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HEALTH RELATED QUALITY OF LIFE AMONG PRETERM CHILDREN: A LATENT PROFILE ANALYSIS

Master’s thesis

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Running head: Latent profiles of HRQoL among preterm children

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Health related quality of life among preterm children: a latent profile analysis

Abstract

Very preterm (VPT) children, in comparison to full-term children, are in greater risk of developing adverse cognitive, social or psychiatric outcomes, and their parents often report a lower health related quality of life (HRQoL) relative to their peers. Adverse outcome is frequently linked to their perinatal complications or socioeconomic (SE) status. The current study aims to find subgroups of preterm HRQoL using latent profile analysis (LPA) and regression analysis, to identify possible predictors among perinatal, SE factors and current problems. VPT children from two national birth cohorts: 2002/03, aged 15-17 (n = 70, M = 16.06) and 2007/08 10-12 (n = 113, M = 11.31) were included in the study. Parents answered questions about child's health and behavioural/emotional problems, study curriculum, and their own education; both the parent and the child filled a HRQoL questionnaire, Kidscreen-52. Four profiles were identified with LPA: "High HRQoL" (n = 22); "Optimal HRQoL" (n = 80); "Suboptimal HRQoL, low Autonomy" (n = 49) and "Low HRQoL, optimal Autonomy" (n = 32). Gestational age, school curriculum, gender, cohort, parent education and several somatic, emotional and behavioural problems were all found to be important predictors of belonging to a specific profile while the number of perinatal complications was not. With this study we explored the internal differences of HRQoL among preterm children in order to understand the trajectories leading to different outcomes.

Keywords: latent profile analysis, very preterm children, health-related quality of life

Tervisega seotud elukvaliteet enneaegsete laste seas: latentsete profiilide analüüs

Lühikokkuvõte

Väga enneaegsetel (EA) lastel on võrreldes õigeaegselt sündinud lastega suurem risk kognitiivsete, sotsiaalsete ja psühhiaatriliste probleemide tekkeks ning tihti hindavad EA laste vanemad oma laste tervisega seotud elukvaliteeti madalaks. Probleeme lapse- ja noorukieas seostatakse sageli perinataalsete tüsistuste ja sotsiaalmajandusliku seisundiga. Käesolevas uuringus kasutatakse latentsete profiilide analüüsi, et tuvastada väga EA laste elukvaliteedi alagrupid, ning regressioonanalüüsi, et leida, millised perinataalsed, sotsiaalmajanduslikud ja muud tegurid ennustavad elukvaliteedi taset. Uuringusse kaasati kaks üleriigilist väga EA laste sünnikohorti: 2002/03 sündinud lapsed, vanuses 15–17 (*n* = 70, *M* = 16.06) ja 2007/08, vanuses 10-12 (*n* = 113, *M* = 11.31). Vanemad vastasid küsimustele lapse tervise ja üldise heaolu, õppekava ja enda sotsiaalmajandusliku seisukorra kohta; nii vanem kui ka laps täitsid elukvaliteedi küsimustiku Kidscreen-52. Analüüsi tulemusena eristati neli profiili: „Kõrge elukvaliteet“ (*n* = 22); „Hea elukvaliteet“ (*n* = 80); „Keskmine elukvaliteet, madal iseseisvus“ (*n* = 49) ja “Madal elukvaliteet, keskmine iseseisvus” (*n* = 32). Profiilidesse kuulumist ennustasid gestatsioonivanus, õppekava, sugu, kohort, vanema haridustase ning paljud somaatilised, emotsionaalsed ja käitumuslikud probleemid. Perinataalsete tüsistuste arv ei ennustanud hästi profiilide jaotust. Grupisisesed erinevused väga EA laste elukvaliteedis, mida käesolevas töös uuriti, aitavad paremini mõista tegureid, mis need erinevused põhjustab.

Märksõnad: latentsete profiilide analüüs, väga enneaegsed lapsed, tervisega seotud elukvaliteet

Introduction

Since the rapid improvement of perinatal medical intervention there has been an increase in children born preterm (PT) who survive into childhood, adolescence and adulthood (Lemola, 2015; Wen et al., 2004). For example, perinatal mortality rate for very preterm children has dropped greatly in Estonia, from 65% in 1992 to 20% in 2013 (Toome, 2014). Nevertheless, there are still several perinatal complications affecting children born that early, and they are still at risk of developing adverse outcomes (Potharst et al., 2013). This raises the question – how do preterm children make it into their childhood, adolescence and adulthood. And more importantly – how do individuals, who are born preterm, make it in their lives. There are various longitudinal studies from other countries addressing prematurely born children that have followed their development in various domains, e.g. Bavarian Birth Cohort in Germany (Wolke et al., 2013) and EPIPAGE in France (Deloubel-Ayoung et al., 2019). Unfortunately, there have not been studies investigating adolescent outcome of prematurity in Estonia.

According to the current national follow-up management guideline for high-risk newborns (Toome et al., 2008), most very premature children are only followed by specialists until they turn 2 corrected[1] years old. After that, the progress of children who were born prematurely is no longer followed, as there are no regulated procedures for follow-up. Considering that they are still a risk group, it is essential we track their outcome, namely quality of life, and determine who are in greater risk than others.

Prematurity and perinatal complications

Preterm birth is defined as birth before gestational age (GA) of 37 weeks. Most research is made on children born before the GA of 32 (including 31 weeks and 6 days), which is considered very preterm (VPT). Children born before GA of 28 (27+6) are considered extremely preterm (EPT) (World Health Organisation, 2015). For the past 10 years an average of 147 children a year were born very preterm in Estonia, making it an average of 1.026% of all births in Estonia (Tervise Arengu Instituut, n.d).

There are various perinatal complications accompanying preterm birth that have an impact on the later health outcome: bronchopulmonary dysplasia (BPD), a chronic lung disease that forms from the damage to the immature lungs caused by multiple factors like infection and mechanical ventilation (Jobe and Bancalari, 2001); intraventricular haemorrhage (IVH), a

[1] Corrected age: chronological age reduced by the number of weeks the infant was born before 40 GW

bleeding in the brain's ventricular system (McCrea and Ment, 2008); periventricular leukomalacia (PVL), a brain injury, necrosis of white matter near the ventricles (Volpe, 2001); necrotizing enterocolitis (NEC), Bell's stages 2 and 3 are considered definite diagnosis that could result in partial bowel necrosis, the child might need surgical intervention and lead to growth failure (Lin and Stoll, 2006); retinopathy of prematurity (ROP), an eye disease that can lead to abnormal vision, caused by abnormal development of retinal blood vessels (International Committee for the Classification of Retinopathy of Prematurity, 2005) and small for gestational age (SGA), birthweight below the 10^{th} percentile (Fenton, 2003). All these perinatal/neonatal complications have been found to be linked with a poorer neurodevelopmental and/or behavioural outcome (Böhm et al., 2002; Johnson and Marlow, 2011; Kersbergen et al., 2016; Moster et al., 2008; Ortinau and Neil, 2019; Potharst et al., 2013; Taylor and Clark, 2016).

Neurodevelopmental and academic outcome among prematurely born children

In general, children born preterm have more health-related problems than children born full-term. Even when excluding congenital anomalies, preterm children have been found to have poorer motor skills than their full-term (FT) peers (Allotey et al., 2017; Kieviet et al., 2009). The occurrence of cerebral palsy (CP) among VPT born children is 9%, in contrast to 0,1% among FT born children (Larroque et al, 2008). Motor impairment is found in up to 32% of PT born children at age 5 years, mediated by complex minor neurological dysfunction and low IQ (Van Hus et al., 2000). The link between cognitive delay and motor impairment might also be working the other way. Oudgenoeg-Paz and others (2017) suggest that motor delay in early childhood might affect the IQ in later life, as impaired children have less chance to explore their surrounding and interact with the world. Sensorimotor deficiencies, such as visual and hearing deficiency are also more common among VPT children than among FT children, the risk increasing with lower gestational age (Larroque, 2008).

