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Supporting infants' mental health and
healthy weight development
through community health nurses' promoting
sensitive parenting

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1 Summary

The project is the first to explore intervention within municipality settings to target the earliest developmental trajectories of mental health problems and overweight via promoting sensitive parenting of infants of cognitive and regulatory vulnerabilities.

Mental health problems and overweight are major challenges to public health in the 21st century. These conditions often co-occur, they have their origin in early childhood, and research evidence suggest a key role of cognitive, emotional and behavioural regulation in the developmental trajectories of both mental health problems and overweight, with mounting evidence pointing to public health strategies of intervention starting in infancy and building on strategies of sensitive parenting. The research group behind this project has validated the conditions on which to build preventive intervention in infancy within the settings of Danish community health nurses, and we have developed a basic programme in which community health nurses are educated to address infants' mental health and development, The PUF (In Danish Psykisk Udvikling og Funktion) programme. Still, though urgently needed, an effective intervention to serve the most vulnerable infants is lacking.

The Infant Health project aims to develop and test an intensified intervention as an add-on to the PUF-programme, to address infants with major cognitive and regulatory vulnerabilities identified at age 9-10 months and adapted to the settings of community health nurses. The intervention (PUF-VIPP) will be created from an evidence-based method, the Video-based Intervention to Promote Positive Parenting (VIPPP), to comprise six therapeutic sessions delivered by the community health nurse during home visits over a three months period. The PUF-VIPP builds on teaching the health nurses to promote parents' sensitivity to meet infants' cognitive and regulatory vulnerabilities, while taking in account the particular needs of families of psycho-social disadvantage. A main part of the project is the development and testing of an intensive educational programme for community health nurses.

The Infant Health project is conducted in 16 municipalities across Denmark, and it builds on an already well-established cooperation between the community health nurses and the research group. We use the Intervention Mapping approach as the study frame and integrate the best practice of the community health nurses. The project includes a pilot phase to assess the fidelity and feasibility of the study measures, prior to a randomized controlled step-wedge study of intervention efficacy. The project has strong potentials of providing new research evidence on options of prevention to break the developmental trajectories of mental health problems and overweight in early childhood.

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2 Background

2.1 The public health challenges of mental health problems and overweight

Mental health problems and overweight are major challenges to population health in modern societies. Both are highly prevalent, also among children, and both have severe long-term prognoses regarding mental and physical health, social functioning, and premature death (1-5). Mental health problems and overweight often co-exist, they share risk factors (6, 7), and they share an origin early in development (6-8). Among children in Western European countries, including Denmark, about 15% of the population suffer from mental health disorders (9-14), with a higher prevalence in psycho-socially deprived populations, and the highest prevalence is seen in children from families of psycho-social disadvantage (12, 13, 15-17). As mental health disorders, overweight is a frequent public health concern, affecting about 20% of the child population from Western European countries, and among Danish children, one in eight is overweight when starting school (18, 19). Furthermore, the psycho-social risk factors associated with mental health problems are also associated with childhood overweight (20-23).

Public health strategies are urgently needed to reduce the prevalence of these common conditions (24-27), but so far, no strategies have shown to be effective (5, 22, 23, 28-31), leaving a gap in knowledge on novel ways of preventing mental health problems and overweight in the early stages of the child's development.

2.2 State of the art: Predictors of mental health problems

The majority of children's mental health problems have their origin within the first years of living (8, 27, 29, 32, 33). Psycho-social disadvantage plays an important role in the risk mechanisms, and increased risk has repeatedly been found in children of young parents, single parents, and parents of low education, parents of foreign ethnicity, and mentally ill parents (7, 13, 34-36). Pre- and perinatal adversities and cognitive and psycho-motor difficulties in infancy are associated with an increased risk of neuro-developmental disorders (13, 36), with infancy problems of language development, inattention, and deviant contact and communication being predictive of autism spectrum disorders, and disorders of hyperactivity and inattention, ADHD (32, 34, 37-40). Regulatory problems of eating, sleep, and emotional and behavioural regulation have shown to be highly predictive of mental health problems and disorders later in preschool to school age (27, 39, 41, 42). Regulatory problems are thus considered to represent the first manifestations of persistent dysregulation trajectories (40, 41, 43), showing an up to tenfold increased risk of mental health

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problems later in childhood, in particular ADHD, eating problems, and emotional- and behavioural problems (44-47).

Overall, and across areas of mental health vulnerability, the early parent-child relation seems to be a main moderator of risk and resilience (27, 48, 49), and challenges to parenting are considered to play a key role in the development of enduring problems (44, 50-54).

2.3 State of the art: Predictors of childhood overweight

Mounting evidence points to the early childhood origin of overweight, and a high risk of persisting health problems in children, who are overweight in infancy (20, 55-60). A study of Danish children has shown that 4% of the infant population in Denmark is classified as overweight according to WHO z-scores, and about 0.5% classified as obese (18, 61) with a more than sevenfold increased risk of persistent overweight from infancy to age 5-8 years, independent of child and family factors (18). The studies of Danish children have replicated findings from the international literature regarding psycho-social risk factors (24, 60, 62, 63) and they show that factors such as young parental age, low maternal education, single parent families, and ethnic minorities are highly associated with an increased risk of overweight in infancy (18, 21). The mechanisms behind the social pattern of overweight are suggested to include the gene-environment interaction (23). In early childhood, maternal obesity impacts the infant's feeding pattern and overall risk of overweight (64, 65) via difficulties related to breastfeeding, a higher risk among obese mothers to introduce high energy and fat foods very early, and difficulties for obese parents to regulate their appetite themselves, leaving them more or less responsive to the infant's hunger and satiety cues. Accordingly, parents with overweight have a tendency of excess food provision and the "over-riding" of the infant's internal satiety cues (66-68). Moreover, parents with overweight have an increased risk of contemporary mental health problems, e.g. ADHD and depression, which may further challenge their parenting (69).

2.4 Co-occurrence of children's mental health problems and overweight

Mental health problems often co-occur with overweight (70-77), and prospective longitudinal data indicate that among children and adolescents, the mental health problems tend to precede the development of overweight (70, 74, 77). The potential mechanisms include cognitive vulnerability regarding inhibitory control/reward sensitivity and sustained attention (78-83) leading to impulsive eating, and difficulties in delaying gratification, which are core features in feeding and eating behaviors demonstrated in children with disorders of hyperactivity and inattention, ADHD and co-occurrent overweight (70, 71, 76, 84). Infants' emotional regulation concern their ability to

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maintain an affective homeostasis confronted with stress-full experiences (49), and problems with emotion regulation are suggested to precede childhood emotional and behavioural problems (41, 53) and emotional eating (83, 85). Emotional eating is considered to develop through pathways of physiological stress responses, and through cardiac reactivity influencing appetite (6, 86). Also, stress exposures may induce hyper- or hypo-activation of the hypothalamic-pituitary-adrenal (HPA) axis, and potentially promote fat accumulation in visceral adipose tissues. These hormonal responses potentially influence appetite and attraction to sweet and fatty foods, mainly by stimulating reward pathways (86-89). Among the few prospective studies published in this area, a study of self-regulation skills and obesity in early childhood has shown that poor emotional regulation and lower inhibitory control at age 2 years is predictive of higher BMI at 5 years of age (81).

2.5 State of the art: Early intervention to target childhood mental health problems and overweight

Prevention of mental health problems and overweight has to start early in life and should include universal strategies as well as targeted interventions for children and families at risk (24, 25, 30, 55, 56). To be effective, the preventive strategies should start no later than infancy (27, 90) and include intervention to reduce risk exposures (26, 28), as well as targeted intervention to the infants most vulnerable (91-93). Across areas of infant vulnerability, the preventive strategies should include the parent-child relation, and in particular include strategies to promote parents' sensitivity to understand and handle the infant's vulnerability, called *sensitive parenting* (54, 94).

