and child behavior problems: A transactional relationship across time. *Am J Intellect Dev Disabil*. 2012;117(1):48-66.
77. Klein TP, Pope AW, Getahun E, Thompson J. Mothers' reflections on raising a child with a craniofacial anomaly. *Cleft Palate Craniofac J*. 2006;43(5):590-7.
78. Klein TP, Pope AW, Tan E. Fathers' perspectives on parenting a child with a craniofacial anomaly. *J Pediatr Health Care*. 2010;24(5):300-4.
79. Ablett K, Thompson AR. Parental, child, and adolescent experience of chronic skin conditions: A meta-ethnography and review of the qualitative literature. *Body Image*. 2016;19(Supplement C):175-85.
80. Barke J, Coad J, Harcourt D. Parents' experiences of caring for a young person with neurofibromatosis type 1 (NF1): a qualitative study. *J Community Genet*. 2016;7(1):33-9.
81. Pinquart M. Parenting stress in caregivers of children with chronic physical condition—a meta-analysis. *Stress Health*. 2018;34(2):197-207.
82. Pinquart M. Featured Article: Depressive Symptoms in Parents of Children With Chronic Health Conditions: A Meta-Analysis. *J Pediatr Psychol*. 2018;44(2):139-49.
83. Feragen KB, Rumsey N, Heliovaara A, Boysen BM, Johannessen EC, Havstam C, et al. Scandcleft randomised trials of primary surgery for unilateral cleft lip and Palate: 9. Parental report of social and emotional experiences related to their 5-year-old child's cleft diagnosis. *J Plast Surg Hand Surg*. 2017;51(1):73-80.
84. Feragen KB, Stock NM, Myhre A, Due-Tønnessen BJ. Medical Stress Reactions and Personal Growth in Parents of Children With a Rare Craniofacial Condition. *Cleft Palate Craniofac J*. 2020:1055665619869146.
85. Hasanzadeh N, Khoda MO, Jahanbin A, Vatankhah M. Coping strategies and psychological distress among mothers of patients with nonsyndromic cleft lip and palate and the family impact of this disorder. *J Craniofac Surg*. 2014;25(2):441-5.
86. Bakker A, Maertens KJP, Van Son MJM, Van Loey NEE. Psychological consequences of pediatric burns from a child and family perspective: A review of the empirical literature. *Clinical Psychology Review*. 2013;33(3):361-71.
87. Berger ZE, Dalton LJ. Coping with a cleft: psychosocial adjustment of adolescents with a cleft lip and palate and their parents. *The Cleft Palate-Craniofacial Journal*. 2009;46(4):435-43.
88. Costa B, Thornton M, Guest E, Meyrick J, Williamson H. The effectiveness of interventions to improve psychosocial outcomes in parents of children with appearance-affecting health conditions: A systematic review. *Child Care Health Dev*. 2021;47(1):15-30.

89. Kent G, Keohane S. Social anxiety and disfigurement: The moderating effects of fear of negative evaluation and past experience. *British Journal of Clinical Psychology*. 2001;40(1):23-34.
90. Costello EJ, Copeland W, Angold A. Trends in psychopathology across the adolescent years: What changes when children become adolescents, and when adolescents become adults? *Journal of Child Psychology and Psychiatry*. 2011;52(10):1015-25.
91. Kessler RC, Avenevoli S, Costello EJ, Georgiades K, Green JG, Gruber MJ, et al. Prevalence, persistence, and sociodemographic correlates of DSM-IV disorders in the National Comorbidity Survey Replication Adolescent Supplement. *Archives of General Psychiatry*. 2012;69(4):372-80.
92. Copeland WE, Angold A, Shanahan L, Costello EJ. Longitudinal Patterns of Anxiety From Childhood to Adulthood: The Great Smoky Mountains Study. *Journal of the American Academy of Child & Adolescent Psychiatry*. 2014;53(1):21-33.
93. Ford T, Goodman R, Meltzer H. The British Child and Adolescent Mental Health Survey 1999: The Prevalence of DSM-IV Disorders. *Journal of the American Academy of Child & Adolescent Psychiatry*. 2003;42(10):1203-11.
94. Wesselhoeft R, Sørensen MJ, Heiervang ER, Bilenberg N. Subthreshold depression in children and adolescents - a systematic review. *Journal of Affective Disorders*. 2013;151(1):7-22.
95. Copeland WE, Shanahan L, Costello EJ, Angold A. Childhood and adolescent psychiatric disorders as predictors of young adult disorders. *Archives of general psychiatry*. 2009;66(7):764-72.
96. Pope SJ, Solomons WR, Done DJ, Cohn N, Possamai AM. Body image, mood and quality of life in young burn survivors. *Burns*. 2007;33(6):747-55.
97. Rivlin E, Faragher EB. The psychological sequelae of thermal injury on children and adolescents: Part 1. *Developmental Neurorehabilitation*. 2007;10(2):161-72.
98. Moher D, Liberati A, Tetzlaff J, Altman DG. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *Annals of internal medicine*. 2009;151(4):264-9.
99. Hiller RM, Meiser-Stedman R, Fearon P, Lobo S, McKinnon A, Fraser A, et al. Research Review: Changes in the prevalence and symptom severity of child post-traumatic stress disorder in the year following trauma - a meta-analytic study. *Journal of Child Psychology and Psychiatry*. 2016;57(8):884-98.
100. National Heart Lung and Blood Institute (NIH). Study Quality Assessment Tools: National Heart, Lung and Blood Institute (NIH); 2018 [Available from: <https://www.nhlbi.nih.gov/health-topics/study-quality-assessment-tools>].
101. Wan X, Wang W, Liu J, Tong T. Estimating the sample mean and standard deviation from the sample size, median, range and/or interquartile range. *BMC medical research methodology*. 2014;14(1):135.
102. Melsen WG, Bootsma MCJ, Rovers MM, Bonten MJM. The effects of clinical and statistical heterogeneity on the predictive values of results from meta-analyses. *Clinical Microbiology and Infection*. 2014;20(2):123-9.

103. Turan E, Kandemir H, Yesilova Y, Ekinici S, Tanrikulu O, Kandemir SB, et al. Assessment of psychiatric morbidity and quality of life in children and adolescents with cutaneous leishmaniasis and their parents. *Postepy Dermatologii i Alergologii*. 2015;32(5):344-8.
104. Cummings CM, Caporino NE, Kendall PC. Comorbidity of anxiety and depression in children and adolescents: 20 years after. *Psychological bulletin*. 2014;140(3):816-45.
105. Valentine JC, Pigott TD, Rothstein HR. How Many Studies Do You Need?: A Primer on Statistical Power for Meta-Analysis. *Journal of Educational and Behavioral Statistics*. 2010;35(2):215-47.
106. Silverberg JI, Simpson EL. Associations of childhood eczema severity: a US population-based study. *Dermatitis*. 2014;25(3):107-14.
107. Bhate K, Williams HC. Epidemiology of acne vulgaris. *British Journal of Dermatology*. 2013;168(3):474-85.
108. Mak WWS, Poon CYM, Pun LYK, Cheung SF. Meta-analysis of stigma and mental health. *Social Science & Medicine*. 2007;65(2):245-61.
109. Clarke A, Thompson AR, Jenkinson E, Rumsey N, Newell R. CBT for Appearance Anxiety. *Psychosocial Interventions for Anxiety Due to Visible Difference*. Oxford: Wiley; 2014.
110. Jones LC, Mrug S, Elliott MN, Toomey SL, Tortolero S, Schuster MA. Chronic Physical Health Conditions and Emotional Problems From Early Adolescence Through Midadolescence. *Academic Pediatrics*. 2017;17(6):649-55.
111. Pao M, Bosk A. Anxiety in medically ill children/adolescents. *Depression and Anxiety*. 2011;28(1):40-9.
112. Vancampfort D, Koyanagi A, Hallgren M, Probst M, Stubbs B. The relationship between chronic physical conditions, multimorbidity and anxiety in the general population: A global perspective across 42 countries. *General Hospital Psychiatry*. 2017;45:1-6.
113. Masnari O, Schiestl C, Rossler J, Gutlein SK, Neuhaus K, Weibel L, et al. Stigmatization predicts psychological adjustment and quality of life in children and adolescents with a facial difference. *J Pediatr Psychol*. 2013;38(2):162-72.
114. Mai CT, Cassell CH, Meyer RE, Isenburg J, Canfield MA, Rickard R, et al. Birth defects data from population-based birth defects surveillance programs in the United States, 2007 to 2011: Highlighting orofacial clefts. *Birth Defects Res A Clin Mol Teratol*. 2014;100(11):895-904.
115. Goodacre T, Swan MC. Cleft lip and palate: current management. *Paediatr Child Health*. 2008;18(6):283-92.
116. Dickison P, Christou E, Wargon O. A prospective study of infantile hemangiomas with a focus on incidence and risk factors. *Pediatr Dermatol*. 2011;28(6):663-9.
117. Munden A, Butschek R, Tom WL, Marshall JS, Poeltler DM, Krohne SE, et al. Prospective study of infantile haemangiomas: incidence, clinical characteristics and association with placental anomalies. *Br J Dermatol*. 2014;170(4):907-13.