In general, preterm children score lower in overall intelligence scores (Aarnoudse-Moens et al., 2009; Allotey et al., 2017; Brydges et al., 2018). Some intelligence subscales are more affected than the others. According to Allotey et al. (2017), the least affected by prematurity is verbal intelligence, while performance intelligence (executive functions) domains are more impaired among children born preterm. Working memory and processing speed are found to be poorer among PT children than their FT peers. Compared to term born children, the difference in general intelligence and executive functions varies from 0.5-0.8 SD (Lemola,

2015) or on average 10.9 points (Bhutta et al., 2002). In addition to poorer cognitive results, the amount of children with moderate and severe neurodevelopmental disabilities (detected in motor, cognitive, speech, hearing, and ophthalmological assessments) that is considered as neurodevelopmental impairment (NDI) among preterm children is greater than among FT children. The number of children with NDI is approximately 19% among EPT children (Adams-Chapman et al., 2018).

Lower results on IQ scores are also reflected on their school performance. Children born preterm in general report poorer academic achievement (Aarnoudse-Moens et al., 2009; Allotey et al., 2017) the effect size being the greatest in reading skills, less so in mathematics and spelling. Deficits in cognitive function partly account for lesser academic skills and their academic trajectories, but problems remain even after excluding major disabilities, such as autism spectrum disorder (ASD) and cerebral palsy (CP) (Moster et al., 2008).

Internalizing and externalizing problems among preterm born children

Johnson and Marlow (2011) have proposed a “preterm behavioural phenotype”, consisting of 3 main problematic domains: social, inattention and anxiety problems.

Lesser social skills among preterm born children has often been observed. Extremely preterm children report more peer and social problems than their FT peers (Linsell, 2019). These skills are evaluated with self-administered test, and it is important to note that there is an inconsistency between child-rated and proxy (parent- and teacher-rated) results: VPT children and adolescents rate their social skills and problems equal to their FT counterparts, while teachers and parents rate their VPT children less socially competent (Twilhaar, 2019). Deficits in social skills are found to be related to deficits in understanding other’s emotions (especially negative ones) (Wocadlo and Riegel, 2006) and cognitive control (Twilhaar et al., 2019). Social and emotional regulation problems among VPT children are, according to MRI studies, linked to both functional and structural brain differences in frontoparietal and orbitofrontal brain areas (Healy et al., 2013; Urbain et al., 2018). Preterm born children are also found to be bullied more often, which itself contributes to an increased risk of emotional problems (Wolke et al., 2015).

While studies show that PT children have more externalising problems than FT children, the most prevalent among them are attention problems (Johnson and Wolke, 2013). For example, the most salient symptom for preterm children with ADHD, a common diagnosis among this group, is inattention (Johnson and Wolke, 2013). It has been suggested that only inattentionhyperactivity and peer problems are more prevalent, whereas conduct problems are not Deloubel-Ayoung et al., 2019). Other studies show an overall increase of all externalising problems among preterm children (Aarnoudse-Moens et al., 2009; Allotey et al., 2017; Farooqi et al., 2007). Behavioural problems are strongly related to cognitive impairment, however, an increased risk of behavioural problems remains even when adjusting for cognitive performance (Deloubel-Ayoung, 2019). In addition to ADHD, autism spectrum disorder (ASD) is very often linked to prematurity (Aarnoudse-Moens et al., 2011; Allotey et al., 2017; Johnson et al., 2010; Johnson and Wolke, 2013).

In addition to externalising problems, preterm children are also reported to have more internalising problems (Aarnoudse-Moens et al., 2009; Allotey et al., 2017; Deloubel-Ayoung et al., 2019). Studies have reported a significantly higher number of emotional problems, including depression and anxiety, among preterm children (Burnett at al., 2011; Lindstörm et al., 2009). Preterm children are found to be especially prone to anxiety, more than depression, compared to FT children (Johnsons and Marlow, 2011). Problems with anxiety among preterm children are often linked to social environmental factors, such as social competence and bullying (Johnson and Wolke, 2013). People (including adolescents and young adults) born preterm are also more vulnerable to bipolar disorder (Nosarti et al., 2012) and schizophrenia (Farooqi et al., 2007; Nosarti et al., 2012). In total, individuals born preterm are about 3.5 times more likely to receive a diagnosis of psychiatric condition (Burnett et al., 2011).

Eventually, the reasons behind adverse outcomes are still not clear. In addition, it is not even clear, whether prematurity accounts for these disabilities, or whether underlying biological factors that cause these cognitive problems, lead to preterm birth (Moster et al., 2008). Nevertheless, the immaturity of the developing brain is usually held responsible for the cognitive delay (Lemola, 2015; Ortinau et al., 2019; Taylor and Clark 2016) and mental health outcome (Johnson and Wolke, 2013; Lindström et al., 2009) of preterm born children. However, it is still important to note a large variety among preterm children. While in total they have more psychiatric problems than FT children, there are many who have consistently favorable outcomes, according to psychiatric research (Johnson and Wolke, 2013).

Environmental and socio-economic factors

It is also important to consider socio-economic factors when interpreting the outcome of prematurity, as low socioeconomic status (SES) has generally an impact on child development and well-being (Bradley and Corwyn, 2002). In addition, socioeconomic disadvantage (lower education and income) is in itself associated with increased risk of adverse birth (preterm or low birthweight) (Blumenshine et al., 2010). Some researchers have found that various environmental factors, such as parental education and SES have a more incremental role on the cognitive outcome than the perinatal factors (Bhutta et al., 2002; Taylor and Clark, 2016). Shah and others (2013) found that very preterm children accompanied with supportive parenting had better IQ outcome at age 36 months than late preterm (32-37 GA) with supportive parenting; unsupportive parenting had the exact reverse effect. While Bhutta and colleagues (2002) proposed that preterm born children's brains are more vulnerable to negative outcome, Shah et al. (2013) suggested more neuroplasticity among children born very preterm. The presence of a low SES also increases the effect that preterm birth has on psychiatric disorders (Lindström et al., 2009).

Health related quality of life (HRQoL) among preterm children

Given that preterm children are at risk of more physical and mental impairments, their and their parents' self-perceived quality of life is an important indicator of the long-term outcome of prematurity.

To understand the general functioning level of a person, we must also take into account the person's own views about one's subjective health (Saigal, 2013). In order to encompass this, multi-dimensional quality of life measures should be used (Ravens-Sieberer, 2005). World Health Organisation defines quality of life (QoL) as "A state of complete physical, mental, and social well-being, not merely the absence of disease . . ." (World Health Organisation). Health related quality of life (HRQoL) is often measured, to understand the psychological complications related to health, to assess outcome and plan interventions. As QoL and HRQoL are used interchangeably in the literature, the following overview uses both terms.

There are various tools to measure QoL or HRQoL, some of which are more condition specific (for example tools that measure the QoL of those, who have been diagnosed with asthma), the others are broader and more general. Most often used QoL and HRQoL measuring tools – questionnaires – for children and adolescents usually have two versions: parent-proxy and child-rated (Saigal, 2013). Most tools measuring HRQoL measure social, physical and psychological/emotional functioning, but the exact dimensions vary from questionnaire to questionnaire (Zwicker and Harris, 2008).

As research has showed us time and time again, prematurity is a risk factor for several problems, including neurodevelopmental impairments, psychiatric disorders, and social adjustment. However, these areas do not assess the overall well-being. Thus, researchers have started calling upon other researchers to investigate quality of life (Saigal, 2013), i.e. to ask the subjects themselves how they feel they are doing. Unfortunately, research into HRQoL outcome among preterm children is not yet as extensive as the research into cognitive/neuropsychological outcome among PT children. Nevertheless, a few researchers have been looking into quality of life as well.

To begin with, preterm children are often compared to those who were full-term. Very preterm children generally score lower in HRQoL (Berbis et al., 2012; Wolke et al., 2013; Zwicker and Harris, 2008), although there are a few exceptions (Saigal, 2013). Berbis and others (2012) note that VPT children scored significantly lower in following domains: body image, vitality, psychological wellbeing, school performance and overall HRQoL; while there was no difference in family relationships, peer relationships, leisure activities, physical well-being and teacher relationship.