Regarding mental health vulnerability, most preventive programmes address pregnancy and perinatal adversities, or exposures associated with psycho-socially disadvantage, such as teenage parents or mothers with mental health problems (95-97), or they address specific problems in high-risk infants, e.g. developmental or behavioural problems, or problems related to attachment (95, 96, 98). Programmes to promote parenting mainly target behavioural problems in toddlers or older children and most are group-based, whereas individually targeted interventions mainly target attachment difficulties in younger children (95, 96, 98). Overall, no preventive interventions have been published that systematically address the range of mental health vulnerabilities seen in the youngest children. Among the methods published so far, the Video-feedback Intervention to Promote Positive Parenting, VIPP, takes an outstanding position however (99), in being highly effective in reducing both behavioural dysregulation and communicative problems in infants and

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toddlers (100) and being successfully used in families of psycho-social disadvantage, including mothers with eating problems (101, 102).

Regarding the early prevention of overweight, universal public health programmes are recommended to start in pregnancy, to promote healthy weight for mother and foetus/ infant, and to optimize breastfeeding and promote healthy nutrition in infancy (23, 24, 63). Moreover, targeted intervention is recommended for families with limited psycho-social resources to optimize the conditions of healthy weight development across early childhood and beyond (24, 31).

Still, although the evidence for obesity prevention in early childhood is growing (24, 31, 103), research on effective strategies is sparse and the outcomes associated with the available strategies have been modest (30, 104, 105). Across the literature on the early childhood trajectories of overweight, the importance of parenting holds a key position (6, 104), with the suggested risk trajectories linking infancy dysregulation to overweight being highly influenced by parenting. Taking novel research evidence on cognitive and regulatory vulnerabilities regarding unhealthy weight development and overweight into account, approaches that address the promotion of sensitive parenting are theoretically sound (6), however not yet fully explored (106).

In sum, there is a strong scientific rationale for public health interventions that include strategies to promote sensitive parenting across the range of cognitive and regulatory vulnerabilities seen in children below two years of age, to address the shared vulnerability traits in the early trajectories of mental health problems and overweight.

Promoting sensitive parenting has the potential of optimizing parents' understanding and regulation of their infant's cognitive, physiological, emotional and behavioural vulnerabilities, and thereby optimize the child's healthy mental development and healthy weight.

2.6 The particular challenges of intervention in disadvantaged families

The literature on interventions that address childhood mental health problems and overweight converges on the importance of parents' resources (7, 21, 29, 35, 107-109). The parents are key mediators of healthy mental development as well as healthy weight development in their child (24, 27, 33, 51, 110). Still, the current literature indicates that parents with a background of mental illness, low education, low income, and young age at the child's birth, more often experience challenges in providing a healthy and stimulating environment for their child, due to their own psychological vulnerabilities, and due to an associated risk of limited social and psychological resources in the external environment (35, 111, 112). Notably, families of ethnic minorities, socio-

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economic adversity, and families in which parents suffer from mental health problems have an increased risk of not benefitting sufficiently from universal efforts (26, 91, 113).

Regarding targeted interventions, parents may experience particular challenges, if the intervention implies that they have to change behaviours and habits that are integrated in their lifestyle and overall way of living (114). Therefore, to compile with the challenges in vulnerable families, the targeted intervention should address the specific needs and vulnerabilities of the family, e.g. in families of ethnic minorities and in families in which the parents suffer from mental health problems (113). The challenges experienced by parents with limited cognitive, mental and social resources and in particular, the vulnerabilities of parents with psychiatric problems are often overlooked aspects in the planning of preventive interventions. Still, these aspects have to be considered both in the ethical considerations and in the detailed planning of an intervention, and they have to be included in the teaching and supervision of the professionals, who deliver the intervention.

2.7 Denmark as a lab for research in community-based strategies to address mental health and healthy weight in infancy

Public health intervention research in childhood has unique opportunities in Denmark, due to a municipality child health surveillance attended by more than 95% of infant families (115, 116) and the comprehensive Danish population registries which comprise data on health and social conditions of all citizens recorded through the unique civil registration system (117). Hereby it is possible to reach and invite all families for research, and to ensure the valid tracking of subjects for examinations and follow-ups, and to assess the influences on study findings due to non-participation (116).

The child health surveillance in Denmark includes home-visits to all families with an infant, delivered by a community health nurse, CHN, and anchored in the municipality social services (27, 97). The CHN assesses child health and development, and measures length and weight, at an average of four times within the first year of the child's life.

It is a part of the standard services that parents are given advices regarding e.g. breastfeeding, nutrition and the overall infant care, as well as advices regarding the stimulation of the child's psycho-motor development and the parent-child relations. Within the administrative and economic limits set by the individual municipality, the CHN may extend the services to target particular problems and needs of the child and the parents. About 20% of all infants receive more visits than included in the standard care, mostly in the form of elaborated parent counseling, e.g. concerning

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infant problems of eating and sleeping, or regarding emotional reactions, or the parent-child relation, or maternal mental health problems (118, 119).

The CHNs follow national guidelines regarding children's eating, meal habits and physical activity (120). Still, no validated intervention is available that specifically address the CHNs' actions to prevent infants' mental health problems and risk of overweight.

2.8 *Targets and potentials of preventive intervention explored in municipality settings*

The lack of preventive intervention to address mental health and healthy weight development in infancy, leaves parents and CHNs without tools to reduce the impact of infants' cognitive and regulatory vulnerabilities, even in a society as the Danish with an otherwise well-functioning child health surveillance.

Pioneering work to specifically address the gap in knowledge on effective prevention within the child health surveillance has been ongoing in Denmark since 2000 (121). Among the results from this work, the recordings of the CHNs' observations and assessments of child health and development have been standardized, and they are currently validated in a collaboration comprising 33 Danish municipalities and the Child Health Database, located at the National Institute of Public Health (121). Research embedded in this collaboration has provided solid evidence on the particular needs and challenges for specified prevention regarding mental health and overweight (13, 18, 27, 34, 40, 43, 61, 85, 121-123). Thus, reliable markers of mental health vulnerabilities have been identified, showing that problems of language, attention, activity and interests, contact and communication, and problems of eating, sleep and emotional regulation are highly predictive of mental health problems later in preschool age (27, 34, 40, 85). The research based on the settings of CHNs in Denmark has replicated international research findings and underscored that the parent-child relation acts as the main moderator of risk and resilience, across domains of child vulnerabilities (27). Notably, the child age of 8 to 10 months has been identified as a window of opportunity regarding the valid identification and subsequent intervention concerning infants' cognitive and regulatory vulnerabilities (123), and a standardized measure has been developed (124), and thoroughly validated (124-126). Hereby, a valid starting point for intervention has been identified in a period of life in which prevention is considered to have the highest impact (33, 127). The measure called PUF (in Danish *Psykisk Udvikling og Funktion*) has recently been integrated in a programme of basic intervention, the PUF-programme (128). The programme includes education, training and guidelines of action within the existing routines. Pilot-testing has demonstrated high face validity

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and feasibility of the basic PUF-programme, which is now implemented in 17 Danish municipalities (128).

Still, the pilot study of the basic PUF-programme has highlighted a group of particularly vulnerable infants in need of a more specific and intensive intervention that addresses major cognitive, physiological, emotional and behavioural problems. Also, the challenges faced by psycho-socially vulnerable parents have been highlighted, and the importance of taking the particular needs of these parents into account in the planning of a more specified intervention has been underscored.

The lack of an effective and feasible preventive intervention for the most vulnerable infants and their families stands in contrast to the mounting evidence on the developmental impact and longterm consequences of mental health problems and overweight in early childhood.

Notably, the promotion of sensitive parenting via specified and intensive support from CHNs to parents stands out as a promising avenue of intervention to capture cognitive and regulatory precursors of mental health problems and overweight, but the specific contents and the potentials within existing services lack to be systematically explored.

2.9 Objectives and hypothesis

The study aims

- 1) to develop an intervention to promote sensitive parenting of infants with cognitive and regulatory problems at ages 9-10 months, which is based on the VIPP-method adapted to the PUF-programme (the PUF-VIPP intervention) to be implemented within the settings of CHNs, and
- 2) to examine the feasibility, fidelity, and the effectiveness of the PUF-VIPP intervention with the outcome early in childhood, and specifically at child ages 18 and 24 months.

