Trials

STUDY PROTOCOL

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The VIA Family 2.0 study: a randomized clinical trial evaluating a family-based intervention for children born to parents with mental illnesses–study protocol

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Abstract

Background Children of parents with mental illness face significant increased risks of developing mental health problems and experiencing developmental delays or other negative life outcomes due to genetic and environmental factors. Parental symptoms often disrupt caregiving, leading to family stress, inadequate routines, and insufficient stimulation and support in the home. Research, including findings from the Danish High Risk and Resilience Study, the VIA cohort, has shown substantial developmental, social, and cognitive challenges in these children.

This study aims to evaluate the efficacy of a team-based, multidisciplinary preventive intervention compared with standard treatment for families with recent parental mental illness via a series of predefined outcome measures.

Methods/design This randomized controlled trial, VIA Family 2.0, includes 304 children aged 3–17 years and 128 children aged 0–2 years with a parent with a psychiatric diagnosis and having received treatment within the past three years. The families will be assessed at baseline and thereafter randomized to either treatment as usual or VIA Family 2.0 intervention. The intervention group will be assigned to a multidisciplinary team with expertise from municipal services, child and adolescent psychiatry, and adult psychiatry. A case manager coordinates all the elements and supports the family with their challenges, on the basis of their own motivation. The study period is 24 months, and all participants will be assessed at baseline and after 24 months.

The primary outcomes are cognitive, language and motor development for infants and toddlers aged 0–2 years (Bayley-4, Bayley Scales of Infant and Toddler Development), well-being and behavioral and social development for children aged 3–17 years (the Strengths and Difficulties Questionnaire (SDQ)), perceived parental stress for parents (Parental Stress Scale, PSS), and family functioning for the family (Family Assessment Device, FAD).

Discussion This study examines the impact of a cross-sectoral intervention that integrates expertise across sectors. This study contributes critical knowledge about whether improving family resilience, supporting children's development, and reducing risk loads through holistic family support is possible. This research highlights the potential

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of preventive public health initiatives to promote well-being and reduce long-term adverse outcomes in a high-risk group of children and adolescents.

Trial registration The study is registered at ClinicalTrials.Gov (NCT06312410) on March 15, 2024.

Keywords Familial high-risk, Offspring, Parental mental illness, Multidisciplinary, Early intervention, Child mental health, Family-based intervention

Introduction

Background and rationale

Children born to parents who suffer from a mental illness constitute a significant yet often overlooked group in society, and in social and health care systems [1]. A comprehensive study combining genetic and registry data revealed that personal history of any previous mental illness diagnosis, familial history of mental illness and birth-related factors were the most influential risk factors for specific psychiatric disorders, whereas GWAS-based genetic factors accounted for only approximately 3–5% of the risk [2]. Extensive research spanning several decades systematically shows the profound impact of parental mental illness as one of the strongest individual risk factors for developing a mental illness [3, 4]. Furthermore, parental mental illness is more likely to be associated with a family climate characterized by higher levels of stress or conflicts, leading to an increased risk of trauma exposure. In addition, the home environment is more likely to lack good routines, and age-appropriate and sufficient stimulation and support because of the impact of symptoms on parenting competence and well-being [5]. While it is important for all parents to provide good parenting, parents with mental illness often face stigmatization, which may affect their willingness to ask for help or to share their mental health problems with, for example, professionals in the social system, which leads to reduced access to parenting training courses or other preventive initiatives [6].

Therefore, there is considerable promise in further exploring and testing interventions that focus on the concept of "familial risk" to potentially change the life trajectories of many children [7]. A prediction model based on a simple screening tool, such as a brief test battery, could inform families and society more precisely about risk. Moreover, adapting a stepped care model that takes into account the whole family's challenges and protective factors could guide the way for relevant and specific prevention and early intervention. The VIA *Family 2.0* randomized clinical trial is an example of a step toward this with an intervention model that seeks to embrace the complexity of these children's challenges in a more holistic way than the many ongoing projects that evaluate the effect of more brief interventions such as Family Talk and Let's Talk about Children [8].