There are several factors contributing to the HRQoL outcome among preterm children. For example, HRQoL among preterm is often found to be associated with the presence of NDI (Berbis et al., 2012; Natalucci et al., 2016; Saigal, 2013). Perinatal factors contributing to the quality of life outcome are neonatal sepsis and surgical intervention (Natalucci et al., 2016). Other contributing factors are earlier disabilities, IQ, internalising problems (Wolke et al., 2013) as well as the presence of ADHD and poorer socioeconomic status (Natalucci et al., 2016).

Another issue often discussed in research on prematurely born children is the problem of parent-proxy vs children rated QoL (Zwicker and Harris, 2008). For example, Wolke and colleagues (2013) found that adolescents rated their quality of life to be lower than their parents did, in contrast to Natalucci and others (2016), who found that children rated their QoL equal to their peers while their parents did not.

Nevertheless, the outcome for preterm-born children is not as grave as it might seem at first glance. Zwicker and Harris (2008) conclude that although there is quite a lot of difference between FT and PT in young childhood, the differences diminish over time, being non-significant by young adulthood. Many researchers note that it’s not the prematurity itself that links to lower HRQoL but what’s in prematurity – developmental delays, presence of psychiatric problems and low SES eventually determines the quality of life (Wolke et al., 2013; Natalucci et al., 2016). Saigal (2013) stresses that prematurely born children still report high or very high quality of life that is often comparable to their term born peers.

Knowing there is a vast heterogeneity among preterm children in terms of their developmental, psychiatric, and socio-economic problems, one could assume there is a similar heterogeneity among HRQoL results as well. That is, among preterm children there is a subgroup of children who are doing well, and a subgroup of children, who are doing not so well. For example, Johnson and colleagues (2017) identified 3 different subgroups of cognitive and behavioural outcomes among moderately and late preterm children (GA of 32 to 37 weeks), and Heeren and others (2017) identified 6 subgroups of different cognitive functioning profiles. Dividing preterm children into such groups permitted them to investigate the possible factors distinguishing the groups from each other.

Objective

With the present study, I aim to further understand how preterm born children function in their adolescence, as they are no longer systematically in the health care provider's sight. Also, considering that not all children are equal, and the outcome among preterm children is diverse, I wish to examine the differences of HRQoL outcome between these children and explore the possible distinguishable profiles of HRQoL among preterm children. Furthermore, I wish to see what are the trajectories leading to a poorer HRQoL; and in contrast, what factors are protective.

Hypotheses

H1: Preterm child-rated and parent-proxy ratings in HRQoL questionnaire are generally lower than control child-rated and parent-proxy HRQoL.

H2: Parent-proxy rating in HRQoL is higher than child ratings among preterm children.

H3: Subgroups of HRQoL among preterm children can be identified.

H4: Subgroups with lower HRQoL are associated with lower primary caregiver's education.

H5: Subgroups with lower HRQoL are associated with more perinatal complications.

H6: Subgroups with lower HRQoL are associated with more emotional, physical, developmental and social problems.

Method

Sample

The sample of this study consists of 2 national population based birth cohorts of very premature (GA < 32 weeks) children born in Estonia in 2002/2003 and 2007/2008. The two original cohorts consist of 501 surviving children. In the preliminary study, 425 children's school information was gathered from the Ministry of Education and Science. 82 children, who follow Russian curriculum, were excluded. Parent contact information could not be gathered from school for 106 children. In total, 243 parents were approached. 6 parents did not wish to participate and 49 failed to respond. Five participants were excluded on the grounds of too little information.

The final sample of this study consists of 183 (a total of 75% of people contacted) participants making it a total of 36.53 % of the 2 cohorts (34% of the 02/03 cohort and 38.3% of the 07/08 cohort). For 19 children only parent-proxy answers were optained, as the children were not able to answer the questionnaire (due to their impairments) or the children failed to answer for other reasons. Four responders were not parents, but either a foster parent or a member of the family taking care of the child. For this reason, the responder to the questionnaire is called primary caregiver in this study. Characteristics of the sample can be found in Table 1.

For control, Estonian national sample for the adaptation project of Kidscreen-52 was used (Konstabel et al., 2016). The sample consisted originally of 1162 parent and 1199 child responses, but only Estonian speaking and age matching groups were included (N = 436). Younger age group was 10-13 years of age (M_{age} = 11.02, SD = .3) and consisted of 135 girls and 94 boys. The older age group consisted of adolescents 15-18 years of age (M_{age} = 17, SD = .34), of whom 125 were girls and 82 were boys. There is no information about control group's perinatal age, so we have no knowledge of how many of them could be born preterm.

Measures

Final data consists of perinatal data, derived from earlier studies on these cohorts (Toome, 2014), information about child school-age outcome and parent socioeconomic status (answered by parent or the primary caregiver); HRQoL measure Kidscreen-52, filled both by the child and the parent/primary caregiver.

Table 1. Sample perinatal and outcome characteristics by cohort

	Cohort		
	02/03 (*n* = 70)	07/08 (*n* = 113)	Total (*N* =183)
Perinatal characteristics			
Gestational age (weeks), *n* (%)			
EPT (GW < 28)	21	34	55 (30)
VPT (GW 28 – 31)	49	79	128 (70)
Gender, *n* (%)			
Boys	28 (40)	57 (50)	85 (46)
Girls	42 (60)	56 (50)	98 (54)
Perinatal morbidities, *n* (%)			
ROP	12 (17)	15 (13)	27 (15)
BPD	15 (23)	24 (21)	40 (22)
IVH	5 (7)	5 (4)	10 (6)
PVL	2 (3)	5 (4)	7 (4)
NEC	5 (7)	12 (10)	17 (9)
SGA	6 (9)	6 (5)	12 (7)
N of perinatal morbidities, *n* (%)			
0	44 (63)	68 (60)	112 (61)
1	21 (30)	28 (25)	49 (27)
2	2 (3)	11 (10)	13 (7)
3	3 (4)	6 (5)	9 (5)
Outcome characteristics			
Mean age (*SD*)	16.06 (0.78)	11.31 (0.77)	13.12 (2.44)
School curriculum(1), *n* (%)			
National curriculum	58 (85)	98 (88)	156 (87)
Individualized curriculum	2 (3)	6 (5)	8 (5)
Simplified curriculum	4 (6)	5 (5)	9 (5)
Special needs management	4 (6)	2 (2)	6 (3)
Caregiver education(2), *n* (%)			
Primary	3 (5)	5 (5)	8 (5)
Secondary	38 (59)	38 (38)	76 (46)
Tertiary	23 (36)	58 (57)	81 (49)
Problematic areas, *n* (%)			
Sleeping	6 (9)	7 (6)	13 (7)
Eating	5 (7)	15 (13)	20 (10)
Physical	17 (24)	36 (32)	53 (29)
Developmental	17 (24)	25 (22)	42 (23)
Social	9 (13)	19 (17)	28 (15)
Behavioural	6 (9)	17 (15)	23 (13)
Emotional	16 (23)	16 (14)	32 (18)

Comments: (1) – missing values (*n* = 3); (2) – missing values (*n* = 18); ROP – retinopathy of prematurity (stages 3 and greater); BPD – bronchopulmonary dysplasia; IVH – intraventricular haemorrhage (grades II and IV); PVL – periventricular leukomalacia; NEC – necrotising enterocolitis (Bell's stages 2 and 3); SGA – small for gestational age

Child neonatal information

1. Gestation week
2. Bronchopulmonary dysplasia (BPD)
3. Intraventricular haemorrhage (IVH)
4. Periventricular leukomalacia (PVL)
5. Necrotizing enterocolitis (NEC)
6. Retinopathy of prematurity (ROP)
7. Small for gestational age (SGA)

Perinatal morbidities (perinatal factors 2 to 7) were combined into one score.

Socioeconomic background and child outcome

Following child outcome and socio-economic information was asked:

1. Current problems with the child: behavioural problems (problems with attention, following instructions or impulsivity); eating problems (problems with appetite and/or chewing, biting); emotional problems (anxiety); physical problems (problems with hearing, seeing, movement, weight, growth or breathing); sleeping problems and developmental problems (problems with speech or learning); social problems (difficulties with social relations).
2. Child’s school curriculum: national curriculum, individualized curriculum, simplified curriculum or special needs management curriculum.
3. Primary caregiver’s education: primary, secondary (high school or vocational training) or tertiary (university or an equal degree).