The primary hypothesis:

The PUF-VIPP intervention is hypothesized to be feasible within the municipality settings of CHNs. Among infants with high levels of cognitive and regulatory problems at age 9-10 months, adding the PUF-VIPP intervention to treatment as usual, will reduce mental health problems (primary outcome).

The secondary hypotheses

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- 1) Among children with high levels of cognitive and regulatory vulnerabilities at age 9-10 months, adding the PUF-VIPP intervention to treatment as usual will promote healthy weight development (secondary outcome).
- 2) Among infants with high levels of cognitive and regulatory vulnerabilities at age 9-10 months, adding the PUF-VIPP intervention to treatment as usual will reduce infant cognitive and regulatory problems (secondary outcome).
- 3) Among infants with high levels of cognitive and regulatory vulnerabilities at age 9-10 months, adding the PUF-VIPP intervention to treatment as usual will reduce parents' experiences of stress and promote sensitive parenting and parents' feeling of competence and relatedness.
- 4) Among infants with high levels of cognitive and regulatory vulnerabilities at age 9-10 months adding the PUF-VIPP intervention to treatment as usual will reduce the development of dysregulation from infancy to age 24 months.

3 Methods

The development, implementation and evaluation of the intervention is guided by the Intervention Mapping approach (129), guides for development of complex interventions from the UK Medical Research Council (130) and the RE-AIM-method (131, 132).

3.1 Study area, settings and population

The study is anchored in the settings of CHNs in the municipalities of the Child Health Database, CHD, (121) and conducted among the municipalities who have implemented the basic PUF-programme in 2018-2019 (128) and 2020. The study municipalities are overall representative of the municipalities in the Child Health Database and the Danish population regarding key background characteristics (133).

Anticipated number of participants

At October 1, 2020, a total of sixteen municipalities have consented participation, and we expect that all of them will complete participation in the study. These 16 municipalities have in total about ~7,760 births/ year (134); and with a recruitment period of 16 months (1.3 2021-30.6 2022) estimated 10,350 infants will reach 9-10 months in the study period. Based on data from the Child Health Database (135), we expect that about 88% of the children born in the study municipalities

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will receive home visits at age 9-10 months and screened by the PUF-assessment (~9,100). In this study, we have to exclude children with severe mental or physical disabilities, and children whose parents have major problems in speaking or understanding Danish or English, in total estimated 4-5 % of the population, which in total leaves estimated (~8,650) children to be eligible for participation. Based on previous research (27, 121, 124, 125, 128), we estimate that about 16 % of them (~1,384) will have three or more (≥ 3) problems which index major cognitive, emotional or behavioral problems, and the parents of these infants will be invited to participate in the study. Assuming a recruitment rate of 80% as estimated from previous work, we anticipate that a total of ~1,107 parent-child dyads will be enrolled, and of them, we estimate that ~775 (70%) will be available for full follow-up at 24 months.

3.2 Design

We have chosen the stepped wedge cluster randomized design (136-138) mainly for two reasons. First, it is more feasible to randomize at the municipality level as compared to the level of the individual child or CHN. An RCTs based on randomization of the individual child or nurse would be associated with more logistical demand on the individual municipality or nurse as compared to the stepped wedge design as they would be having both the intervention and the control condition running simultaneously. For practical reasons, all municipalities cannot be trained at the same time but have to be split into three groups, and with the stepped wedge design we utilize this and randomly allocate the 16 participating municipalities to the time at which their health nurses have been trained and start offering the intervention to families. Also, with the SWD spill over is reduced by the randomization of clusters as compared to individual randomization. Second, in the stepped wedge design, interventions are introduced in a stepwise manner to all participating clusters (municipalities in this case) which encourages participation for those who would otherwise have been randomized to the control condition. Initial feedback from our interactions with the municipalities reveals that their motivation is strongly associated with being able to offer the intervention, as many municipalities prioritize early intervention highly. Also, with the stepped wedge design control families are recruited in the early phases of the trial, which enhances the recruiting of a control group with the level of usual care offered at the beginning of the trial. In the control period no participants receive intervention and sequential random crossover to the intervention cannot be reversed (139).

An important advantage of the stepped wedge design is that families only need to consent to participate in a research study and not to be randomized. In our experience this makes a big

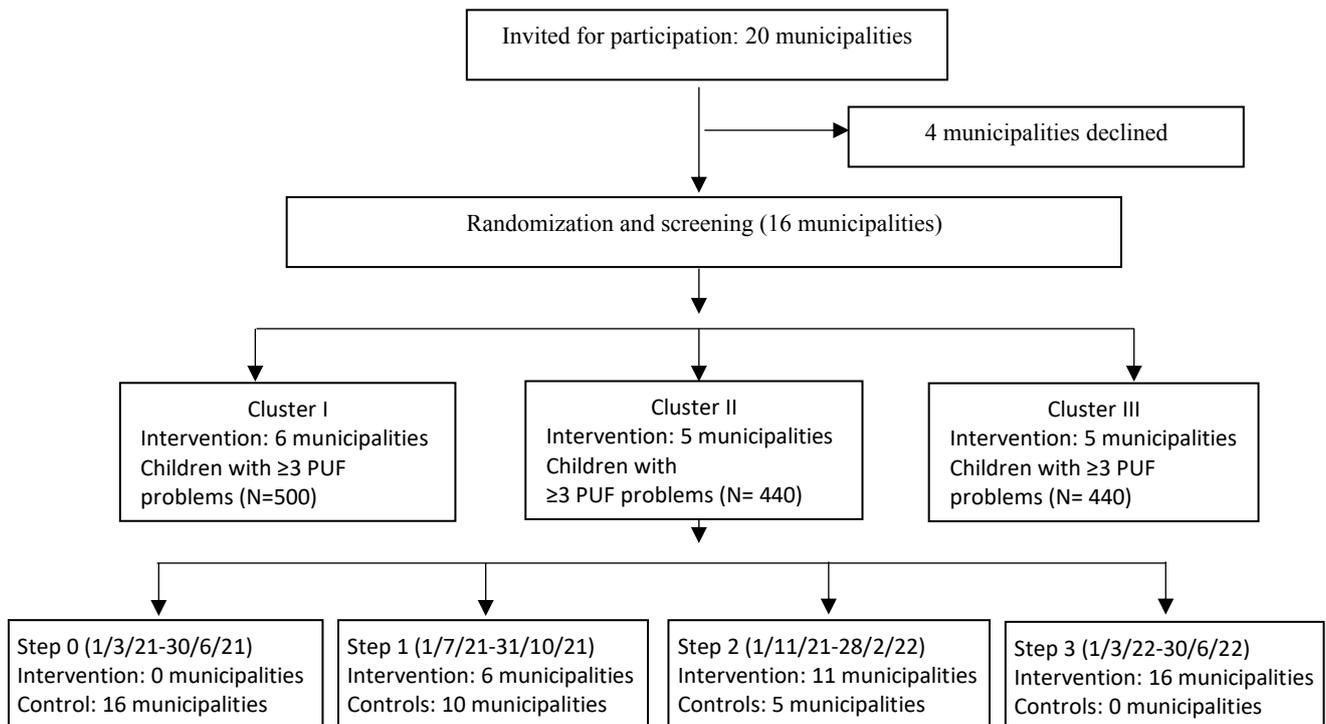
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difference not only to the families, but also the front personnel who are recruiting the families. With a longer recruitment period and higher expected acceptance rates, the stepped wedge design will result in a larger sample size and less frustration about recruitment among the CHNs who find it very hard to deliver standard care to families, when they have introduced an intervention they believe is superior. Thus, we believe that the stepped wedge design is associated with the least dropout.

On a practical level, the 16 participating municipalities will be randomly distributed into three clusters (6+5+5), and clusters will be randomized to initiate intervention at three different time points, according to the stepped-wedge design (Figure 1) (Detailed overview of the design, see Appendix 1).

Figure 1. Study flow diagram



According to the randomization of municipalities, all children assessed to have ≥ 3 problems will function as controls and receive care as usual from Step 0 until the municipalities initiate the intervention in Step 1- 3, respectively.

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Recruitment of municipalities, children and parents

All municipalities that have implemented the basic PUF-programme are invited, and the leading CHNs from the becoming study municipalities are invited as key stakeholders to join the study planning group.