The Danish High Risk and Resilience Study—the VIA cohort—has provided valuable insights over the last decade about children born to parents with severe mental illness. The cohort was recruited from Danish national registers and included 522 7-year-old children born to parents diagnosed with either schizophrenia or bipolar disorder or controls from 2012 to 2015, all thoroughly examined at the age of seven years [9]. The cohort has been followed from age seven through comprehensive assessments at ages 11 [10], 15 [11], and 19 (ongoing, study protocol in preparation).

The results from the VIA cohort are highly concerning. Children with a familial predisposition for severe mental illness (defined here as schizophrenia or bipolar disorder) systematically demonstrated impaired or delayed development across various life domains by age seven persisting through age 11. For example, they exhibit motor skill deficits [12, 13], language and social communication impairments [14], cognitive delays [15, 16], and an increased likelihood of living in inadequate home environments [17, 18]. Additionally, they experienced more social difficulties [19, 20], higher levels of psychopathology [21, 22], and suboptimal parenting conditions than controls did [23].

Cluster analysis of data from the cohort identified a subgroup of children with several widespread impairments at age seven, which emphasizes the heterogeneity of this population [24]. Moreover, parental functioning significantly influences the quality of the home environment i.e., the level of stimulation, structure, and support provided in the home to the child, which highlights the association between the family context and child development [25].

While severe mental illnesses such as schizophrenia, bipolar disorder, and recurrent depression carry significant hereditary components, they are not static conditions but should be viewed as dynamic presentations that can change over time. Studies indicate considerable variability in symptomatology and diagnoses over time, with substantial genetic overlap among psychiatric disorders [26–35]. However, from a child's perspective, the parental diagnosis itself may not be important. Rather, what matters is how parenting, everyday routines, and care are affected by parental psychiatric symptoms, side effects of medication treatment, cognitive difficulties,

socioeconomic disadvantages and other consequences of having a parent with a mental illness [36].

Given this complexity and the heterogeneity of the affected families, effective preventive strategies and early interventions must be flexible, adaptive and comprehensive and should include the whole family. The intervention being tested in this trial is a multidisciplinary, holistic, and cross-sectoral team model, which is developed with strong inspiration from the multidisciplinary model for first episode psychosis, "the OPUS team treatment" that has shown clear and positive results on complex problems and is now implemented at a national level in Denmark [37]. The experimental VIA *Family 2.0 team* model is a slightly modified version of the first version of the team model, which was tested in a large pilot study, the VIA Family 1.0 [38–40]. Similarly, it aims to address the multifaceted needs of families with parental mental illness through a multidisciplinary approach, tailored to each family's specific life circumstances. Among the changes from VIA Family 1.0 to VIA Family 2.0 are the inclusion of peer-support on the basis of the following knowledge. The evidence for the effectiveness of family-based peer-support targeting individuals with mental illnesses and their relatives is limited [41]. However, peer-support for people with mental illnesses supports their well-being and personal recovery from mental illness [42, 43]. The results from systematic reviews and meta-analyses of cofacilitated interventions have indicated that equal collaboration between professional and peer-support staff improves support for the personal recovery process among the recipients of the intervention [42, 44]. Furthermore, in a family where one parent has a mental illness, the other parent is almost always affected somehow. Research shows that co-parents are more likely to have poorer daily functioning than the general population is and that co-parents have increased rates of mental health problems—so-called assortative mating [37, 45]. A peer intervention called the "Family-to-Family Education Program" for family members of adults with mental illness showed in a randomized study that the intervention was effective in enhancing coping and empowerment for family members [46]. Finally, a systematic review revealed that children of parents with a mental illness referred to resources that helped them or could help them learn to overcome difficulties that they had experienced while living with a parent with a mental illness, including support from mental health services, social support, and information [47]. Peer-support might be a way to help [48].