Kidscreen-52

Kidscreen is a health-related quality of life (HRQoL) questionnaire for children and adolescents aged 8 to 18 years. The questionnaire consists of 52 questions and is divided into 10 dimensions (see Figure 1). All questions are on 5-point Likert-scale. Higher scores in each dimension indicate higher HRQoL. There is a separate questionnaire to be filled by the parent (parent-proxy) and child (child-rated).

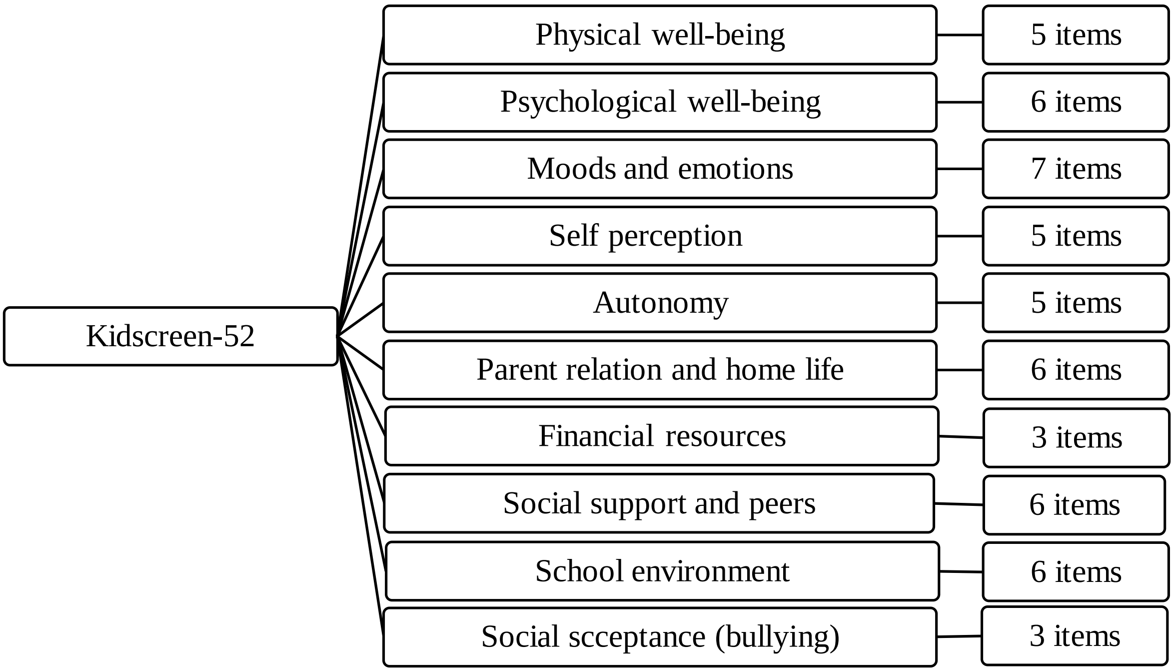

Figure 1. KIDSCREEN-52 dimensions and the number of items corresponding to each dimension.

The questionnaire was developed by Kidscreen Group, a project that had 13 European countries contributing to the development (Ravens-Sieberer et al, 2005). The questionnaire was adapted into Estonian by Konstabel and others (2016). The psychometric properties of Estonian Kidscreen have been tested on 781 children ages 7 to 19. Reliability among child and parent-proxy answers (Cronbach Alpha measured from α =.70 to α =.87 within different dimensions) of the instrument range from satisfactory to good (Konstabel et al, 2016).

Procedure

Prior to the main study, a pre-study was conducted to find the contacts of the 2 cohorts. Information about the child school was retrieved from the Ministry of Education and Research; child contact information was received from corresponding school psychologists.

The participants were recruited to the study via a phone call to their parents. The parents were asked to participate on the grounds of contributing to research of long-term effects of preterm birth. All the subjects have previously been participants to other studies regarding prematurity. The parents were asked to fill a questionnaire via their preferred method (mail or online). All the questions were asked on trust-basis, the parent’s responses about the child’s health situation were not checked from medical databases.

Both pre-study and the current study have been approved by Tartu University Ethics Committee (permission numbers 288T_10 and 291/T-24, respectively).

Statistical analyses

All the data analyses were conducted using RStudio (R Core Team, 2020), version 1.2.5042. Following R packages were used: *mclust* (Scrucca et al., 2016), *nnet* (Venables and Ripley, 2002), *psych* (Revelle, 2019), *tidyverse* (Wickham et al, 2019), *careless* (Yentes et al., 2018), *ez* (Lawrence, 2016) and *stargazer* (Hlavak, 2018).

Internal reliabilities of both parent-proxy and self-report Kidscreen-52 were measured using Cronbach Alpha. To measure the difference between parent-proxy and self-report, paired-samples t-test was used. Independent t-test measured differences between preterm sample and control. Report differences in Kidscreen-52 between sexes and cohorts were checked with independent t-tests.

To distinguish subgroups of preterm born children with different profiles in HRQoL, latent profile analysis (LPA) was used with parent-proxy Kidscreen-52 results. LPA is a statistical method to determine hidden subgroups within a sample. (Gibson, 1959). It classifies individuals into new subgroups, based on their response patterns. This makes it possible to create groups, or profiles, and then examine these profiles separately.

Model selection (the number of profiles) was based on following information criteria: (1) BIC: Bayesian Information Criteria (Scwarz, 1978), (2) AIC: Akaike Information Criteria (Akaike, 1987); (3) Log-L: Log-Likelihood (Fisher, 1950) and (4) ICL: Integrated Completed Likelihood (Biernacki, Celeux and Govaert, 2000) and (5) BLRT: Bootstrap Likelihood Ratio Test. Entropy (Celeux and Soromenho, 1996), which is often used to fit models into classes, was not taken into account, as entropy criteria is taken into consideration when calculating ICL. Among the most commonly used are BIC, AIC and entropy (Tein, Coxe and Cham, 2013), while BIC and BLRT are found to be the most accurate indices (Nylund, Asparouhov and Muthen, 2007). BLRT uses the likelihood ratio test to compare every model to the previous one, to determine whether adding one class improves the model significantly. The final model was chosen based on these criteria and the usability and interpretability of latent subgroups.

Model validity was tested with multivariate analysis of variance (MANOVA), all profiles were compared to each other with independent t-test.

To analyse the differences between different profiles, we added perinatal and outcome factors as predictors to the model. For this, multinominal logistic regression was used. Prior to regression analysis, multicollinearity was tested among the predictors, using tetrachoric correlation between binary predictors and polyserial correlation between non-binary predictors. Variance inflation factor (VIF) was calculated to assess multicollinearity. Cut-off of VIF < 5 was chosen as criteria (Vatcheva et al., 2016).

Results

As this is the first time Kidscreen-52 is used to measure HRQoL of preterm children in Estonia, Cronbach Alpha of all dimensions was checked. Cronbach Alpha varied from acceptable (α = .75) to very good (α =.92) among parent-proxy and from acceptable (α =.74) to good (α =.89) among child-rated results (Appendix 1 Table 1). Correlations between Kidscreen-52 dimensions can be found in Appendix 2 Table 1.

T-tests between Kidscreen-52 dimensions

First, independent t-tests were run to identify possible differences between preterm sample and control. Preterm parents rated their children's Autonomy (*M* = 19.71, *SD* = 3.67) significantly higher ($t(350) = 2.52$, $p = .012$) than did control parents (*M* = 18.95, *SD* = 3.74); Social relations ($t(294) = -3.11$, *p* = . 0.002) and Social acceptance (bullying) ($t(280) = -2.4$, *p* = . 0.017) was rated significantly lower by preterm children's parents. Between child-rated Kidscreen-52, preterm children rated their Moods and Emotions ($t(289) = 2.48$, $p = .014$) and Autonomy ($t(322) = -2.55$, $p = .011$) higher; Social relations ($t(247) = 2.48$, $p = .014$) and Social acceptance ($t(251) = -2.04$, $p = .043$) lower than did control children. Control parent-proxy and child-rated dimensions' means and t-test results between preterm sample and control can be found in Appendix 3 Table 1. Results do not confirm hypothesis 1, where we predicted that preterm parents and children rate their HRQoL generally lower than does control.