118. Anderson KR, Schoch JJ, Lohse CM, Hand JL, Davis DM, Tollefson MM. Increasing incidence of infantile hemangiomas (IH) over the past 35 years: Correlation with decreasing gestational age at birth and birth weight. *J Am Acad Dermatol*. 2016;74(1):120-6.
119. Léauté-Labrèze C, Harper JL, Hoeger PH. Infantile haemangioma. *Lancet*. 2017;390(10089):85-94.
120. Hunt O, Burden D, Hepper P, Johnston C. The psychosocial effects of cleft lip and palate: a systematic review. *Eur J Orthod*. 2005;27(3):274-85.
121. Pinckston M, Dalton L, Farrar S, Hotton MT. The Psychosocial Adjustment of Children Born With a Cleft Lip and/or Palate: Cross-Sectional and Longitudinal Analyses. *Cleft Palate Craniofac J*. 2020;57(11):1280-90.
122. Snyder H, Pope AW. Psychosocial adjustment in children and adolescents with a craniofacial anomaly: diagnosis-specific patterns. *Cleft Palate Craniofac J*. 2010;47(3):264-72.
123. Zeraatkar M, Ajami S, Nadjmi N, Faghihi SA, Golkari A. A qualitative study of children's quality of life in the context of living with cleft lip and palate. *Pediatric Health Med Ther*. 2019;10:13-20.
124. Murray L, Arteche A, Bingley C, Hentges F, Bishop DV, Dalton L, et al. The effect of cleft lip on socio-emotional functioning in school-aged children. *J Child Psychol Psychiatry*. 2010;51(1):94-103.
125. Feragen KB, Stock NM. When there is more than a cleft: psychological adjustment when a cleft is associated with an additional condition. *Cleft Palate Craniofac J*. 2014;51(1):5-14.
126. Berger ZE, Dalton LJ. Coping with a cleft: psychosocial adjustment of adolescents with a cleft lip and palate and their parents. *Cleft Palate Craniofac J*. 2009;46(4):435-43.
127. Brand S, Blechschmidt A, Müller A, Sader R, Schwenzer-Zimmerer K, Zeilhofer H-F, et al. Psychosocial Functioning and Sleep Patterns in Children and Adolescents with Cleft Lip and Palate (CLP) Compared with Healthy Controls. *Cleft Palate Craniofac J*. 2009;46(2):124-35.
128. Pope AW, Snyder HT. Psychosocial Adjustment in Children and Adolescents with a Craniofacial Anomaly: Age and Sex Patterns. *Cleft Palate Craniofac J*. 2005;42(4):349-54.
129. Hunt O, Burden D, Hepper P, Stevenson M, Johnston C. Parent reports of the psychosocial functioning of children with cleft lip and/or palate. *Cleft Palate Craniofac J*. 2007;44(3):304-11.
130. Hoornweg MJ, Grootenhuis MA, van der Horst CM. Health-related quality of life and impact of haemangiomas on children and their parents. *J Plast Reconstr Aesthet Surg*. 2009;62(10):1265-71.
131. Cohen-Barak E, Rozenman D, Shani Adir A. Infantile haemangiomas and quality of life. *Arch Dis Child*. 2013;98(9):676-9.
132. Masnari O, Landolt MA, Roessler J, Weingaertner SK, Neuhaus K, Meuli M, et al. Self-and parent-perceived stigmatisation in children and adolescents with congenital or acquired facial differences. *J Plast Reconstr Aesthet Surg*. 2012;65(12):1664-70.

133. Dieterich-Miller CA, Cohen BA, Liggett J. Behavioral Adjustment and Self-Concept of Young Children with Hemangiomas. *Pediatr Dermatol.* 1992;9(3):241-5.
134. Moyakine AV, Spillekom-van Koulil S, van der Vleuten CJM. Propranolol treatment of infantile hemangioma is not associated with psychological problems at 7 years of age. *J Am Acad Dermatol.* 2017;77(1):105-8.
135. Feragen KB, Stock NM. Psychological adjustment to craniofacial conditions (excluding oral clefts): A review of the literature. *Psychol Health.* 2017;32(3):253-88.
136. Gee C, Maskell J, Newcombe P, Kimble R, Williamson H. Australian health professionals' perspectives of psychosocial adjustment to visible differences: A qualitative analysis of pediatric populations. *Body Image.* 2020;33:13-26.
137. Clarke A, Thompson AR, Jenkinson E, Rumsey N, Newell R. Psychosocial interventions for anxiety due to visible difference. Chichester, UK: John Wiley & Sons, Ltd; 2014.
138. Feragen KB, Stock NM. Risk and Protective Factors at Age 10: Psychological Adjustment in Children with a Cleft Lip and/or Palate. *Cleft Palate Craniofac J.* 2016;53(2):161-79.
139. Wesseldijk LW, Dieleman GC, van Steensel FJA, Bleijenberg EJ, Bartels M, Bögels SM, et al. Do Parental Psychiatric Symptoms Predict Outcome in Children With Psychiatric Disorders? A Naturalistic Clinical Study. *J Am Acad Child Psy.* 2018;57(9):669-77.e6.
140. van Dalen M, Leemreis WH, Kraaij V, de Laat PCJ, Pasmans SGMA, Versnel SL, et al. Parenting children with a cleft lip or infantile haemangioma: a cross-sectional study of parenting stress and distress. *Cleft Palate Craniofac J.* 2021.
141. Stifter C, Augustine M, Dollar J. The role of positive emotions in child development: A developmental treatment of the broaden and build theory. *J Posit Psychol.* 2020;15(1):89-94.
142. Tyler MC, Wehby GL, Robbins JM, Damiano PC. Separation Anxiety in Children Ages 4 through 9 with Oral Clefts. *Cleft Palate Craniofac J.* 2013;50(5):520-7.
143. Wehby GL, Collet B, Barron S, Romitti PA, Ansley TN, Speltz M. Academic Achievement of Children and Adolescents With Oral Clefts. *Pediatrics.* 2014;133(5):785-92.
144. Feragen KB, Særvold TK, Aukner R, Stock NM. Speech, Language, and Reading in 10-Year-Olds with Cleft: Associations with Teasing, Satisfaction with Speech, and Psychological Adjustment. *Cleft Palate Craniofac J.* 2017;54(2):153-65.
145. Verhulst FC, van der Ende J. Handleiding ASEBA: vragenlijsten voor leeftijden 6 t/m 18 jaar: CBCL/6-18, YSR, TRF: ASEBA Nederland; 2013.
146. Achenbach TM, Rescorla LA. Manual for the ASEBA preschool forms and profiles: Burlington, VT: University of Vermont, Research center for children, youth and families; 2000.
147. Zondervan-Zwijnenburg MAJ, Veldkamp SAM, Neumann A, Barzeva SA, Nelemans SA, van Beijsterveldt CEM, et al. Parental Age and Offspring Childhood Mental Health: A Multi-Cohort, Population-Based Investigation. *Child Dev.* 2020;91(3):964-82.