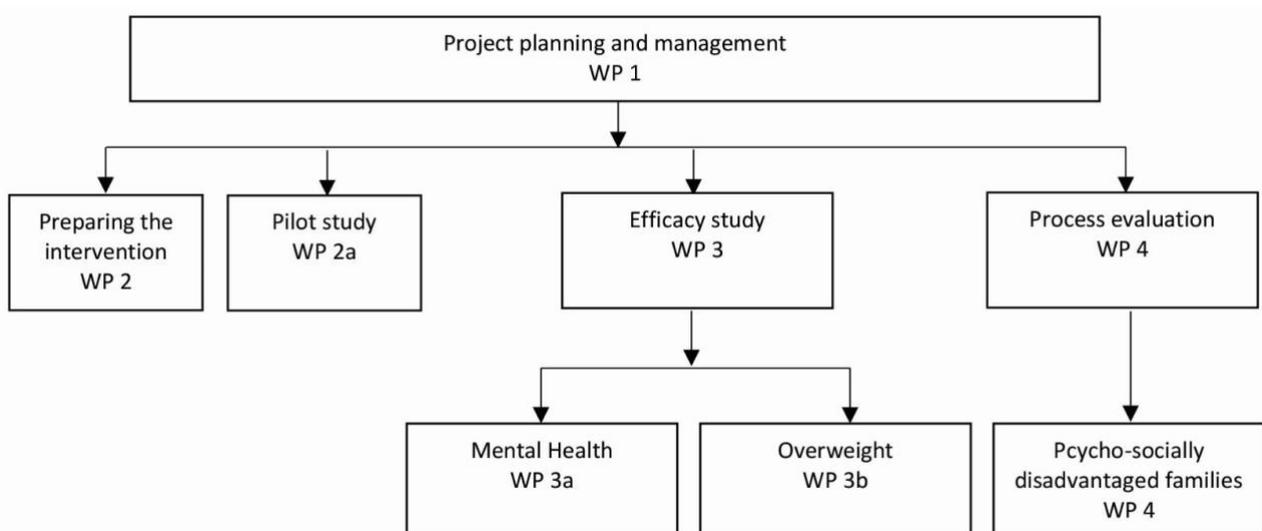
In the participating municipalities, the parents of children becoming 9-10 months in the study period are informed about the project by the CHNs, and via written folders and information on the study home page (<https://www.sdu.dk/da/sif>). At the the scheduled home visit at child age 9-10 months, the CHNs complete PUF-assessment and offer the parents feedback in accordance with the basic PUF-programme and the existing routines. All parents of children who have been assessed to have three or more problems are offered extended service. In the control phase of the study, the extended service comprises treatment as usual, in which the CHN does as she is used to according to existing municipality services. In the intervention phase, the CHN offers the parents the PUF-VIPP intervention. The CHN informs the parents about the details in the Infant Health project, and if parents agree to participate, they are invited by e-post and sms.

Parents make their final agreement for participation by answering the web-based questionnaires at the study web-site.

Parents who have difficulties in completing the questionnaires are offered assistance from the CHN.

Participating parents join a lottery with gift certificate of about 40 euro.

Figure 2. The Work Packages (WP) of the project



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3.3 Measurements

Social and emotional development at ages 9-10, 18 and 24 months

The Ages and Stages Questionnaire, Social-Emotional 2, ASQ SE2 (version for children aged 1 to 60 months) (140) is used to measure the child's self regulation, compliance, communication and adaptive functioning. It comprises 19 to 33 items rated by parents and includes a box parents in which parents may check if the behavior is a concern for them. The ASQ:SE2 is well-validated and the most commonly used measure of young children's social and emotional development, internationally as well as in Denmark (141-143).

Mental health problems at ages 18 months

The Child Behaviour Checklist, CBCL-version for children aged 1 ½ -5 years answered by parents (144) is used to measure problems of eating, sleep, emotional problems, behavioural problems and problems of hyperactivity, concentration, communication, language and social interaction (41, 45-47). The CBCL 1 ½ -5 years comprises 99 items, including problems of overeating and problems of dysregulation (145). CBCL is predictive of persistent emotional and behavioural dysregulation, including overt symptoms of ADHD (146, 147). It is one of the internationally most used and validated psychometric tools (148), and the version for children aged 1 ½ -5 years has been used in several population based studies in Denmark (13, 125).

Mental health problems at ages 24 months

The Strengths and Difficulties Questionnaire, SDQ answered by parents (149) (www.sdqinfo) is used at ages 24 months in order to use this very short (25-items) and feasible measure both at age 24 months and at the planned follow-up at older ages. SDQ is highly predictive of persistent child mental health problems and suitable for the prospective investigation of mental health from ages 24 months and onwards (149, 150). SDQ has been validated for use in children down to the age of 2 years (151, 152), and used in epidemiological research worldwide (152), also in Danish populations, with Danish norms being available (34, 153) (www.sdq.dk).

Weight and height measures at ages 9-10 months and 24 months

Weight and lengths are measured by CHNs at four home visits between ages 0-10 months using a hand-held beam scale (In Danish Bismervægt) or a hand-held hanging scale (In Danish babyvægt/hængevægt) and a tape measure, as described in the Danish National guidelines (97).

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At age 24 months, no official guidelines are available for measurements of weight and height, and for this assessment, the measurements will be standardized as far as possible by providing the CHNs with uniform equipment for transportable scales and height carts and guidelines on how to perform the measurements.

Eating behaviour at ages 12, 18 and 24 months

Video-recordings of mealtimes at child ages 12 and 24 months are used to examine the child's eating behaviour, the parents feeding behaviour, and the parent-child interaction with regard to parental sensitivity, intrusiveness and limit setting, regarding the child's involvement, withdrawal and compliance and concerning the overall dyadic reciprocity during a meal.

At 18 months parents answers questions on eating behaviour as part of the *CBCL 1 ½ -5*. At 24 months parents answer a short questionnaire on the child's eating behaviour, including questions on appetite and overeating.

Parenting and parental stress and family impairment at child age 9-10, 18 and 24 months

The Mother and Baby Interaction Scale, MABISC (at 9-10 months) (154, 155); the Being a Mother, BaM13 (at 18 and 24 months) (156); the Parental Stress Scale, PSS, (157, 158); and the WHO-5 well-being index, WHO-5 (159, 160); all well validated, internationally and in Danish public health settings (95, 141).

Sensitive parenting will be examined from observer-ratings of video-recording of parent-infant interaction at age 18 months and 24 months using the Child Interaction Behavior (CIB) system (161) to assess the parent-child relationship (162). The CIB system contains 22 parent behavior codes, 16 child behavior codes, and five dyadic codes which can be aggregated into the following composites: sensitivity, intrusiveness, limit setting, involvement, withdrawal, compliance, dyadic reciprocity, and dyadic negative states. The CIB system has been validated in normative as well as high-risk populations, and shows stability over time, predictive validity and adequate psychometric properties (161, 163-166).

Coders will be trained to intercoder reliability ICC > .65, Pearson's $r > .70$, and regular meetings and checks will be organized to prevent coder drift.

Child physical health and the social-economic conditions of the family

Data on pregnancy, birth, perinatal factors and physical and mental health problems diagnosed at hospital are obtained from the Medical birth registry and Danish patient registries (133, 167).

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Information on ethnicity, parental age, family structure, parents' education, and family economic position are obtained from Danish population registries (133, 167). Information on mental health problems in parents and parent-child relation problems recorded by CHNs at home visits between the child's birth and age 6 months are obtained from the Child Health Database (118-121).

3.4 Project planning and management (WP 1)

The project is an extension of our previous work in the study municipalities, and we have previously evaluated the organizational capacity and the structure and content of CHNs' home visits, including descriptions of themes covered in the existing routines at home visits, such as child development and nutrition.

It is a core feature of this project that we use the settings and the best practices of the CHNs as the starting point to develop the specified PUF-VIPP intervention. In line with the Intervention Mapping approach, the first phase of the study includes the establishing of a participatory planning group comprising the principal investigators and the leading CHNs. Furthermore, CHNs from each participating municipality will join the project planning, and will be trained in the original VIPP method (99), from which the PUF-VIPP will be developed. These CHNs function as municipality stakeholders; they facilitate the municipality supervision-groups to be established, and they function as the first generation of PUF-VIPP co-trainers and supervisors in the municipality.