Second, paired t-tests were conducted to compare the HRQoL results between preterm parent-proxy and child-report (Table 2). Difference was observed in four dimensions: in Physical well-being, Psychological well-being, Social relations and Social Acceptance, where children scored their HRQoL significantly higher than did their parents. This is contrary to our hypothesis, where it was assumed that children generally rate their HRQoL lower than do their parents.

To classify children by their HRQoL, parent-proxy Kidscreen-52 was used. As both cohorts and sexes were analysed together, differences were checked with t-tests. There were no differences in any dimensions between boys and girls. The sole difference found between cohorts was in Social Acceptance dimensions ($t(174) = 2.79$, $p = .006$).

Table 2. T-test between preterm parent-proxy and child-rated Kidscreen-52

Kidscreen-52 dimensions	Parent-proxy Mean (*SD*)	Child-rated Mean (*SD*)	*t-value (df)*	*p*
1. Physical well-being	18.14 (3.75)	18.96 (3.44)	-2.11 (162)	.036*
2. Psychological well-being	22.85 (3.60)	24.09 (4.69)	-3.34 (163)	.001**
3. Moods and emotions	30.31 (3.46)	30.68 (4.55)	.24 (163)	.807
4. Self-perception	20.86 (3.23)	20.89 (3.93)	.17 (163)	.868
5. Autonomy	19.71 (3.67)	19.92 (4.1)	-.67 (163)	.506
6. Parent relation and home life	24.06 (3.72)	24.75 (4.7)	-1.78 (163)	.078
7. Financial resources	11.45 (2.82)	11.57 (3.2)	.31 (163)	.756
8. Social relations and peers	20.67 (5.44)	22.26 (5.82)	-2.93 (163)	.004**
9. School environment	21.69 (4.08)	22.1 (4.82)	-1.52 (163)	.132
10. Social acceptance (bullying)	13.60 (1.85)	13.92 (1.71)	-2.68 (162)	.005**

Comment: * $p < .05$; ** $p < .01$

Latent profile analysis

To decide the number of profiles, BIC, AIC, Log-L, ICL and BLRT were used. Lower values of AIC, BIC and ICL and higher value of Log-L indicate better fit. BLRT *p*-values were checked. As can be seen in Table 3, either 2 or 4 profile models are recommended. Based on BIC, considered a superior statistic to AIC and entropy (ICL is using entropy as penalty) (Tein, Coxe and Cham, 2013), and considering theoretical meaningfulness, four class model was selected.

Table 3. Model fit indices

Number of classes	BIC	AIC	Log-L	ICL	BLRT
2	4729.518	4453.502	-2140.751	4742.151	-
3	4724.960	4612.628	-2271.314	4746.576	.001
4	**4723.292**	**4572.446**	**-2239.223**	**4762.223**	**.001**
5	4741.403	4552.043	-2217.022	4796.493	.004
6	4757.807	4529.934	-2193.967	4809.522	.003
7	4784.883	4518.495	-2176.248	4833.207	.034

Comments: Best fitting model per criteria is depicted in bold. BIC: Bayesian Information Criteria; AIC: Akaike Information Criteria; Log-L: Log-Likelihood; ICL: Integrated Completed Likelihood; BLRT: Bootstrap Likelihood Ratio Test. Chosen model is indicated in bold.

As hypothesized, latent profiles were identified. All four profiles of preterm HRQoL are pictured on Figure 2. Profile 4 (n = 22) consists of children with the highest HRQoL and could be named “High HRQoL”. Profile 3 is the largest group (*n* = 80) and has the “optimal HRQoL”. Profile 2 (*n* = 49) has second lowest HRQoL values in all but Autonomy and Home life dimensions and could be described as “Suboptimal HRQoL, low Autonomy” profile. Profile 2 (*n* = 32) has mostly the lowest values and could be named “Low HRQoL, optimal Autonomy”.

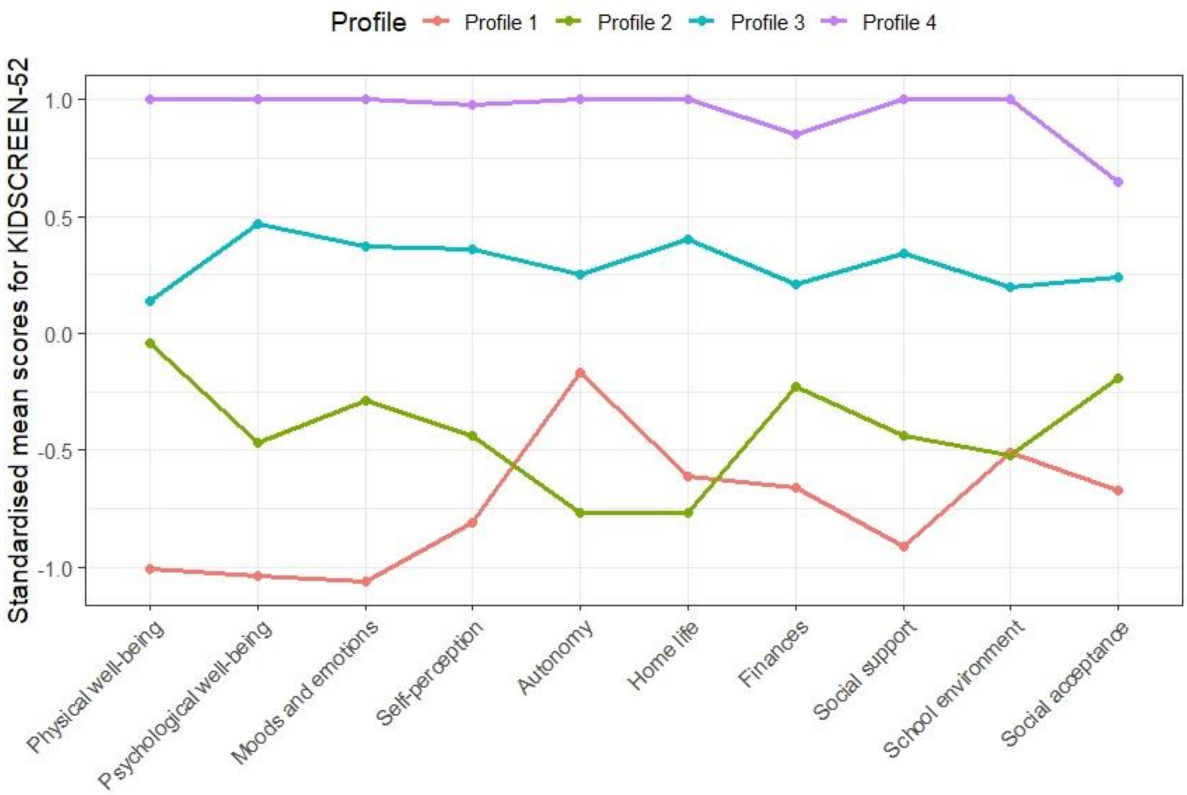

Figure 2. Four-profile model with standardized mean scores for all Kidscreen-52 dimensions

Validation analyses were conducted for the four profile model with MANOVA on all 10 Kidscreen-52 subscales (Table 4), all groups were found to be significantly different in all dimensions. Independent t-tests served as post-hoc tests of differences between profiles.