148. World Medical Association. World Medical Association Declaration of Helsinki: ethical principles for medical research involving human subjects. *JAMA*. 2013;310(20):2191-4.
149. Von Elm E, Altman DG, Egger M, Pocock SJ, Gøtzsche PC, Vandenbroucke JP, et al. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) Statement: guidelines for reporting observational studies. *Int J Surg*. 2014;12(12):1495-9.
150. CBS. Niveau ISCED 2011: CBS; 2011 [Available from: <https://www.cbs.nl/nl-nl/onz-diensten/methoden/classificaties/onderwijs-en-beroepen/isced/niveau-isced-2011>].
151. Achenbach TM, Rescorla LA. Manual for the ASEBA school-age forms & profiles: an integrated system of multi-informant assessment Burlington, VT: University of Vermont 2001.
152. Watson D, Clark LA, Tellegen A. Development and validation of brief measures of positive and negative affect: the PANAS scales. *J Pers Soc Psychol*. 1988;54(6):1063-70.
153. Crawford JR, Henry JD. The Positive and Negative Affect Schedule (PANAS): Construct validity, measurement properties and normative data in a large non-clinical sample. *Br J Clin Psychol*. 2004;43(3):245-65.
154. RStudio Team. RStudio: Integrated Development for R.: RStudio, PBC, Boston, MA; 2020 [Available from: <http://www.rstudio.com/>].
155. van Buuren S, Groothuis-Oudshoorn K. MICE: Multivariate Imputation by Chained Equations in R. *J Stat Softw*. 2011;45(3):1-67.
156. Benjamini Y, Hochberg Y. Controlling the False Discovery Rate: A Practical and Powerful Approach to Multiple Testing. *J R Stat Soc Series B Stat Methodol*. 1995;57(1):289-300.
157. Cohen J. A power primer. *Psychol Bul*. 1992;112(1):155-9.
158. Stock NM, Feragen KB. Psychological adjustment to cleft lip and/or palate: A narrative review of the literature. *Psychol Health*. 2016;31(7):777-813.
159. Kenny SA, Majeed N, Zhand N, Glikstein R, Agid R, Dos Santos MP. Psychological comorbidities and compliance to interventional treatment of patients with cutaneous vascular malformations. *Interv Neuroradiol*. 2016;22(4):489-94.
160. Hoek IH, Kraaimaat FW, Admiraal RJ, Kuijpers-Jagtman AM, Verhaak CM. [Psychosocial adjustment in children with a cleft lip and/or palate] Sociaal-emotionele gezondheid bij kinderen met schisis. *Ned Tijdschr Geneesk*. 2009;153:B352.
161. Pinquart M. Do the parent-child relationship and parenting behaviors differ between families with a child with and without chronic illness? A meta-analysis. *J Pediatr Psychol*. 2013;38(7):708-21.
162. Crandell JL, Sandelowski M, Leeman J, Havill NL, Knafl K. Parenting behaviors and the well-being of children with a chronic physical condition. *Fam Syst Health*. 2018;36(1):45-61.
163. Smolak L. Appearance in Childhood and Adolescence. In: Rumsey N, Harcourt D, editors. *The Oxford handbook of the psychology of appearance*. Oxford: Oxford University Press; 2012. p. 123-41.

164. Dion J, Blackburn M-E, Auclair J, Laberge L, Veillette S, Gaudreault M, et al. Development and aetiology of body dissatisfaction in adolescent boys and girls. *Int J Adolesc Youth*. 2015;20(2):151-66.
165. Vannucci A, Ohannessian CM. Body Image Dissatisfaction and Anxiety Trajectories During Adolescence. *J Clin Child Adolesc*. 2017:1-11.
166. Flores-Cornejo F, Kamego-Tome M, Zapata-Pachas MA, Alvarado GF. Association between body image dissatisfaction and depressive symptoms in adolescents. *Braz J Psychiatry*. 2017;39(4):316-22.
167. Sprangers MAG, Schwartz CE. Integrating response shift into health-related quality of life research: a theoretical model. *Soc Sci Med*. 1999;48(11):1507-15.
168. Castro E, Cotov M, Brovedani P, Coppola G, Meoni T, Papini M, et al. Associations between Learning and Behavioral Difficulties in Second-Grade Children. *Children*. 2020;7(9).
169. Visser L, Kalmar J, Linkersdörfer J, Görgen R, Rothe J, Hasselhorn M, et al. Comorbidities Between Specific Learning Disorders and Psychopathology in Elementary School Children in Germany. *Front Psychiatry*. 2020;11:292.
170. Achenbach TM, McConaughy SH, Howell C. Child/adolescent behavioral and emotional problems: Implications of cross-informant correlations for situational specificity. *Psychol Bull*. 1987;101(2):213-32.
171. Alakortes J, Fyrstén J, Bloigu R, Carter AS, Moilanen IK, Ebeling HE. Parental Reports of Early Socioemotional and Behavioral Problems: Does the Father's View Make a Difference? *Infant Ment Health J*. 2017;38(3):363-77.
172. Spijkers W, Jansen DEMC, Reijneveld SA. Parental internalizing problems in a community sample: association with child psychosocial problems. *Eur J Public Health*. 2013;24(1):11-5.
173. van der Bruggen CO, Stams GJ, Bögels SM. Research review: the relation between child and parent anxiety and parental control: a meta-analytic review. *J Child Psychol Psychiatry*. 2008;49(12):1257-69.
174. Hettema JM, Neale MC, Kendler KS. A Review and Meta-Analysis of the Genetic Epidemiology of Anxiety Disorders. *Am J Psychiatry*. 2001;158(10):1568-78.
175. Dishion TJ, Patterson GR, Griesler PC. Peer adaptations in the development of antisocial behavior: A confluence model. *Aggressive behavior: Current perspectives*. Plenum series in social/clinical psychology. New York, NY, US: Plenum Press; 1994. p. 61-95.
176. Ainsworth MDS, Bell SM, Stayton DF. Infant-mother attachment and social development: Socialization as a product of reciprocal responsiveness to signals. *The integration of a child into a social world*. New York, NY, US: Cambridge University Press; 1974. p. 99-135.
177. McLeod BD, Weisz JR, Wood JJ. Examining the association between parenting and childhood depression: a meta-analysis. *Clin Psychol Rev*. 2007;27(8):986-1003.
178. Miller ML, Williams BM, McCabe JE, Williamson JA, King S, Laplante DP, et al. Perinatal anxiety and depressive symptoms and perception of child behavior and temperament in early motherhood. *J Dev Orig Health Dis*. 2020:1-10.
179. Bowling A. Mode of questionnaire administration can have serious effects on data quality. *J Public Health*. 2005;27(3):281-91.