The participatory planning group are thus involved in the decisions of measurements in the efficacy study to be completed in WP 2 and pilot-tested in WP 2a.

Our ongoing collaboration with the CHNs (121) and our previous research related to the implementation of the basic PUF-programme (121, 124, 128) has provided a thorough knowledge on local political priorities of child health prevention related to structure and resources for the CHNs' visiting practice and administration, e.g. manpower, number of CHNs, and the administrative structure of CHNs daily work. Further, we have assessed the capacity of implementation and evaluated specific local challenges (e.g. high proportion of families of ethnic minorities or with low socioeconomic status) and local staff competences, interest and engagement, training, and management support.

The informations already available from our close collaboration with managing and practising CHNs in the study municipalities is currently updated in WP 1, and they will be taken into account

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when developing the PUF-VIPP intervention, and in the strategies necessary to ensure fidelity and deliver valid results for the efficacy trial.

Overall, the PUF-VIPP will be designed as an add-on to the basic PUF-programme for use in the CHNs' ordinary routines between child age 9 and 14 months, taking into account the traditions and strategies of the particular municipality, and the recommendations from the National Board of Health (97) that include guidelines regarding the prevention of overweight (120).

Notably, the PUF-VIPP intervention will be embedded in the already existing need-based health visiting system, in which practice is already established and working well. As such our intervention could be viewed as further specialization or professionalization of the current health visiting practice. The thorough organizational capacity assessment already done will ensure that the PUF-VIPP is relevant and applicable to the administrative and practical organization of the current home-based health visiting system.

3.5 Preparing the PUF-VIPP intervention (WP 2)

The goal, scientific foundation and setting of the intervention

The overall goal is to develop a targeted intervention that 1) address infants of particular vulnerability regarding mental health problems and the development of overweight, and specifically target cognitive and regulatory problems, and which 2) can be delivered by CHNs, and 3) is feasible within the municipality child health surveillance.

The intervention will be designed as an add-on to the basic PUF-programme (128), which includes a) a basic education of CHNs, b) the CHNs' systematic evaluation of infants aged 9-10 month, c) their communication with parents about the infants needs, and d) the planning of support within existing service-settings, all in accordance with the manualized guidelines of the basic PUF-programme (168). According to these guidelines, the basic PUF programme builds on the existing municipality care to address the needs the individual families and in particular the needs of families of socio-economic and psycho-social disadvantages. The primary focus of the PUF-VIPP intervention is to educate CHNs in promoting sensitive parenting, and the PUF-VIPP will be developed to fulfil the following demands:

1) address infants with major vulnerabilities regarding mental health problems and healthy weight development indexed as three or more problems of cognitive and regulatory functioning at the PUF assessment at age 9-10 months (children with two or less problems receive care as usual including the basic PUF-programme),

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- 2) be acceptable for parents, taking into account challenges experienced by families of immigrants, young parents and parents with limited cognitive, mental and social resources,
- 3) not stress the participating children or families,
- 4) be sustainable and integrated into the existing structure of CHNs' home visiting programme and education,
- 5) adhere to the official guidelines within the CHNs' practice,
- 6) be acceptable and appropriate for the CHN, who will be the main responsible professional for the implementation and delivery of the intervention.

Parenting as a core ingredient of intervention to promote healthy development in early childhood

The VIPP is basically a highly structured intervention to promote parents' observational skills and capacity to empathize with the child (169). The intervention is delivered at home, by health professionals and across six to seven sessions of about one hour. Each session is standardized and includes education of the parents on topics covering infant and toddler development, using video recordings and feedback to promote parents' sensitive responsiveness and sensitive discipline (170). The VIPP is based on attachment theory and theories of social learning (171, 172). The method has been thoroughly validated as a cost-effective tool to promote parental sensitivity and child attachment in vulnerable infants (171, 172), and has been shown to be modifiable to various areas of infant mental health (170) e.g. regulatory problems (173); feeding and eating problems (170), and behavioural problems (174); and it has shown to be feasible in various cultural settings and populations, e.g. families of ethnic minorities, and families of limited cognitive or psycho-social resources (175), and mothers with eating problems (101, 102). Meta-analyses of RCT studies of VIPP show a substantial combined effect size for increased caregiver sensitivity, and a robust combined effect size for improved child outcomes (99). Importantly, being short and with a clear behavioural focus, VIPP has shown to be more effective compared to longer lasting programmes (100).

The VIPP has been developed in the Netherlands, in populations comparable to the Danish and the fidelity has been documented in community settings, and also in families of socio-economic and psycho-social disadvantages, e.g. families of immigrants, young parents and parents with limited cognitive, mental and social resources (176).

Adapting the VIPP to the PUF-programme to address infant vulnerabilities within the settings of community health nurses

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The VIPP method does not systematically address the full range of infancy vulnerabilities regarding mental health and healthy weight, and the measure has not been tested in settings like the Danish CHNs. Still, we consider the VIPP method to be an obvious starting point for the development of the focused intervention in Danish municipality settings. Firstly, because VIPP is short, effective and highly feasible in populations which are comparable to the Danish. Secondly, because it has shown effectiveness regarding intervention towards a range of infant problems and parental vulnerabilities as e.g. families of ethnic minorities, socio-economic adversity, and parental mental health vulnerabilities including parental eating problems. Accordingly, we collaborate with the the VIPP Institute and the PI of the VIPP research professor Marian Bakermans-Kranenburg to adapt the VIPP to the PUF-programme.

The PUF-VIPP intervention is planned to be of a duration and frequency like the core VIPP methods (170), comprising a package of six to seven sessions of approximately 60 minutes. Moreover, the PUF-VIPP will build on actual practices in the Danish home-visiting programme, and experiences from the pilot-testing of the PUF-programme (97, 128).

Education of community health nurses

The core essence of the PUF-VIPP intervention is the CHNs' supporting and training the parents. The education builds on the education in the PUF-programme, which covers baseline knowledge for CHNs regarding infants' health, development and vulnerabilities (168). The active ingredient in the PUF-VIPP is the CHN's training and supervision in the VIPP based video-feedback approach to promote parents' knowledge and understanding of age related behaviour and reactions. Specifically, the CHNs are trained and supervised to address the promotion of parents' sensitivity and sensitive responsiveness regarding the cognitive and regulatory difficulties identified in the child.

Initially, a group of CHNs are educated in the original VIPP method to enable them to contribute to the adaptation of the VIPP into the PUF-VIPP intervention. Further, these CHNs participate in the pilot testing of the PUF-VIPP, and they function as co-trainers and supervisors of the next generation of CHNs educated in the PUF-VIPP during the project period.

We estimate that 50 CHNs will be educated in the project period based on an estimated inclusion of 16 study municipalities with a total of about 1,400 infants aged 9-10 months reaching the inclusion criterias of ≥ 3 PUF problems and a need of minimum two CHNs educated in the PUF-VIPP method per municipality.

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Development of intervention components

The specific tools and activities of the intervention will be developed in a participatory planning group and in dialogue with the Project Steering Group.

Educational experts, graphic- and web-designers, videographers and writers will be consulted to develop the web-platform and extended scripts, plans, visual and written outlines (booklets, leaflets/handouts/newsletters) and video demos (visual presentation of information, skills training and case situations).

Focus discussions involve CHNs from the study area and parents, recruited by local CHNs (WP4).

3.6 The pilot study (WP 2a)

The aim of the pilot study is to a) evaluate the face validity and feasibility of the PUF-VIPP intervention developed in WP2 and b) assess face validity and feasibility of baseline and outcome measurements. A core aim of the pilotstudy is the comprehensive evaluation of 1) the recruitment procedures, 2) the feasibility and effectiveness of the CHNs education and training, 3) the feasibility of the PUF-VIPP intervention within the existing routines of CHNs 4) the parents' motivation, compliance and acceptance of the intervention, 5) the function of the web-platform, and 6) the practical procedures. Further, we will 7) evaluate the measures of the efficacy study (WP3), adjust the process evaluation (WP4), and to evaluate 8) the overall study frame, the particular delivery tools, and to assess the overall feasibility of the primary, intermediate and secondary measures planned to be used.