Table 3. Means and standard deviations between four profiles on Kidscreen-52 dimensions with results in MANOVA

	Profile 1	Profile 2	Profile 3	Profile 4	MANOVA
	M (SD)	*M (SD)*	*M (SD)*	*M (SD)*	*F* (1, 181)
1. Physical well-being	13.84(3.72) (2)(3)(4)	18.23 (2.87) (1)(4)	18.6 (2.81) (1) (4)	22.55 (1.87) (1) (2) (3)	94.87***
2. Psychological well-being	18.59 (4.02) (2)(3)(4)	21.18 (1.97) (1) (3)(4)	24.56 (2.03) (1) (2) (4)	26.55 (2.11) (1) (2) (3)	198.88***
3. Moods and emotions	26.25 (4.3) (2)(3)(4)	29.29 (2.49) (1) (3)(4)	31.6 (1.95) (1) (2) (4)	33.82 ((1.18) (1) (2) (3)	146.29***
4. Self-perception	18.09 (4.6) (3)(4)	19.33 (2.29) (3)(4)	22.03 (1.83) (1) (2) (4)	24.05 (1.25) (1) (2) (3)	99.7***
5. Autonomy	19 (4.39) (2)(4)	16.86 (2.68) (1) (3)(4)	20.6 (2.77) (2) (4)	23.86 (1.49) (1) (2) (3)	46.11***
6. Home life	21.69 (3.73) (3)(4)	21.04 (2.58) (3)(4)	25.51 (2.30) (1) (2) (4)	28.91 (1.31) (1) (2) (3)	134.23***
7. Financial resources	9.53 (3.58) (3)(4)	10.65 (2.56) (3)(4)	12.03 (2.18) (1) (2) (4)	13.86 (1.55) (1) (2) (3)	47.5***
8. Social relations and peers	15.29 (6.13) (2) (3)(4)	18.29 (3.92) (1) (3)(4)	22.4 (3.39) (1) (2) (4)	27.55 (2.11) (1) (2) (3)	150.29***
9. School environment	19.41 (4.4) (3)(4)	19.55 (3.19) (3)(4)	22.51 (3.16) (1) (2) (4)	26.82 (2.44) (1) (2) (3)	72.2***
10. Social acceptance	12.47 (2.59) (3)(4)	13.16 (1.66) (3)(4)	13.99 (1.4) (1) (2) (4)	14.77 (0.75) (1) (2) (3)	31.58***

Comments: *** < .001; (1) – statistically significant difference (< .05) from Profile 1; (2) – statistically significant difference (< .05) from Profile 2; (3) – statistically significant difference (< .05) from Profile 3; (4) – statistically significant difference (< .05) from Profile 4

Regression analysis

Following variables were chosen to use as predictors for regression analysis: gestational age, cohort, number of perinatal morbidities, primary caregiver's education, school curriculum, social problems, behavioural problems, eating problems, emotional problems, physical problems, sleeping problems and developmental problems. Prior to regression analysis, a frequency table (Table 4) was created to see how the variables were distributed among the 4 profiles.

Table 4. Frequencies of possible predictors by profiles

	Profile 1 *n* = 32	Profile 2 *n* = 49	Profile 3 *n* = 80	Profile 4 *n* = 22	Total *N* = 183
Gender, *n* (%)					
Boys	12 (37)	21 (43)	46 (58)	6 (27)	85 (46)
Girls	20 (63)	28 (57)	34 (42)	16 (73)	98 (54)
N of perinatal morbidities, *n* (%)					
0	13 (40)	31 (63)	49 (61)	19 (86)	112 (61)
1	11 (34)	15 (31)	21 (27)	2 (9)	49 (27)
2	6 (19)	1 (2)	5 (6)	1 (5)	13 (7)
3	2 (6)	2 (4)	5 (6)	-	9 (5)
Gestational age (weeks)$^{(1)}$, *n* (%)					
EPT (GW < 28)	16 (50)	14 (29)	21 (26)	4 (18)	55 (30)
VPT (GW 28 – 31)	16 (50)	35 (61)	59 (74)	18 (82)	128 (70)
Cohort, *n* (%)					
02/03	18 (56)	13 (27)	29 (36)	10 (45)	70 (38)
07/08	14 (44)	36 (73)	51 (64)	12 (55)	113 (62)
School curriculum$^{(2)}$, *n* (%)					
National curriculum	19 (61)	45 (94)	71 (91)	21 (96)	156 (87)
Individualized curriculum	2 (7)	1 (2)	4 (5)	1 (4)	8 (5)
Simplified curriculum	5 (16)	1 (2)	3 (4)	-	9 (5)
Special needs management	5 (16)	1 (2)	-	-	6 (3)
Caregiver's education$^{(3)}$, *n* (%)					
Primary	3 (11)	1 (2)	4 (5)	-	8 (5)
Secondary	11 (41)	14 (32)	41 (53)	10 (59)	76 (46)
Tertiary	13 (48)	29 (66)	32 (42)	7 (41)	81 (49)
Problematic areas, *n* (%)					
Sleeping	10 (31)	-	3 (4)	-	13 (7)
Eating	9 (28)	7 (14)	4 (5)	-	20 (10)
Physical	18 (56)	9 (18)	21 (26)	5 (23)	53 (29)
Developmental	16 (50)	11 (23)	14 (18)	1 (5)	42 (23)
Social	11 (35)	8 (16)	9 (11)	-	28 (15)
Behavioural	13 (40)	4 (8)	5 (6)	1 (5)	23 (13)
Emotional	11 (34)	9 (18)	10 (12)	2 (9)	32 (18)

Comments: (1) – in later analyses GA was used as a continuous variable; (2) – missing values (*n* = 3); (2) – missing values (*n* = 18)

To detect possible multicollinearity between predictors, correlation analyses were run and VIF was calculated. Highest calculated VIF, between school curriculum and developmental problems, was 1.6 (< 5). Therefore, all factors were included as predictors to the regression analysis.

Multinominal logistic regression analysis was conducted (Table 5). The regression was run four times, with each profile serving as a reference in turn. Profiles 3 and 4 were considered, as they are the most stable ones (Figure 2). Eventually Profile 3, as a stable and most numerous one, was chosen to be the reference group.

Table 5. Multinominal logistic regression odds rations and 95% confidence intervals. All comparisons were made in reference to Profile 3.

	Profile 1	Profile 2	Profile 4
	OR (95% *CI*)	*OR* (95% *CI*)	*OR* (95% *CI*)
Gestational age	0.90*** (0.52, 1.28)	0.98*** (0.74, 1.23)	1.12 *** (0.75, 1.49)
Perinatal morbidities			
0	1.00	1.00	1.00
1	0.85 (-.81, 2.51)	0.4 (-0.77, 1.56)	0.41 (-1.37, 2.18)
2	2.87* (-.35, 6.09)	0.08 (-2.96, 3.12)	1.55 (-1.35, 4.46)
3	1.16 (-1.83, 4.14)	0.23 (-2.05, 2.50)	0.00
School curriculum			
National	1.00	1.00	1.00
Individualized	12.79*** (9.21, 16.38)	0.27 (-2.53, 3.06)	3.95** (0.69, 7.22)
Simplified	11.31*** (8.04, 14.57)	1.88 (-0.90, 4.65)	0.00
Special	3×10^{10}*** (3×10^{10}, 3×10^{10})	6×10^{9} (6×10^{9}, 6×10^{9})***	27.91*** (27.91, 27.91)
Caregivers' education			
Primary	1.00	1.00	1.00
Secondary	0.14 (-3.93, 4.21)	5.90*** (2.84, 8.97)	4×10^{7}*** ($4\times^{107}$, 4×10^{7})
Tertiary	0.38 (-3.73, 4.49)	18.85*** (15.75, 21.96)	4×10^{7}*** (4×10^{7}, 4×10^{7})
Cohort			
02/03	1.00	1.00	1.00
07/08	0.06 (-1.93, 2.05)	1.43*** (0.47, 2.39)	0.93 (-0.33, 2.18)
Gender			
Boy	1.00	1.00	1.00
Girl	50.10*** (47.70, 52.49)	2.38*** (1.48, 3.28)	4.92*** (3.56, 6.29)
Current problems			
Developmental	0.89 (-1.301 3.07)	2.04*** (0.70, 3.38)	.43 (-2.61, 3.47)
Emotional	3.60*** (1.52, 5.68)	3.80*** (2.26, 5.35)	0.00
Sleep	6.84*** (4.13, 9.55)	0.00	0.03*** (0.03, 0.03)
Behavioural	35.78*** (33.24, 38.32)	1.25(-0.67, 3.17)	2.25(-.84, 5.34)
Physical	1.80** (0.04, 3.56)	.77(-0.34, 1.88)	0.97(-.57, 2.52)
Eating	12.80*** (10.17, 15.42)	1.73** (.12, 3.34)	0.00
Social	2.23** (0.40, 4.06)	2.74*** (1.28, 4.20)	0.00

*Comments: **p<0.05; ***p<0.01*

Regression analysis identified predictors, which were more likely to predict profile belonging. Contrary to our hypothesis, the number of perinatal complications did not predict well profile belonging (with the sole exception of 2 perinatal complications in Profile 1). Gestational age, gender and school curriculum were found to be important indicators of all profile belongings. We hypothesized that primary caregivers educational level is associated with profile belonging and so was found – primary caregiver's educational level predicted belonging to Profiles 2, 3 and 4. All problems increased a likelihood belonging to some group or another, with the most problematic areas found among Profile 1 members (Table 1). In return, the lack of sleep problems was identified as a protective factor for Profile 4. As hypothesized, various problems are good indicators of HRQoL group belonging.