180. Thompson A, Kent G. Adjusting to disfigurement: processes involved in dealing with being visibly different. *Clinical Psychology review*. 2001;21(5):663-82.
181. Rumsey N, Harcourt D. Visible difference amongst children and adolescents: issues and interventions. *Developmental Neurorehabilitation*. 2007;10(2):113-23.
182. Barankin B, DeKoven J. Psychosocial effect of common skin diseases. *Canadian Family Physician*. 2002;48:712-6.
183. Magin PJ, Pond CD, Smith WT, Watson AB, Goode SM. A cross-sectional study of psychological morbidity in patients with acne, psoriasis and atopic dermatitis in specialist dermatology and general practices. *Journal of the European Academy of Dermatology and Venereology*. 2008;22(12):1435-44.
184. van Dalen M, Dierckx B, Pasmans SGMA, Aendekerk EWC, Mathijssen IMJ, Koudstaal MJ, et al. Anxiety and depression in adolescents with a visible difference: A systematic review and meta-analysis. *Body Image*. 2020;33:38-46.
185. van Dalen M, Pasmans SGMA, Aendekerk M-L, Mathijssen I, Koudstaal M, Timman R, et al. Investigating online psychological treatment for adolescents with a visible difference in the Dutch YP Face IT study: protocol of a randomised controlled trial. *BMJ Open*. 2021;11(1):e041449.
186. Williamson H, Hamlet C, White P, Marques EMR, Paling T, Cadogan J, et al. A web-based self-help psychosocial intervention for adolescents distressed by appearance-affecting conditions and injuries (Young Persons' Face IT): Feasibility study for a parallel randomized controlled trial. *JMIR mental health*. 2019;6(11):e14776.
187. Sekhon M, Cartwright M, Francis JJ. Acceptability of healthcare interventions: an overview of reviews and development of a theoretical framework. *BMC Health Services Research*. 2017;17(1):88.
188. O'Brien BC, Harris IB, Beckman TJ, Reed DA, Cook DA. Standards for reporting qualitative research: a synthesis of recommendations. *Academic Medicine*. 2014;89(9):1245-51.
189. Williamson H, Hamlet C, White P, Marques EM, Cadogan J, Perera R, et al. Study protocol of the YP Face IT feasibility study: comparing an online psychosocial intervention versus treatment as usual for adolescents distressed by appearance-altering conditions/injuries. *BMJ Open*. 2016;6(10):e012423.
190. Heath J, Williamson H, Williams L, Harcourt D. "It's just more personal": Using multiple methods of qualitative data collection to facilitate participation in research focusing on sensitive subjects. *Applied Nursing Research*. 2018;43:30-5.
191. La Greca AM, Lopez N. Social anxiety among adolescents: Linkages with peer relations and friendships. *Journal of Abnormal Child Psychology*. 1998;26(2):83-94.
192. Mendelson BK, Mendelson MJ, White DR. Body-esteem scale for adolescents and adults. *Journal of Personality Assessment*. 2001;76(1):90-106.
193. Harter S. Self-perception profile for adolescents: Manual and questionnaires. Denver Uo, editor. Denver2012.

194. Treffers PDA, Goedhart AW, Veerman JW, Van den Bergh BRH, Ackaert L, De Rycke L. Competentie belevingsschaal voor Adolescenten. Tijdschrift voor Psychiatrie. 2004;7:468-9.
195. Herdman M, Gudex C, Lloyd A, Janssen MF, Kind P, Parkin D, et al. Development and preliminary testing of the new five-level version of EQ-5D (EQ-5D-5L). Quality of Life Research. 2011;20(10):1727-36.
196. Atkinson MJ, Diedrichs PC. Assessing the impact of body image concerns on functioning across life domains: Development and validation of the Body Image Life Disengagement Questionnaire (BILD-Q) among British adolescents. Body Image. 2021;37:63-73.
197. Kovacs M. CDI-2. Screeningsvragenlijst voor depressie bij kinderen en jongeren. Nederlandse bewerking door Denise Bodden CBeYS, editor. Amsterdam: Hogrefe Uitgevers BV; 2016.
198. Okkerse JME, Dessens AB. Spiegeltje, spiegeltje.. Vragenlijst voor adolescenten en volwassenen over (on)tevredenheid met het lichaam en gerelateerde lijdensdruk. 2016.
199. Braun V, Clarke V. Using thematic analysis in psychology. Qualitative Research in Psychology. 2006;3(2):77-101.
200. VERBI Software. MAXQDA 2018. Berlin, Germany: VERBI Software; 2017.
201. Guest G, Bunce A, Johnson L. How Many Interviews Are Enough?: An Experiment with Data Saturation and Variability. Field Methods. 2006;18(1):59-82.
202. Centraal Bureau voor de Statistiek. Internet; toegang, gebruik en faciliteiten 2020 [Available from: <https://opendata.cbs.nl/statline#/CBS/nl/dataset/83429NED/table?dl=4B34>].
203. March S, Donovan CL, Baldwin S, Ford M, Spence SH. Using stepped-care approaches within internet-based interventions for youth anxiety: Three case studies. Internet Interv. 2019;18:100281.
204. Paulhus DL. Two-component models of socially desirable responding. Journal of personality and social psychology. 1984;46(3):598.
205. Turner SR, Rumsey N, Sandy JR. Psychological aspects of cleft lip and palate. European Journal of Orthodontics. 1998;20(4):407-15.
206. Inderbitzen-Nolan HM, Walters KS. Social anxiety scale for adolescents: Normative data and further evidence of construct validity. Journal of Clinical Child Psychology. 2000;29(3):360-71.
207. Cragun D, DeBate RD, Ata RN, Thompson JK. Psychometric properties of the Body Esteem Scale for Adolescents and Adults in an early adolescent sample. Eating and Weight Disorders. 2013;18(3):275-82.
208. Haubrock I. Body-self-unity: Gender difference concerning the body self unity. Do the genders differ in the evaluation of their self and body? [Bachelor thesis]. Enschede: University of Twente; 2009.
209. Janssen MF, Pickard AS, Golicki D, Gudex C, Niewada M, Scalone L, et al. Measurement properties of the EQ-5D-5L compared to the EQ-5D-3L across eight patient groups: a multi-country study. Quality of Life Research. 2013;22(7):1717-27.

210. Diedrichs PC, Atkinson MJ, Steer RJ, Garbett KM, Rumsey N, Halliwell E. Effectiveness of a brief school-based body image intervention 'Dove Confident Me: Single Session'when delivered by teachers and researchers: Results from a cluster randomised controlled trial. *Behaviour Research and Therapy*. 2015;74:94-104.
211. Eysenbach G. The Law of Attrition. *J Med Internet Res*. 2005;7(1):e11.
212. Meyerowitz-Katz G, Ravi S, Arnolda L, Feng X, Maberly G, Astell-Burt T. Rates of Attrition and Dropout in App-Based Interventions for Chronic Disease: Systematic Review and Meta-Analysis. *J Med Internet Res*. 2020;22(9):e20283.
213. Singer JD, Willett JB. *Applied longitudinal data analysis: Modeling change and event occurrence*: Oxford university press; 2003.
214. Rounsaville BJ, Carroll KM, Onken LS. A Stage Model of Behavioral Therapies Research: Getting Started and Moving on From Stage I. *Clinical Psychology: Science and Practice*. 2001;8(2):133-42.
215. Cunningham JA, Kypri K, McCambridge J. Exploratory randomized controlled trial evaluating the impact of a waiting list control design. *BMC Medical Research Methodology*. 2013;13(1):150.
216. Williamson H, Harcourt D, Halliwell E, Frith H, Wallace M. Adolescents' and parents' experiences of managing the psychosocial impact of appearance change during cancer treatment. *Journal of Pediatric Oncology Nursing*. 2010;27(3):168-75.
217. Tiemens K, Nicholas D, Forrest CR. Living with difference: experiences of adolescent girls with cleft lip and palate. *The Cleft Palate-Craniofacial Journal*. 2013;50(2):27-34.
218. Shapiro DN, Waljee J, Ranganathan K, Buchman S, Warschausky S. Gender and satisfaction with appearance in children with craniofacial anomalies. *Plastic and reconstructive surgery*. 2015;136(6):789e-95e.
219. Armstrong-James L, Cadogan J, Williamson H, Rumsey N, Harcourt D. An evaluation of the impact of a burn camp on children and young people's concerns about social situations, satisfaction with appearance and behaviour. *Scars, burns & healing*. 2018;4:2059513118816219.
220. Pell C. What to do when people stare: a workshop to teach individuals with disfiguring conditions to contend with staring and improve control of social interactions. *Journal of Burn Care & Research*. 2019;40(6):743-51.
221. Blakeney P, Thomas C, Holzer C, Rose M, Berniger F, Meyer WJ. Efficacy of a short-term, intensive social skills training program for burned adolescents. *The Journal of burn care & rehabilitation*. 2005;26(6):546-55.
222. Edwards TC, Topolski TD, Kapp-Simon KA, Aspinall CL, Patrick DL. What difference can a minute make? Social skills and first impressions of youth with craniofacial differences. *The Cleft palate-craniofacial journal*. 2011;48(1):91-7.
223. Maddern LH, Cadogan JC, Emerson MP. 'Outlook': A psychological service for children with a different appearance. *Clinical child psychology and psychiatry*. 2006;11(3):431-43.
224. National institute for health and clinical excellence. Final appraisal determination - Computerised cognitive behaviour therapy for depression (review) 2005 [Available from: <https://www.nice.org.uk/guidance/ta97>.