Methods: The pilot study will be conducted in two strategically sampled municipalities of at least 500 births a year with estimated 6-10 CHNs and takes into account diversities regarding background population and municipality resources. To evaluate the feasibility of the PUF-VIPP intervention, the acceptability and usefulness of the web-based questionnaires, web-platform (RedCap, e-box delivery and dunning procedures) and the needs of assistance to the parents of limited cognitive or psycho-social resources, the strategic sample includes high as well as low-resource families, families of different ethnic and cultural backgrounds, and in particular families of disadvantaged psycho-social conditions.

Procedures: The practical procedures are elaborated by the Participatory Planning Group and tested in the two pilot study municipalities.

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Parents of infants going to be assessed at age 9-10 months according to existing routines are invited for participation 2-4 weeks prior to the homevisit at age 9-10 months. Parents of infants becoming 18 and 24 months during the study period are invited for participation in the testing of intermediate and outcome measures at these ages, including the measurement of weight and height at an extra home visit at child age 24 months.

The PUF-VIPP intervention is offered to infants with ≥ 3 problems at the PUF assessment at age 9-10 months, and across a 3 month period. Baseline, intermediate and outcome measures are obtained via webbased questionnaires to parents of children aged 9-10 months, 18 months and 24 months respectively. Home visits at child age 9-10 months and 24 months include the CHN's assessments of the child's height and weight. Moreover the CHNs offer help to the parents to fill in questionnaires, if needed.

Estimated 2-4 infants per CHNs will have ≥ 3 problems at the PUF assessment and therefore be offered intervention, of which estimated 2-3 of the families agree to participate, leaving a total of 4-6 infant families to participate in the pilot-intervention and asked to fill out the parent questionnaires at child age 9-10 months. Further, four families per municipality, who have infants previously tested with the PUF-measure at ages 9-10 months and are invited for the pilottesting of web-questionnaires and practical procedures at ages 18 and 24 months.

The feasibility of the PUF-VIPP intervention is evaluated as part of the overall Process evaluation (WP 4), which run in parallel to the preparing process (WP1), the intervention planning (WP2) and the present pilot-study and involves both CHNs and parents. The evaluation includes questionnaires to CHNs regarding the adherence to the intervention e.g. the extent to which activities are possible to implement in accordance with the intervention designed. Further, the process evaluation comprises participant observations at home visits, focus group interviews with participating CHNs and with parents involved in the pilot-intervention (Detailed description of the Process evaluation (WP4), see section 3.7).

Included in the pilot study is the assessment of the test-retest and interrater-reliability of the anthropometric measures at ages 9-10 and 24 months, and the coding of sensitive parenting at ages 24 months.

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Focus group interviews of CHNs will be undertaken to evaluate the feasibility and effectiveness of CHNs education and training, and to explore the recruitment procedures, the function of the web-platform, the feasibility of the practical procedures related to the specified intervention and to the follow-up assessment, including the parents need of CHN's assistance to fill out the questionnaires. Also, the CHNs' experiences in using the specified intervention will be explored.

Semi-structured interviews of parents of infants with ≥ 3 problems will explore the parents' experiences of the recruitment procedures and the web-based questionnaires. Both mothers and fathers are invited, and we will evaluate the particular needs in families of different social and cultural-ethnic composition, and to what extent parents of limited cognitive or psycho-social resources need particular support.

Specifically, we will explore the parents' experiences regarding recruitment, information, and communication about the PUF-VIPP- intervention; and the parents' evaluation of the frame, setting and content of the intervention.

Data analyses and results: We will assess face validity, feasibility and reliability of core measures of the main study, and use the results from the pilot study to decide the further progress of the study, including a stop-go decision or the continuing of WP3 and WP4. Should the pilot study suggest major problems of recruitment of municipalites and/or families, it will be considered whether a full trail is feasible, or whether minor needs of adjustment have to be implemented in the final study set.

3.7 The efficacy study (WP 3)

The efficacy of the PUF-VIPP intervention is measured as a significant reduction in mental health problems (WP 3a) and BMI-z scores at age 24 months (WP 3b) among infants who have received the PUF-VIPP intervention, compared to control infants, who have received care as usual.

Outcomes

The primary child outcome is child mental health at age 24 months measured by the Ages and Stages Questionnaire, Social-Emotional 2, ASQ-SE2 (140) and the Strenghths and Difficulties Questionnaire, SDQ (149).

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The secondary outcomes measured at child age 24 months include BMI z-scores measured by CHNs at home visits, and parental well-being, parental stress, and parents' experiences of family impairment measured by the Being a Mother questionnaire, BaM1 (156); the Parental Stress Scale, PSS, (157, 158); and the WHO-5 well-being index, WHO-5 (159, 160).

Measures of eating behaviour at 24 months include items in the ASQ-SE, specific questions on the child's eating behaviour at 24 months and ratings of child involvement, withdrawal and compliance during a meal, as well as the parent's feeding behaviour, sensitivity, intrusiveness and limit setting, and the overall parent-child interaction and dyadic reciprocity based on video-recordings of two mealtimes at child age 24 months.

Intermediate outcomes measured at child age 18 months include child mental health and development measured by the the Ages and Stages Questionnaire, Social-Emotional 2, ASQ-SE2 (140) and the Child Behaviour Checklist, CBCL-version for children aged 1 ½ -5 years (144), which includes information on regulatory problems of eating, sleep, emotions, behavioural and cognitive functions (41, 45-47).

The intermediate outcomes at age 18 months include measures of sensitive parenting, the Mother and Baby Interaction Scale, MABISC (at 9-10 months) (154, 155); and measures of parents' well-being and feeling of competence and relatedness, and parents' experiences of stress, the Parental Stress Scale, PSS, (157, 158) and the WHO-5 well-being index, WHO-5 (159, 160).

WP 3a: The efficacy of on the child' mental health

The efficacy of the PUF-VIPP intervention is measured as differences in cognitive and regulatory problems between infants receiving the PUF-VIPP intervention compared to infants receiving care as usual. As potential predictors of effect, we include the CHN's evaluation of infant development and socio-emotional and regulatory functions at ages 2-4 weeks, and 2-3 and 4-6 months.

Moreover, the ASQ:SE2 answered by parents will be used to measure socio-emotional development at age 9-10 months.

The effect of the intervention will be investigated in relation to early developmental and regulatory vulnerabilities (from birth to ages 6 months); and the influences of gender, perinatal adversities, parent-child relational problems will be explored, as well as in addition to parental age, ethnicity parents' educational level, household income, marital status, and parents' mental health problems.

WP 3b: Weight development

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The effects of the PUF-VIPP intervention on weight development is measured as differences in BMI z-scores among children with cognitive and regulatory problems at age 9-10 months who receive the PUF-VIPP intervention compared to infants who receive care as usual, CAU. We will adjust for BMI z-score at birth (177, 178), and specifically, we will examine the role of pre-and postnatal risk factors for childhood overweight on BMI z-score at age 24 months (179, 180).

Weight trajectories from birth to age 9-10 months will be analyzed, we will examine the influences of early feeding, eating, sleep and overall regulatory problems between ages 2 and 6 months as evaluated by CHN's at home visits ages 2-4 weeks, 2-3 and 4-6 months. These evaluations are based on the CHNs overall conclusion about the infants' feeding/eating/ sleep or crying and rated by the CHNs as being of concern or not (121).

We will examine the role of ethnicity, socioeconomic position of the parents and parental mental health problems informed from National registries or recorded by CHNs at home visits between ages 0 and 6 months. Specifically, we will explore whether trajectories of feeding and eating behavior and of dysregulation (eating, sleep and emotional expression) measured between 2 and 9 months (43) and 18 and 24 months will be modified by the intervention, and to what degree eating behavior and dysregulation influences the BMI-z scores at ages 24 months. Also, we will investigate the influences of parental experienced stress and parent-child relational problems at ages 9 month and 18 months on BMI z scores at age 24 months.