Discussion

The main aim of this study was to explore the HRQoL of preterm children and adolescents. Health related quality of life is a broad term that indicates the self-perceived psychological, physical and social well-being (Zwicker and Harris, 2008). Several factors contribute to HRQoL, including disabilities, IQ, psychiatric and socioeconomic factors (Natalucci et al., 2016; Ravens-Sieberer et al., 2005; Wolke et al., 2013). As preterm children are a vulnerable group, many of whom have had various perinatal complications (Böhm, 2002; Potharst at al., 2013) and continue to have several developmental, medical and psychological problems (Brydges et al., 2018; Johnson and Marlow, 2011; Twilhaar et al., 2019), their self-perceived HRQoL should be examined (Saigal, 2013). However, as most preterm children are still doing well in terms of general functioning and quality of life (Zwicker and Harris, 2018), determining those who are at risk and more vulnerable is necessary to plan interventions and predict outcome.

In this study, our focus was on exploring the heterogeneity among preterm children and looking for the hidden subgroups in HRQoL of preterm children. Although latent profiles in preterm children's outcome (cognitive and behavioural) have been explored before (Heeren et al., 2017, Johnson et al., 2017), to our knowledge, LPA has not been used on HRQoL of premature children to this day. In our study, we found that four different profiles can be distinguished. Gestational age, school curriculum, primary caregiver's education and various somatic and/or behavioural, social and emotional problems were identified as predictors of the profiles. In addition, some differences were found between PT children and their parents as well the differences between PT group and control group in Kidscreen-52 ratings.

Firstly, it was hypothesized that both parents and children from preterm sample rate their HRQoL lower than does the control (H1). However, in most areas (Physical and Psychological well-being, Self-perception, Home life and School environment) both parents and children rated their quality of life equal to general population of the same age. Some areas were rated even higher among preterm sample; for example, both preterm children and their parents rated the Autonomy to be higher than that of their FT peers. Nevertheless, Social relations and Social acceptance (bullying) dimensions of preterm children were rated lower than the same dimensions by control (both in parent-proxy and child ratings). This is different from earlier findings by Berbis (2012), who found differences in other areas, but not in areas related to peer relationship. Saigal (2013), however, concludes in her review that there is no agreement whether preterm children rate their HRQoL lower than their peers, as the results by different researchers are confounding. However, relying on theory, according to which preterm children are socially less competent (Linsell, 2019; Twilhaar, 2019) and are bullied more often (Wolke et al, 2019) than their peers, these results are likely to reflect the reality.

Secondly, in contrast to earlier findings (Wolke et al, 2013) and the hypothesis in this work (H2), preterm children rated their HRQoL generally higher than did their parents. Significant differences were found in Physical and Psychological well-being, Social relations and Social acceptance.

The main purpose of this study was to explore the hidden groups within the sample. Saigal (2013) points out that most preterm children still have high HRQoL, despite of belonging to a risk group. Considering those, we decided to use a more individual-centred approach. Analysing HRQoL with latent profile analysis, four profiles emerged (H3). All these profiles were significantly different from each other and portrayed the heterogeneity within preterm children. **Profile 4**, the smallest group (n = 22), stands out as the “High HRQoL” profile. Their results are relatively steady and high across all dimensions. **Profile 3**, the “Optimal HRQoL” group, represents the children who still do well in terms of quality of life, but are still significantly different from Profile 4. Profile 3 has the most members in the group (n = 80), and most male members of all four profiles (58%). They too can be described as having stable results in different dimensions. **Profile 2** (n = 49) has generally a below average score in HRQoL and the lowest scores in Autonomy and Home life dimensions, whereas their Physical well-being is comparable to the Physical well-being in Profile 3. Profile 2 could be called the “Suboptimal HRQoL, low Autonomy” group. **Profile 1** (n = 32) has the lowest scores in HRQoL, with the exception of Autonomy and Home life. They are called “Low HRQoL, optimal Autonomy”. Profile 1 has particularly low results in Physical well-being, Psychological well-being and Moods and emotions. Profile 1 has the most members from the older (02/03) cohort (56%) of all four profiles.

In comparison to Profile 3, children in Profile 4 were more likely to be born later (in terms of gestational weeks), less likely to have various perinatal complications, more likely to be a girl and their primary caregiver is more likely to have a secondary or tertiary education. In comparison to Profile 3 they are also less likely to report sleep problems.

Profile 3 has more likely higher GA than Profiles 2 and 1, but younger than Profile 4. Children in Profile 3 are less likely than children in Profiles 1 and 2 to currently experience various problems, and are less likely to follow a special management curriculum. Also, in comparison to Profile 2, who in terms of HRQoL are doing less well, the primary caregivers in this profile have generally a lower education. This group has the greatest number of boys (58%), in comparison to other groups that were all more likely to have more girls.

Profile 2 (in comparison to Profile 3) is more likely to have smaller gestational age; are more likely studying in special needs curriculum; are more likely younger (from 07/08 cohort), are more likely girls; report more developmental, emotional, eating and social problems and their primary caregiver is more likely to have a secondary or tertiary education.

In comparison to Profile 3, Profile 1 is more likely to have a lower gestational age; more likely to be studying with either individualized, simplified or special need curriculum; are more likely to have 2 perinatal morbidities; are more likely girls and more likely have emotional, sleep, behavioural, physical, eating and social problems. School curriculum was also a very important predictor, as a total of 39% of preterm children from this profile do not study in the national curriculum (in comparison, this number stays below 10% in all other profiles). However, they do not differ from Profile 3 in terms of primary caregiver's education and developmental problems, whereas Profile 2 did.

It was hypothesized that more perinatal complications are associated with lower HRQoL (H4). Perinatal morbidities are not good predictors for HRQoL outcome, as the number of perinatal morbidities did not differ significantly in most profiles (the sole exception being the Profile 1). However, higher gestational age (a perinatal factor) was significantly linked to better HRQoL outcome. Lower GA is often linked to a poorer cognitive and psychiatric outcome (Bhutta, et al., 2008; Moster et al., 2008), and therefore could also be a predictor of a poorer HRQoL outcome. Individualized, simplified and special needs management curricula were also significant predictors of lower HRQoL profiles, and might be mediating the effect of low GA.

With our fifth hypothesis, we assumed that primary caregiver's education is associated with preterm children's HRQoL outcome (H5). There was an increase of caregivers with secondary or tertiary degree in Profiles 2 and 4, compared to Profile 3. That means that in our study caregiver's education did not have a linear effect on HRQoL, as Profile 3, the "optimal HRQoL" profile, had less caregivers with secondary and tertiary degree than has Profile 2. Lower SES, including parental education, is associated with various adverse outcomes among preterm children (Bradley and Corwin, 2002), including HRQoL (Natalucci et al., 2016). In this study, primary caregiver's education was found to be a more important predictor of HRQoL than were perinatal complications. SES is also found to be a more important indicator of low cognitive outcome than are perinatal factors (Bhutta et al., 2002; Taylor and Clark, 2016).