225. Nordgreen T, Gjestad R, Andersson G, Carlbring P, Havik OE. The implementation of guided Internet-based cognitive behaviour therapy for panic disorder in a routine-care setting: effectiveness and implementation efforts. *Cognitive behaviour therapy*. 2018;47(1):62-75.
226. Carlbring P, Andersson G, Cuijpers P, Riper H, Hedman-Lagerlof E. Internet-based vs. face-to-face cognitive behavior therapy for psychiatric and somatic disorders: an updated systematic review and meta-analysis. *Cogn Behav Ther*. 2018;47(1):1-18.
227. Stjerneklar S, Hougaard E, McLellan LF, Thastum M. A randomized controlled trial examining the efficacy of an internet-based cognitive behavioral therapy program for adolescents with anxiety disorders. *PloS one*. 2019;14(9):e0222485.
228. Topooco N, Byléhn S, Nysäter ED, Holmlund J, Lindegaard J, Johansson S, et al. Evaluating the efficacy of internet-delivered cognitive behavioral therapy blended with synchronous chat sessions to treat adolescent depression: randomized controlled trial. *Journal of medical Internet research*. 2019;21(11):e13393.
229. Franko DL, Cousineau TM, Rodgers RF, Roehrig JP. BodiMojo: Effective Internet-based promotion of positive body image in adolescent girls. *Body image*. 2013;10(4):481-8.
230. Rodgers RF, Donovan E, Cousineau T, Yates K, McGowan K, Cook E, et al. BodiMojo: Efficacy of a mobile-based intervention in improving body image and self-compassion among adolescents. *Journal of youth and adolescence*. 2018;47(7):1363-72.
231. van Dalen M, Pasmans SGMA, Aendekerk EWC, Mathijssen IMJ, Koudstaal MJ, Williamson H, et al. Acceptability and feasibility of an online psychosocial intervention for adolescents with a visible difference: a mixed-method study. Preprint. 2021.
232. Riobueno-Naylor A, Williamson H, Kogosov A, Wang S, Drexler A, Canenguez K, et al. 432 Feasibility and Implementation of the YP Face IT Online Program for Youth Recovering from Burn Injuries. *Journal of Burn Care & Research*. 2019;40(Supplement_1):S188-S9.
233. Schulz KF, Altman DG, Moher D. CONSORT 2010 Statement: updated guidelines for reporting parallel group randomised trials. *BMJ*. 2010;340:c332.
234. Brislin RW. Back-translation for cross-cultural research. *Journal of cross-cultural psychology*. 1970;1(3):185-216.
235. Nelson SC, Kling J, Wängqvist M, Frisén A, Syed M. Identity and the body: Trajectories of body esteem from adolescence to emerging adulthood. *Developmental Psychology*. 2018;54(6):1159.
236. Lawrence JW, Rosenberg L, Mason S, Fauerbach JA. Comparing parent and child perceptions of stigmatizing behavior experienced by children with burn scars. *Body Image*. 2011;8(1):70-3.
237. Ranta K, Junttila N, Laakkonen E, Uhmavaara A, La Greca AM, Niemi PM. Social Anxiety Scale for Adolescents (SAS-A): measuring social anxiety among Finnish adolescents. *Child Psychiatry & Human Development*. 2012;43(4):574-91.
238. Fauerbach JA, Spence RJ, Patterson DR. *Adult Burn Injury*. 2006.

239. Willemse H, Geenen R, Van Loey NE. Reliability and structural validity of the Dutch version of Perceived Stigmatization Questionnaire in adults with burns. *Burns*. 2020.
240. Diedrichs PC, Atkinson MJ, Garbett KM, Williamson H, Halliwell E, Rumsey N, et al. Randomized controlled trial of an online mother-daughter body image and well-being intervention. *Health Psychology*. 2016;35(9):996.
241. Cohen J. A power primer. *Psychol Bull*. 1992;112(1):155-9.
242. Moss TP, Bailey C, Griffiths C, Lawson V, Williamson H. Development of new psychometric instruments to measure appearance distress during adolescence: the Adolescent Appearance Distress Scales. *PeerJ PrePrints*, 2014 2167-9843.
243. Frisén A, Lunde C, Berg AI. Developmental patterns in body esteem from late childhood to young adulthood: A growth curve analysis. *European Journal of Developmental Psychology*. 2015;12(1):99-115.
244. Folker AP, Mathiasen K, Lauridsen SM, Stenderup E, Dozeman E, Folker MP. Implementing internet-delivered cognitive behavior therapy for common mental health disorders: A comparative case study of implementation challenges perceived by therapists and managers in five European internet services. *Internet Interventions*. 2018;11:60-70.
245. Gee C, Williamson H, Maskell J, Kimble R, Newcombe P. Challenges of recruiting adolescents for appearance-related research in a specialist tertiary hospital. *J Paediatr Child Health*. 2018.
246. Axén I, Björk Brämberg E, Galaasen Bakken A, Kwak L. Recruiting in intervention studies: challenges and solutions. *BMJ Open*. 2021;11(1):e044702.
247. Vall-Roqué H, Andrés A, Saldaña C. The impact of COVID-19 lockdown on social network sites use, body image disturbances and self-esteem among adolescent and young women. *Progress in Neuro-Psychopharmacology and Biological Psychiatry*. 2021;110:110293.
248. Wallander JL, Varni JW, Babani L, DeHaan CB, Wilcox KT, Banis HT. The social environment and the adaptation of mothers of physically handicapped children. *J Pediatr Psychol*. 1989;14(3):371-87.
249. Goodacre T, Swan MC. Cleft lip and palate: current management. *Paediatrics and Child Health*. 2012;22(4):160-8.
250. Darrow DH, Greene AK, Mancini AJ, Nopper AJ. Diagnosis and Management of Infantile Hemangioma. *Pediatrics*. 2015;136(4):e1060-e104.
251. Deater-Deckard K, Scarr S. Parenting stress. New Haven, CT: Yale Univ. Press; 2004.
252. Abidin RR, Abidin RR. Parenting Stress Index (PSI): Pediatric Psychology Press Charlottesville, VA; 1990.
253. Abidin RR. Parenting Stress Index: Manual, Administration Booklet,[and] Research Update. Charlottesville, VA: Pediatric Psychology Press; 1983.
254. Deater-Deckard KD, Panneton RK. Parental stress and early child development: adaptive and maladaptive outcomes. Cham: Springer; 2017. Available from: 10.1007/978-3-319-55376-4.
255. Pinquart M. Meta-Analysis of Anxiety in Parents of Young People with Chronic Health Conditions. *J Pediatr Psychol*. 2019;44(8):959-69.