3.8 *Proces evaluation- What works for the vulnerable families? (WP 4)*

The aims of the process evaluation is 1) to document the development of the PUF-VIPP intervention, and 2) to explore and analyse the implementation process to obtain knowledge about activities and effects, and to extend the understanding of the relationship between the intervention and the outcome (181). We will evaluate whether the intervention is implemented as intended (fidelity), and whether and to what degree it has reached all families within the intended target group and across various risk groups (reach), and with a specific focus on families of psycho-social disadvantage. Also, we will assess the acceptability of the intervention among CHNs and parents, and their appreciation of and satisfaction with the intervention programme, to get a deeper understanding of how, why and for whom the intervention was effective or not (182).

Data collection and analysis will run in parallel to the preparing process (WP1), the intervention planning (WP2), the pilot study (WP 2a), and the efficacy study (WP3), and includes

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questionnaires and interviews of the CHNs, parents and stakeholders to explore the fidelity and reach of the intervention.

Ad 1) The process of intervention development and pilot testing (WP2 and 2a) involves both CHNs and parents. We will, therefore, collect qualitative data on the process by participant observations at home visits (183), focus groups interviews (184) with participating CHNs and with parents of different socio-cultural background. Also, we will conduct individual, semistructured interviews (185) with the involved parents, and fathers and mothers will be interviewed separately to explore potential differences in experiences and needs.

Ad) 2 The process evaluation will combine quantitative and qualitative methodologies. Datacollection and analysis run in parallel to the preparing process and evaluation, WP1, WP2, WP3 and WP4, and will be based on questionnaires and interviews of the CHNs, parents and stakeholders in the study area concerning the implementation of the study e.g. the fidelity and reach of the intervention.

Fidelity

In order to gain a comprehensive picture of the implementation of the intervention, we will measure implementation by multiple aspects of implementation fidelity; such as structural aspects, adherence to the intervention and dosage of implementation. Also we will explore procedural aspects, such as quality of delivery and participant responsiveness (181, 186).

The measurement of fidelity of the intervention implementation will include information on the variability allowed in the different municipalities, and among CHNs, as based on the child and the family. In particular, we will evaluate whether the PUF-VIPP intervention has reached all families across various risk groups, and assess the particular needs and experiences among families of high vulnerability and low socio-economic position.

Quantitative data relating to the administration and delivery of the CHN's educational and training courses include recordings of the adaptation of programme skills and self-monitoring checklists for each intervention session. In order to reflect the implementation fidelity and impact of implementation on mental health problems and weight all main components of the PUF-VIPP intervention will be addressed according to the guidelines elaborated in the pilot-study (WP2) e.g. specified videotape during daily situations at homevisits; themes of the program delivered for each session and successively elaborated during the intervention period according to the guidelines; the

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CHNs' use of the manualised instruction for feed-back to the parent according to each theme of the program; delivery of written material on sensitive parenting and sensitive responding in daily situations about e.g. eating and feeding (169). Questionnaire surveys will be set up to collect information on contextual factors including competing health promotion activities targeting families with infants.

Qualitative data will be collected to inform the intervention processes and to explore the translation of the CHNs' intervention skills into practice and these data will be used investigate how parents experience and respond to the intervention. Data will be collected using focus groups with CHNs, and individual interviews with participating parents. We will conduct participant observations at a selected number of home visits at different times throughout the study, to collect data on the learning, uptake, use of the programme in the home visit, and to explore the maintainance of the techniques. Semi-structured interviews with parents will be used to explore both their acceptability of the intervention, and hopes and priorities for change in relation to the intervention provided. At the municipal level, individual and focus group interviews will be conducted to further investigate barriers at the organisational level.

Questionnaire surveys will be set up to collect information on contextual factors including competing health promotion activities targeting families with infants (187). The evaluation includes telephone interviews with heads of health departments, health administrators, health planners, and managing CHNs, to collect data on differential use of CHNs' services, the attribution to the CHNs being trained, and the perception of the settings of the intervention among other available sources of support.

Interview guides will be developed for both the focus groups and the semi-structured individual interviews. Interviews will be audiorecorded and transcribed verbatim and anonymised (187).

3.9 Health economic evaluation

Health economic expertise will be consulted to plan the evaluation of the cost-effectiveness of the PUFF-VIPP intervention, including data from Danish national registers and data on service use from the Child Health Database.

4 Data analysis

4.1 *Analyses of qualitative data*

The empirical material (i.e. transcriptions of interviews and field notes) will be analysed following general principles for qualitative data analysis (188, 189). We will perform a systematic coding approach to identify important themes across the empirical material. We will read through and code the material in order to group the codes and categories into overall themes. Recurrent topics will be identified, compared and categorised. The analytical process will be inspired from ‘collaborative data analysis’ (190), through which different perspectives are brought to bear on the analysis and interpretation of the data. The analysis and interpretation of results will be brought into dialogue with the existing research on the research topic.

Summary and illustrative data relevant to the aims of the quantitative and qualitative research for each phase in the different WPs will be available, to facilitate further interpretation and discussion of which processes worked well or not so well within the study.

Thematic analyses of interview and focus group data will be driven by the research question and allow for more inductive analysis whereby emergent themes are also identified (188).

4.2 *Statistical analyses*

Comparisons between the children and parents receiving care as usual (CAU) and children and parents receiving the PUF-VIPP intervention will use the intention to treat principle, where the randomized children are analyzed according to their CAU/ intervention status. Random effects linear regression models will be fitted to compare means for continuous outcomes (including the primary outcome measured as the SDQ total difficulties score) and random logistic regression will be fitted to compare binary outcomes (e.g. border line/abnormal versus normal SDQ score) between CAU and children receiving PUF-VIPP intervention, allowing for the correlation between outcomes of children from the same municipality. Prognostic factors identified from the literature *á priori* will be included in analyses. Examples include parents’ education, employment status, household income, and marital status (all obtained from national registers) (185-187); at the child level, sex, birth parameters, BMI z-scores from birth to age 9 months, regulatory problems from ages 2-9 months, and ASQ:SE2 score at 9-10 months; family parameters including parents age, educational level, ethnicity, and parental mental health problems; and at the municipality level, e.g. level of social disadvantage. Tests of interaction is conducted for each outcome to investigate whether the intervention effect differs across the three waves of inclusion.

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Interaction terms will be included to explore possible differences in intervention effect (on the primary outcome SDQ score only) between gender, pre-defined subgroups based on BMI z-scores 0-9 months, low versus high scores of regulatory problems 2-9 months (0-2 problems versus ≥ 3 problems of eating, sleep or emotional dysregulation); low versus high baseline ASQ:SE2 scores and parental characteristics. Also, additional analyses of effect modification will further explore the effect by different population groups (socio-economic position, family structure and migration status).

We will use path analysis to explore whether the effect of the intervention on BMI z-score at age 18 and 24 months are mediated through the above-mentioned risk factors for childhood overweight. Using path analysis, we can assess the direct effect of the intervention, corresponding to the proportion not mediated through risk factors for child overweight, and the indirect effects of the intervention, corresponding to the proportion mediated through selected risk factors for childhood overweight. The total effect is the sum of the direct and indirect effects.

Power calculation

We expect that the mean SDQ score in children with ≥ 3 problems are 13 (153) and that it will be reduced by the intervention to 11 (150). Further, we expect that the standard deviation of SDQ is 8 (www.sdqinfo.org/DK). Uncorrected for clustering and repeated measurements, a sample size of 790 children would be required to detect this effect (power of 80% and significance level of 0.05). The intra-cluster correlation coefficient (ICC) for SDQ is anticipated to be no higher than 0.05. Taking the design effect of the stepped wedge design into account, a sample size of 690 is required to detect the anticipated effect, as the stepped wedge designs could reduce the required sample size in cluster randomized trials (138). As we expect that it will be possible to enroll and obtain full follow-up on about 775 children, the power in the study allows for testing moderator effects.

5 Ethics

The study is approved by the Research Ethics Committee of the University of Southern Denmark , case nr. 20/61404; and registered and approved by the University of Southern Denmark in accordance with the Data Protection Regulation and the General Data Protection Regulation (GDPR) (EU) 2016/679; Notification number: 11.090.