With the last hypothesis (H6), we predicted that various problems, such as physical and/or emotional, behavioural and social, predict belonging to a specific profile. We found that different problems were greatly associated with different profiles. Behavioural and physical difficulties were most strongly related to the lower HRQoL (Profile 1). Both internalising and externalising problems is associated with poorer HRQoL (Natalucci et al., 2016; Wolke et al., 2013). Interestingly, developmental problems did not predict Profile 1 belonging, even though that profile had the lowest results in Physical and Psychological well-being.

Limitations

This study has several limitations. Firstly, there is the eternal problem of sample group (n = 183) size. For research in prematurity, international collaboration for pooling data should be considered.

In terms of interpreting the results of regression analysis, caution about the results must be taken. For example, the odds ratios for some factors (for example regarding school curriculum, the $OR = 3\times10^{10}$) are extremely high because there were very few (or no) children in respective factor levels (thus yielding unstable estimates). Factors such as gender should be taken with caution, as the reference profile (3) had the most boys in the subgroup, thus inflating the probability of having more girls in other profiles.

It is also worth noting that this study has little objective measurements, HRQoL is a fully subjective questionnaire. In addition, as this study did not have diagnosis of children, we had to rely on parents' evaluation on their children's problems, another subjective measurement.

Future directions

Dividing people into groups and assessing them in terms of their profiles is an interesting measure and in my opinion, vastly underused. LPA is also often used within different scales, for example in Heeren and others' (2017) article, scales from two different measures were combined. For example, in next research on dividing preterm children into latent classes, other measurements (such as IQ test) should be used together with HRQoL measures.

For future research, LPA analysis on preterm children should also be either pooled together with controls' results or used to create profiles for control (similar to Johnson and other, 2017), in order to determine the "preterm profile". This approach would give a better overview of how and whether preterm children really differ from general population.

To maximize sample size, using international data sources should be an option. For example, a research platform such as RECAP Preterm (Zeitlin et al., 2020), an international collaborative project helping to pool data, aids researchers in connecting perinatal factors to outcome.

Conclusions

While previous research has studied HRQoL of preterm children as a homogenous group, this study took a more exhaustive look into the differences within preterm sample. In addition to evaluating the HRQoL of preterm children, we determined the possible risk factors as well as protective factors for children. Preterm children differ from each other in terms of their HRQoL and there are various factors, most notably gestational age, study curriculum, caregiver education and various current problems listed by the parent that contribute to the outcome. Taking all these into considerations will hopefully help future specialists in providing better care for preterm children and their parents.

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Appendix 1

Table 1. Cronbach α and means of preterm parent-proxy and child rated Kidscreen-52 dimensions.

	Parent-proxy		*Child-rated*	
	Mean (SD)	*α*	*Mean (SD)*	*α*
Physical well-being	18.14 (3.75)	.84	18.96 (3.44)	.84
Psychological well-being	22.85 (3.60)	.89	23.95 (5.04)	.89
Moods and emotions	30.31 (3.46)	.87	30.5 (5.12)	.87
Self-perception	20.86 (3.23)	.74	20.89 (3.93)	.75
Autonomy	19.71 (3.67)	.82	19.92 (4.1)	.82
Home life	24.06 (3.72)	.88	24.75 (4.7)	.85
Financial resources	11.45 (2.82)	.87	11.44 (3.42)	.89
Social relations	20.67 (5.44)	.89	22.26 (5.82)	.92
School environment	21.69 (4.08)	.87	22.1 (4.82)	.86
Social acceptance	13.60 (1.85)	08	13.84 (2.02)	.88

Appendix 2

Tabel 1: Correlation table of Kidscreen-52 dimensions, method = Pearson

	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20
Parent-proxy																				
1. Physical w-b(1)	–																			
2. Psychological w-b(1)	.58**	–																		
3. Moods and emotions	.43**	.62**	–																	
4. Self-perception	.29**	.43**	.56**	–																
5. Autonomy	.19*	.36**	.28**	.41**	–															
6. Home life	.34**	.55**	.44**	.43**	.53**	–														
7. Finances	.23**	.27**	.15	.15*	.31**	.36**	–													
8. Social support	.43**	.40**	.37**	.31**	.39**	.52**	.41**	–												
9. School environment	.24**	.37**	.29**	.36**	.33**	.53**	.28**	.34**	–											
10. Social acceptance	.13	.17*	.27**	.31**	.17*	.27**	.25**	.24**	.24**	–										
Child-rated																				
11. Physical w-b(1)	.65**	.46**	.43**	.38**	.23**	.26**	.22**	.32**	.35**	.32**	–									
12. Psychological w-b(1)	.45**	.60**	.52**	.36**	.21*	.35**	.21*	.22**	.37**	.18*	.64**	–								
13. Moods and emotions	.44**	.44**	.46**	.15	.08	.27**	.25**	.27**	.37**	.10	.47**	.68**	–							
14. Self-perception	.37**	.40**	.38**	.46**	.18*	.25**	.25**	.16*	.29**	.16*	.47**	.57**	.64**	–						
15. Autonomy	.30**	.37**	.25**	.27**	.39**	.35**	.35**	.23**	.36**	.20*	.43**	.55**	.48**	.51**	–					
16. Home life	.38**	.50**	.40**	.33**	.26**	.56**	.36**	.29**	.43**	.27**	.49**	.71**	.63**	.64**	.63**	–				
17. Finances	.33**	.29**	.20*	.17*	.18*	.27**	.51**	.30**	.31**	.22*	.32**	.36**	.40**	.43**	.49**	.57**	–			
18. Social support	.27**	.40**	.36**	.25**	.25**	.35**	.34**	.47**	.45**	.26**	.42**	.52**	.46**	.42**	.53**	.56**	.46**	–		
19. School environment	.30**	.41**	.33**	.25**	.20**	.31**	.29**	.21**	.68**	.18*	.53**	.65**	.59**	.49**	.53**	.61**	.48**	.55**	–	
20. Social acceptance	.10	.19*	.24 **	.05	.00	.18*	.13	.15	.16*	.48**	.19*	.27**	.33**	.13	.15	.23**	.15*	.16*	.23**	–

Comments: ** < .01; * < .05; (1) w-b – well-being

Appendix 3

Table 1. Means and standard deviations of all Kidscreen-52 dimensions, independent t-tests between sample and control

	Preterm		Control		Parent-proxy/ parent-proxy	Child-rated/ child-rated
Kidscreen dimensions	Parent-proxy Mean (*SD*)	Child-rated Mean (*SD*)	Parent-proxy Mean (*SD*)	Child-rated Mean (*SD*)	*t-value (df)*	*t-value (df)*
Physical well-being	18.14 (3.75)	18.96 (3.44)	18.42 (3.3)	18.7 (3.59)	-.87 (309)	.81 (303)
Psychological well-being	22.85 (3.60)	24.09 (4.69)	23.03 (3.57)	23.95 (4.11)	-.56 (242)	.35 (266)
Moods and emotions	30.31 (3.46)	30.68 (4.55)	30.53 (3.52)	29.66 (4.47)	-.73 (345)	2.48* (289)
Self-perception	20.86 (3.23)	20.89 (3.93)	18.9 (3.05)	20.21 (3.85)	.35 (324)	1.89 (288)
Autonomy	19.71 (3.67)	19.92 (4.1)	18.95(3.74)	18.99 (4.46)	2.52* (347)	2.42* (322)
Home life and parent relation	24.06 (3.72)	24.75 (4.7)	23.72 (3.99)	24.68 (4.52)	1.0 (368)	.16 (282)
Financial resources	11.45 (2.82)	11.57 (3.2)	11.27 (2.73)	12.12 (2.84)	.71 (334)	-2.09* (263)
Social relations and peers	20.67 (5.44)	22.26 (5.82)	22.1 (4.47)	23.55 (4.62)	-3.11** (294)	-2.55* (247)
School environment	21.69 (4.08)	22.1 (4.82)	21.65 (4.3)	21.5 (4.64)	.13 (366)	1.35 (287)
Social acceptance (bullying)	13.60 (1.85)	13.92 (1.71)	13.97 (1.42)	14.23 (1.47)	-2.4* (280)	-1.35* (251)

Comment: * $p < .05$; ** $p < .01$

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