256. Stock NM, Costa B, White P, Rumsey N. Risk and Protective Factors for Psychological Distress in Families Following a Diagnosis of Cleft Lip and/or Palate. *Cleft Palate Craniofac J.* 2020;57(1):88-98.
257. Collett BR, Cloonan YK, Speltz ML, Anderka M, Werler MM. Psychosocial Functioning in Children with and without Orofacial Clefts and Their Parents. *Cleft Palate Craniofac J.* 2012;49(4):397-405.
258. Baker SR, Owens J, Stern M, Willmot D. Coping strategies and social support in the family impact of cleft lip and palate and parents' adjustment and psychological distress. *Cleft Palate Craniofac J.* 2009;46(3):229-36.
259. Cazeau C, Blei F, Gonz  les Hermosa MdRF, Cavalli R, Boccara O, F  lster-Holst R, et al. Burden of Infantile Hemangioma on Family: An International Observational Cross-Sectional Study. *Pediatr Dermatol.* 2017;34(3):295-302.
260. Hatfield E, Cacioppo JT, Rapson RL. Emotional contagion. *Curr Dir Psychol Sci.* 1993;2(3):96-100.
261. ISCED. ISCED 2011 Operation Manual. Guidelines for classifying national education programmes and related qualifications. 2011.
262. de Brock AJLL, Vermulst AA, Gerris JRM, Abidin RR. Nijmeegse ouderlijke stress index: meetinstrument voor de vaststelling van stress bij opvoeders: een uitgebreide versie (NOSI) voor psychodiagnostische doeleinden en een verkorte versie (NOSIK) voor signaleringsdoeleinden: Swets & Zeitlinger; 1992.
263. van der Pal SM, Maguire CM, Bruil J, Cessie S, van Zwieten P, Veen S, et al. Very pre-term infants' behaviour at 1 and 2 years of age and parental stress following basic developmental care. *Br J Dev Psychol.* 2008;26(1):103-15.
264. Meijssen DE, Wolf MJ, Koldewijn K, van Wassenae AG, Kok JH, van Baar AL. Parenting stress in mothers after very preterm birth and the effect of the Infant Behavioural Assessment and Intervention Program. *Child: Care, Health and Development.* 2011;37(2):195-202.
265. van der Veek SMC, Kraaij V, Garnefski N. Cognitive coping strategies and stress in parents of children with Down syndrome: A prospective study. *Intellect Dev Disabil.* 2009;47(4):295-306.
266. Arrindell WA, Ettema JHM. SCL-90: Handleiding bij een multidimensionele psychopathologie-indicator [SCL-90: Manual for a multifaceted measure of psychopathology]. Lisse: Swets & Zeitlinger; 1986.
267. Nelson P, Glenn AM, Kirk S, Caress AL. Parents' experiences of caring for a child with a cleft lip and/or palate: a review of the literature. *Child Care Health Dev.* 2012;38(1):6-20.
268. IBM Corp. IBM SPSS Statistics for Windows, Version 25.0. Armonk, NY: IBM Corp; 2017.
269. Scorgie K, Sobsey D. Transformational outcomes associated with parenting children who have disabilities. *Ment Retard.* 2000;38(3):195-206.
270. Li Y, Cao F, Cao D, Wang Q, Cui N. Predictors of posttraumatic growth among parents of children undergoing inpatient corrective surgery for congenital disease. *J Pediatr Surg.* 2012;47(11):2011-21.
271. Jayawickreme E, Blackie LER. Post-traumatic Growth as Positive Personality Change: Evidence, Controversies and Future Directions. *Eur J Pers.* 2014;28(4):312-31.

272. Schwartz CE, Bode R, Repucci N, Becker J, Sprangers MAG, Fayers PM. The clinical significance of adaptation to changing health: A meta-analysis of response shift. *Qual Life Res.* 2006;15(9):1533-50.
273. Lee CY, Lee Y, Wang LJ, Chien CY, Fang FM, Lin PY. Depression, anxiety, quality of life, and predictors of depressive disorders in caregivers of patients with head and neck cancer: A six-month follow-up study. *J Psychosom Res.* 2017;100:29-34.
274. Lockhart E. The mental health needs of children and adolescents with cleft lip and/or palate. *Clin Child Psychol Psychiatry.* 2003;8(1):7-16.
275. van Dalen M, Hermans MM, Leemreis WH, Kraaij V, De Laat PCJ, Pasmans SGMA, et al. Emotional and behavioural problems in children with a cleft lip with or without palate or an infantile haemangioma. Manuscript submitted for publication.
276. Lukaviciute L, Navickas P, Navickas A, Grigaitiene J, Ganceviciene R, Zouboulis CC. Quality of life, anxiety prevalence, depression symptomatology and suicidal ideation among acne patients in Lithuania. *Journal of the European Academy of Dermatology and Venereology.* 2017;31(11):1900-6.
277. Egeberg A, Hansen PR, Gislason GH, Thyssen JP. Patients with rosacea have increased risk of depression and anxiety disorders: a Danish nationwide cohort study. *Dermatology.* 2016;232(2):208-13.
278. Stock NM, Feragen KB. Psychological adjustment to cleft lip and/or palate: A narrative review of the literature. *Psychology & Health.* 2016;31(7):777-813.
279. Williams JM, Currie C. Self-Esteem and Physical Development in Early Adolescence::Pubertal Timing and Body Image. *The Journal of Early Adolescence.* 2000;20(2):129-49.
280. van der Toorn SLM, Huizink AC, Utens EMWJ, Verhulst FC, Ormel J, Ferdinand RF. Maternal depressive symptoms, and not anxiety symptoms, are associated with positive mother-child reporting discrepancies of internalizing problems in children: a report on the TRAILS Study. *European Child & Adolescent Psychiatry.* 2010;19(4):379-88.
281. Kahn RS, Brandt D, Whitaker RC. Combined effect of mothers' and fathers' mental health symptoms on children's behavioral and emotional well-being. *Arch Pediatr Adolesc Med.* 2004;158(8):721-9.
282. Azuine EA, Singh GK. Father's Health Status and Inequalities in Physical and Mental Health of U.S. Children: A Population-Based Study. *Health Equity.* 2019;3(1):495-503.
283. Alleva JM, Sheeran P, Webb TL, Martijn C, Miles E. A Meta-Analytic Review of Stand-Alone Interventions to Improve Body Image. *PLoS One.* 2015;10(9):e0139177.
284. Tsangaris E, Riff KWW, Goodacre T, Forrest CR, Dreise M, Sykes J, et al. Establishing content validity of the CLEFT-Q: a new patient-reported outcome instrument for cleft lip/palate. *Plastic and Reconstructive Surgery Global Open.* 2017;5(4).
285. Catalogue of Bias Collaboration, Nunan D, Bankhead C, Aronson JK. Selection Bias: Catalogue Of Bias; 2017 [Available from: <https://catalogofbias.org/biases/selection-bias/>].