The parents are informed that their participation is fully voluntary, and that families who do not wish to participate, receive care as usual. It is underscored that at any stage of the project, the

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parents can withdraw their participation, and then receive care as usual.

The study comprises a specified intervention as an add-on to existing services provided by CHNs in the study municipalities. The usual care of CHNs, which is well accepted and used by more than 90% of the population, already involves assessment, counselling and information on sensitive issues related to challenges of the health and well-being of the child e.g. mental health and overweight. In this study, the CHNs use a more standardized and specified method to address the needs of the most vulnerable infants and their families, which more than 20% of the population is offered already within the existing routines. Video-feedback which is a core ingredient of the PUF-VIPP intervention, is already frequently used among Danish CHNs as a pedagogic way of communicating infants needs to the parents (191), and experiences show that the video-feedback approach is well accepted among parents, and regarded as a helpful supplement for the parents to understand the CHNs guidance (192).

6 Timeline and economy

The project was planned to be conducted from January 2020 through December 2024. Due to the COVID-19 situation, the first stages of the study have been delayed three months.

(Detailed and updated timeline with milestones, see Appendix 2)

The Infant Health project has October 2019 received 5.8 mill DKK from the Independent Research Fund Denmark, and May 2020, 20 mill DKK from the Novo Nordisk Foundation.

7 The project organization

The study is hosted at the National Institute of Public Health, NIPH, University of Southern Denmark, SDU, associated to the Center for Intervention Research and the Research group of Child and Adolescent Health (www.sdu.dk/da/sif) and led by Anne Mette Skovgaard (PI) and Janni Ammitzbøll (co-PI). The PI and co-PI will take responsibility for the daily transactions of the study activities, and the NIPH will provide support for the project including the Data Manager clerical support to the trial, organising all aspects of the postal questionnaires (mailing, tracking, and entering returned data using the study web-based data entry portal) and the web-page administrator maintaining the study web-page.

Research group

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Anne Mette Skovgaard, MD, DM SCI, Professor in Child Psychiatry, NIPH, SDU experienced in research in community-based studies of developmental epidemiology of mental health (WP 1-4).

Janni Ammitzbøll, Health nurse, MPH, PhD, Researcher, NIPH, SDU, experienced in community health nursing, and research collaborations with CHNs (WP 1-3).

Katrine Rich Madsen, MSc, PhD, Postdoc, NIPH, SDU experienced in process evaluation and social inequality (WP 4)

Tine Tjørnhøj-Thomsen, MA, PhD, Professor in Anthropology, NIPH, SDU (WP 4)

Janne Schurmann Tolstrup, MS, PhD, DM SCI, Professor in Epidemiology, NIPH, SDU (WP 3)

Rodney Stephen Taylor, PhD, Professor in Health Services Research, University of Glasgow and Exeter, and adjunct Professor at NIPH, SDU. Main methodological research expertise in medical statistics and clinical trial design, in particular complex interventions and design of trials to inform reimbursement and health policy (WP 3).

Else Marie Olsen, MD, PhD, Consultant child psychiatrists, Associate clinical professor in Child and Adolescent Psychiatry, Institute of Clinical Medicine, University of Copenhagen, and Centre of Clinical Research and Prevention, Capital Region, Denmark. Experienced in population-based research on mental health, eating and overweight among children (WP 3b).

Maiken Pontoppidan, PhD, Senior Researcher, the Danish Center for Social Science Research, Health Department. Experienced in RCT studies of CHNs' interventions in municipality settings (WP 2, WP 3).

Marian Bakermans-Kranenburg, PhD, Professor, Clinical Child and Family Studies Vrije Universiteit, Amsterdam, The Netherlands. Leading international expert in the dynamics and efficiency of parent-based interventions to young children, and the developer of the VIPP method (WP 2).

Trine Pagh Pedersen, Msc, PhD, Project Manager and research leader of the Child Health Database, NIPH, SDU (WP 2)

Lotte Finseth Health Nurse, stud MPH, NIPH, SDU, experienced in community health nursing (WP 2).

Ida Voss, Msc, Research assistant, NIPH, SDU (WP 2-3)

PhD Student A. Efficacy study (WP 3) and Mental Health (WP 3a)

PhD Student B. Efficacy study (WP 3) and Weight (WP 3b)

PhD Student C. Process evaluation and Psycho-socially disadvantaged families (WP 4).

Consultant health economic expert (WP 3)

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Project Steering Group

The study will be supervised by a Project Steering Group (PSG). The chair of this group will be *Anne Mette Skovgaard* and will consist of *Janni Ammitzbøll*, *Katrine Rich Madsen*, *Else Marie Olsen*, *Maiken Pontoppidan*, leading health nurse *Helle Erstling Rasmussen*, municipality of Roskilde, leading health nurse *Ulla Dupont*, municipality of Vejle, leading health nurse *Lone Dahlstrøm*, municipality of Høje-Tåstrup and *Anna Paldam Folker*, Head of NIPH research. The role of the PSG is to monitor and support the progress of the study. The PSG will meet monthly for the first six months and every second month hereafter.

Participatory Planning Group

The chair of the Participatory Planning Group (PPG) will be *Janni Ammitzbøll* and will consist of *Anne Mette Skovgaard*, the *PUF-VIPP health nurses* and *leading health nurses* from all participating municipalities. The role of the PPG is to participate in the development of tools and intervention to strengthen the fidelity and acceptability among stakeholders and CHNs in the municipalities. The PGG will meet monthly from June 2020 to March 2021 hereafter among every fourth month until the end of the intervention.

Trial and Data Steering Committee

An independent Trial and Data Steering Committee (TDSC) will be convened. The chair of the committee will be Associate Professor PhD *Pia Jeppesen*, University of Copenhagen, further the committee will consist of Associate professor *Sarah Fredsted-Villadsen*, Department of Public Health, University of Copenhagen, Professor PhD *Helle Terkildsen Maindal*, Department of Public Health, Section for Health Promotion and Health Services Research, University of Aarhus; Associate professor PhD, *Katrine Strandberg-Larsen*, Department of Public Health, Section of Epidemiology, University of Copenhagen, Leading Health Nurse *Ulla Dupont*, *Vejle*, PI *Anne Mette Skovgaard* and co-PI *Janni Ammitzbøll*. The role of the TDSC is to provide the overall supervision of the trial and assess the progress of the trial, the safety of data, and the critical efficacy endpoints. Specifically, the TDSC monitors the progress of the trial and advises on scientific credibility, monitor the accumulating trial data and make recommendations to the TDSC as to whether the trial can continue or underline if there are any ethical or safety issues that may necessitate a modification to the protocol or closure of the trial, or if there is evidence of systematic recruitment or attrition bias. The TDSC ultimately carries the responsibility for deciding whether the trial need to be

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stopped on grounds of efficacy or safety. The TSC will meet twice a year in the data collecting period and ad hoc.

8 Publication strategy

We will pre-register the study protocol, and expect to publish 10-12 scientific manuscripts, including the study design paper (1), papers on process evaluation (3), and papers on effect evaluation within the areas explored, mental health (3), weight (3) and psycho-social disadvantaged families (2) to be submitted to international peer-reviewed journals. Moreover, three PhD thesis will be produced.

All publications follow the Vancouver declarations on authorship and comply with the SDU Open Science Policy including Open Access publishing of results.

The results will be presented at international meetings and conferences, and presented to the public via the home pages of the institutes (www.sdu.dk/da/sif/forskning) and public medias.

9 Perspectives

The project's scientific and potential societal perspectives and relevance.

This project is the first to examine the mental health and weight outcome at 24 months of a focused intervention delivered at child age 9-12 months, addressing sensitive parenting of infants of cognitive and regulatory vulnerability. Future follow-up at age 36 and 60 months are planned to explore the long-term outcomes.

The project is innovative in that it systematically targets regulatory and cognitive problems in infants from the general population, addressing vulnerability markers of mental health problems and overweight in infancy, and using methods to promote sensitive parenting, which are delivered by CHNs. Using an already well-established collaboration between the research group and CHNs as the frame, and including data from a well established municipality database, as well as information from Danish national registries in a randomized controlled design, the project will provide important knowledge on future effective, individually targeted and much needed public health interventions to address mental health problems and overweight in early childhood.

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