286. Price J, Kassam-Adams N, Alderfer MA, Christofferson J, Kazak AE. Systematic review: A reevaluation and update of the integrative (trajectory) model of pediatric medical traumatic stress. *Journal of Pediatric Psychology*. 2016;41(1):86-97.
287. Alexander M. Managing patient stress in pediatric radiology. *Radiol Technol*. 2012;83(6):549-60.
288. Bevilacqua F, Morini F, Ragni B, Braguglia A, Gentile S, Zaccara A, et al. Pediatric medical traumatic stress (PMTS) in parents of newborns with a congenital anomaly requiring surgery at birth. *Journal of Pediatric Surgery*. 2021;56(3):471-5.
289. Ben Ari A, Margalit D, Udassin R, Benarroch F. Traumatic Stress among School-Aged Pediatric Surgery Patients and Their Parents. *Eur J Pediatr Surg*. 2019;29(5):437-42.
290. Thornton M, Harcourt D, Deave T, Kiff J, Williamson H. "Have We Done Enough?" A Cross-condition Exploration of the Experiences of Parents Caring for A Child with an Appearance-affecting Condition or Injury. *Developmental Neurorehabilitation*. 2021:1-11.
291. Cousino MK, Hazen RA. Parenting Stress Among Caregivers of Children With Chronic Illness: A Systematic Review. *Journal of Pediatric Psychology*. 2013;38(8):809-28.
292. Douma M, Maurice-Stam H, Gorter B, Krol Y, Verkleij M, Wiltink L, et al. Online psychosocial group intervention for parents: Positive effects on anxiety and depression. *Journal of Pediatric Psychology*. 2020.
293. Tanner JL, Dechert MP, Frieden IJ. Growing up with a facial hemangioma: parent and child coping and adaptation. *Pediatrics*. 1998;101(3):446-52.
294. Johansson B, Ringsberg KC. Parents' experiences of having a child with cleft lip and palate. *Journal of advanced nursing*. 2004;47(2):165-73.
295. Rumsey N, Harcourt D. *The Oxford handbook of the psychology of appearance*. Oxford: Oxford University Press; 2012. Available from: <https://doi.org/10.1093/oxfordhb/9780199580521.001.0001>.
296. Gan LL, Lum A, Wakefield CE, Nandakumar B, Fardell JE. School Experiences of Siblings of Children with Chronic Illness: A Systematic Literature Review. *Journal of Pediatric Nursing*. 2017;33:23-32.
297. Knecht C, Hellmers C, Metzger S. The Perspective of Siblings of Children With Chronic Illness: A Literature Review. *Journal of Pediatric Nursing*. 2015;30(1):102-16.
298. Spek V, Cuijpers P, Nyklíček I, Riper H, Keyzer J, Pop V. Internet-based cognitive behaviour therapy for symptoms of depression and anxiety: a meta-analysis. *Psychol Med*. 2007;37(3):319-28.
299. Zucchelli FA, Donnelly O, Sharratt ND, Hooper N, Williamson HM. Patients' Experiences of an Acceptance and Commitment Therapy-Based Approach for Psychosocial Difficulties Relating to an Appearance-Affecting Condition. *The European Journal of Counselling Psychology*. 2021;9(1):29-40.
300. Boswell JF, Kraus DR, Miller SD, Lambert MJ. Implementing routine outcome monitoring in clinical practice: Benefits, challenges, and solutions. *Psychotherapy Research*. 2015;25(1):6-19.

301. Gee C, Maskell J, Newcombe P, Kimble R, Williamson H. Opening a Pandora's Box that can't be salvaged: Health professionals' perceptions of appearance-related care in an Australian pediatric specialist hospital. *Body Image*. 2019;31:1-12.

List of abbreviations

ACT	Acceptance and Commitment Therapy
AFB	Absence of Friendly Behaviour
ANOVA	Analysis of Variance
ANCOVA	Analysis of Covariance
BESAA	Body Esteem Scale for Adolescents and Adults
BILD-Q	Body Image Life Disengagement Questionnaire
CAU	Care As Usual
CBSA	Competentiebelevingsschaal voor Adolescenten
CBT	Cognitive Behavioural Therapy
CBCL	Child Behaviour Checklist
CDI-2	Child Depression Inventory-2
CL/P	Cleft Lip and/or Palate
CL±P	Cleft Lip with or without Palate
CSB	Confused and Staring Behaviour
EQ-5D-5L	EuroQol-5D-5L
FNE	Fear of Negative Evaluation
HB	Hostile Behaviour
iCBT	Internet-delivered Cognitive Behavioural Therapy
IH	Infantile Haemangioma
ISCED	International Standard Classification of Education
LES	Life Engagement Scale
NF1	Neurofibromatosis Type 1
NOSI-K	Nijmeegse Ouderlijke Stress Index (verkorte vorm)
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-analyses
PSI	Parenting Stress Index
PSQ	Perceived Stigmatisation Questionnaire
RCT	Randomised Controlled Trial
ROM	Routine Outcome Monitoring
SAD-General	Social Avoidance and Distress in general
SAD-New	Social Avoidance and Distress specific to new situations or unfamiliar peers
SAS-A	Social Anxiety Scale for Adolescents
SCL-90	Symptom Checklist – 90
SDQ	Strengths and Difficulties Questionnaire
SIST	Social Interaction Skills Training
SPPA	Self-Perception Profile for Adolescents
SST	Social Skills Training
YPF	Young People's Face IT
YP Face IT	Young People's Face IT

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Publications

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Van Dalen, M., Hermans, M.M., Leemreis, W. Kraaij, V., de Laat, P.C.J., Pasmans, S.G.M.A., Versnel, S.L., Koudstaal, M.J., Hillegers, M.H.J., Utens, E.M.W.J. & Okkerse, J.M.E. (2021). Emotional and behavioural problems in children with a cleft lip with or without palate or an infantile haemangioma. *The Cleft Palate-Craniofacial Journal*.

Van Dalen, M., Pasmans, S.G.M.A., Aendekerk, E.W.C., Mathijssen, I.M.J., Koudstaal, M.J., Williamson, H., Hillegers, M.H.J., Utens, E.M.W.J. & Okkerse, J.M.E. (2021). Acceptability and feasibility of an online psychosocial intervention for adolescents with a visible difference: a mixed-method study. doi: 10.31234/osf.io/fbj9g

Van Dalen, M., Leemreis, W. Kraaij, V., de Laat, P.C.J., Pasmans, S.G.M.A., Versnel, S.L., Koudstaal, M.J., Hillegers, M.H.J., Utens, E.M.W.J. & Okkerse, J.M.E. (2021). Parenting children with a cleft lip with or without cleft palate or a visible infantile haemangioma: a cross-sectional study of distress and parenting stress. *The Cleft Palate-Craniofacial Journal*. doi: 10.1177/1055665621993298

Van Dalen, M., Pasmans, S.G.M.A., Aendekerk, E.W.C., Mathijssen, I.M.J., Koudstaal, M.J., Timman, R., Williamson, H., Hillegers, M.H.J., Utens, E.M.W.J. & Okkerse, J.M.E. (2021). Investigating online psychological treatment for adolescents with a visible difference in the Dutch YP Face IT study: protocol of a randomised controlled trial. *BMJ Open*, 11. doi: 10.1136/bmjopen-2020-041449

Van Dalen, M., Dierckx, B., Pasmans, S.G.M.A., Aendekerk, E.W.C., Mathijssen, I.M.J., Koudstaal, M.J., Timman, R., Williamson, H., Hillegers, M.H.J., Utens, E.M.W.J. & Okkerse, J.M.E. (2020). Anxiety and depression in adolescents with a visible difference: A systematic review and meta-analysis. *Body Image*, 33, 38-46. doi: 10.1016/j.bodyim.2020.02.006

Kennis, M., Gerritsen, L., **van Dalen, M.**, Williams, A., Cuijpers, P. & Bockting, C. (2020). Prospective biomarkers of major depressive disorder: A systematic review and meta-analysis. *Molecular Psychiatry*, 25, 321-338. doi: 10.1038/s41380-019-0585-z

Utens, E., Stapersma, L., van der Mheen, M., **van Dalen, M.** & Dessens, A. (2019). Depressie en angst bij kinderen en jongeren met een lichamelijke aandoening: screening en behandeling. *Kinder- & Jeugdpsychotherapie*, 46(1).

Kennis, M., Gerritsen, L., **van Dalen, M.**, Williams, A., Cuijpers, P., & Bockting, C. (2018). T149. Do We Have Evidence for Predictive Biomarkers for Major Depressive Disorder? A Meta-Analysis and Systematic Review of Prospective Studies. *Biological Psychiatry*, 83(9), S186. doi: 10.1016/j.biopsych.2018.02.486

PhD portfolio

Name PhD student: Marije van Dalen
 Erasmus MC department: Child and Adolescent Psychiatry/
 Psychology
 Research school: NIHES
 PhD period: November 2017 – June 2021
 Promoters: Prof.dr. E.M.W.J. Utens
 Prof.dr. M.H.J. Hillegers
 Supervisor: Dr. J.M.E. Okkerse

1. Phd training	Year	Workload (ECTS)
General academic skills		
Gemstracker & Limesurvey, Erasmus MC	2017	1.0
Basic course Rules and Organisation for Clinical Researchers (BROK), Erasmus MC	2018	1.5
CPO: Patient Oriented Research, Erasmus MC	2018	0.3
Integrity in Science, Erasmus MC	2019	0.3
Specific research skills		
Basic Course on R, Molmed	2019	1.8
Biostatistical methods I: Basic Principles, NIHES	2019	5.7
Biostatistical Methods II: Classical Regression Models, NIHES	2019	4.60
Repeated measurements in Clinical Studies, NIHES	2020	1.70
Workshops		
Award winning presentation by Rikkert Stuve	2018	0.15
Deel Basiskwalificatie Onderwijs (BKO, Erasmus MC):		
Teach the Teacher	2019	0.70
Individual Guidance	2019	0.15
Presentation workshop by Rikkert Stuve	2020	0.3
International and national conferences and presentations		
Science Café Child and Adolescent Psychiatry/Psychology, Erasmus MC (attende	2017-2020	2.0
Research Meetings Child and Adolescent Psychiatry/Psychology, Erasmus MC (attende	2017-2021	2.0
Member's day Nevus Netwerk Nederland (oral presentation)	2018	0.3
Sophia Research Day, Erasmus MC (attende	2018-2019	0.3
PhD Day, Erasmus MC (attende	2018	0.3
European Pediatric Psychology Conference (EPPC), Ghent, Belgium (poster presentation)	2019	0.5
Member's day, vereniging voor Hemangiomen en Vasculaire Malformaties (HEVAS) (oral presentation)	2018	0.3

Day for Psychologists, Dutch Burns Association (oral presentation)	2018	0.3
Yearly Alopecia Conference, Alopecia Vereniging (oral presentation)	2019	0.3
Kinderdag Alopecia Vereniging (oral presentation)	2019	0.3
PhD weekend, department of Dermatology, Erasmus MC (oral presentation)	2019	0.3
RTL Nieuws (oral presentation)	2019	0.15
World Psoriasis Day, Psoriasispatiënten Nederland (oral presentation)	2019	0.30
R.I.O.T. Science Club (attendee)	2020	0.10
Nederlandse Vereniging voor Schisis en Craniofacial Afwijkingen (NVSCA) meeting (attendee)	2020	0.15
Research Meeting, Levvel, Amsterdam (oral presentation)	2021	0.15
Sophia Research Day, Erasmus MC (oral presentation)	2021	0.15
Research Meeting Department of Pediatrics, Erasmus MC (oral presentation)	2021	0.15
Research Meeting Pediatric Psychology, Erasmus MC (oral presentation)	2021	0.15
Appearance Matters 9 (AM9), virtual conference (oral presentation)	2021	1.0

Other

Coordination of Research Meetings Child and Adolescent Psychiatry/Psychology, Erasmus MC	2018-2020	1.0
Member of organising committee for the Sophia Research Day	2019-2020	0.3

2. Teaching

Medical students

Practical: Normal Development 0-18 years	2018	0.3
Supervision of systematic reviews, 3 rd year medical students	2018	0.5
Practical: Social Interaction	2019-2020	0.75
Practical: Observation Techniques	2019	0.3

Supervising Master's theses and research interns

Yasmine Khaddamallah (Clinical Child and Adolescent Psychology, Erasmus University Rotterdam)	2018-2019	3.0
<i>Symptomen van Aandachtsdeficiëntie-/hyperactiviteitsstoornis als Verklarende Factor in de Relatie tussen Single-Suture Craniosynostose en Intelligentie</i>		
Fiorella Huijgens (Health Sciences – Prevention & Public Health, VU)	2019	3.0
<i>Intelligence of Children with Different Types of Single Suture Craniosynostosis: Trigenocephaly and Scaphocephaly</i>		
Lisa Vogel (Clinical Psychology, Erasmus University Rotterdam)	2019-2020	3.0
<i>The Relationship between Perceived Stigmatization and Social Anxiety in Adolescents with a Visible Difference</i>		
Shreta Maskey (Medicine, Erasmus MC)	2019-2020	3.0

Is the location of a visible difference associated with symptoms of depression and social anxiety in adolescents? A cross-sectional study

Mette Alkema (Psychology, Utrecht University) – no thesis 2019-2020 1.0

Sara Meijer (Clinical Psychology, VU) 2020 3.0

Het verband tussen stigmatisering, lichaamsbeleving en sociale angst bij jongeren met een zichtbare aandoening en het verschil hiertussen in geslacht; een cross-sectionele studie

Aleksandra Kacperski (psychology, VU) – no thesis 2020 1.0

Suze van Capelleveen (psychology, VU) – no thesis 2020 1.0

Rianne Stuivenberg (health & medical psychology/developmental psychology, Leiden University) – no thesis 2020-2021 1.0

Asiye Sezer (medicine, Erasmus MC) 2020-2021 3.0

De relatie tussen subjectieve zichtbaarheid en stigmatisering en sociale angst en depressie bij jongeren met een zichtbare aandoening

Supervising bachelor's theses

Lisa Vogel (Psychology, Erasmus University Rotterdam) 2019 1.0

Quality of Life of Adolescents with a Visible Difference: A Literature Review

Marije Dinkelberg (Psychology, Erasmus University Rotterdam) 2020 1.0

Effectiviteit van Posttraumatische Sociale Ondersteuning aan Kinderen en Adolescenten met Brandwonden en hun Ouders

About the author

Marije van Dalen was born on November 28th, 1994 in De Lier, The Netherlands as a daughter to Liesbeth and Wim. She grew up with a younger sister and brother, Inge and Joost. In 2011, at 16 years old, she completed her secondary education (Atheneum, Grotius College, Delft) and International Baccalaureate in English (Grotius College, Delft). She then proceeded to study psychology at the Erasmus University Rotterdam (EUR), specialising in Clinical Psychology. During her bachelor she spent a semester abroad at Glasgow Caledonian University (United Kingdom). During her master she specialised in Clinical Child and Adolescent Psychology and was part of the Advanced Research Program. Her master's thesis focused on parenting practices and child emotion regulation and was graded 9/10.



After graduating she consecutively worked as an academic teacher at the Erasmus University Rotterdam (EUR) in the Clinical Child and Adolescent Psychology and Orthopedagogy master's, as an education and research assistant focusing on internationalising the psychology bachelor's track at Utrecht University (UU) and as a flex-worker working with people with an intellectual disability at 's Heeren Loo. In November 2017 she started her PhD project at the department of Child and Adolescent Psychiatry/Psychology at the Erasmus MC Sophia Children's hospital in Rotterdam, which resulted in the work described in this thesis. Her project was supervised by dr. J.M.E. Okkerse, Prof. dr. E.M.W.J. Utens and Prof. dr. M.H.J. Hillegers. During her PhD, the Dutch YP Face IT project was awarded the audience award from the *Nationale Jeugdhulpprijzen*. During her PhD project she also worked for ERN CRANIO and developed educational videos for patients affected by a craniofacial condition and their family. In April 2021 she started working as a research psychologist for the TIC-Genetics project at Levvel/Amsterdam UMC. Marije currently lives in De Lier with David.