Objectives

This randomized clinical trial, called the VIA *Family 2.0* study, aims to evaluate the efficacy of a team-based, multidisciplinary preventive intervention compared with standard treatment for families with recent parental mental illness across various predefined outcomes. By addressing the needs of these families comprehensively, this study endeavors to increase resilience and promote positive mental health outcomes for children and parents alike and for the whole family. As infants and toddlers aged 0–2 years have not been specifically targeted in previous studies, a separate substudy with a single primary outcome for this group is planned.

Trial design

The VIA *Family 2.0* study is a two-armed parallel-group randomized clinical trial of a complex intervention [49]. Randomized clinical trials are the gold standard for evaluating the effects of interventions that might ameliorate disease processes and improve outcomes [50].

The trial includes families with at least one child aged 0–17 years. This decision reflects the family-system approach to the intervention and the need for preventive support across developmental stages [51–54]. Because the model is modular and individually tailored, it is feasible to include the full age span while adapting components to the child's age and the family's circumstances. For infants and toddlers, intervention components primarily target parents/caregivers, whereas children and adolescents may participate in age-appropriate elements according to preference and relevance. Environmental factors in the early years have a strong impact on a child's psychological, cognitive, motor, and emotional development [51–54]. Therefore, families who are dealing with recent consequences of parental mental illness while also having caregiving responsibilities for infants, toddlers, and children in middle childhood are often stressed, worried, and in need of advice and support—which is the focus of the intervention.

Treatment as usual (TAU) consists of three family consultations and optional children's groups, and minor regional differences apply.

Method

Study settings

The VIA *Family 2.0* study is one of the main activities of the Research Center for Family-Based Interventions, which is a well-established and close collaboration between the research unit at Child and Adolescent Mental Health Center, the Adult Mental Health Research Center Copenhagen (CORE), both in the Capital Region of Denmark, and the Research Unit for Child and Adolescent Psychiatry, Aalborg University Hospital, North Denmark Region. Families are recruited from both sites, the North Denmark Region and the Capital Region of Denmark. Together, these two regions constitute

approximately 40% of the Danish population. The intervention teams are situated at one location at each site, one in Aalborg in the North Denmark Region and one in Copenhagen in the Capital Region of Denmark. The intervention elements provided may take place in the families' homes or in locations in the municipality or in the local area of the family, depending on their preferences and needs. These settings are geographically separate from the research teams, who perform the assessment at baseline and follow-up owing to the blinding of the researchers.

Recruitment

Participants can be referred directly from all clinical departments within the mental health service system in the catchment areas of the Capital Region of Denmark or the North Denmark Region, as well as from private adult psychiatrist practitioners, GPs, municipalities, and other primary sector entities. Additionally, individual families may self-refer for inclusion in the trial if they meet the inclusion criteria. Folders and post cards with a QR-code provide information about the simple procedure. When a family is referred to the study, a research assistant will reach out to the family via telephone or email and invite the family to an information meeting regarding participation in the study. The families are informed about their right to have some time to consider if they are interested in participating, and information about ethical aspects is provided in a folder.

Eligibility criteria

The inclusion criteria are:

- Families where at least one parent with a mental illness lives in the catchment area and where at least one biological child under age 18 lives with one of the biological parents.
- Parents with any psychiatric diagnoses (ICD-10 DF00-DF99) that have been diagnosed and/or treated in mental health services at some time point in life. are eligible and confirmed by entry into the patient record if possible. Parents, who may have been eligible for treatment in the secondary sector but have not been treated there due to e.g. lack of capacity or too long waiting time, can also be included.
- To ensure the relevance of the intervention for the family, the parent with mental illness must have received some kind of treatment or support for mental health issues within the previous three years.

All adult participants must consent themselves to participate in the research study, and all biological parents with custody of their children must consent to the child's participation. Children from the age of 15 are also asked for consent.

The exclusion criteria are:

- Families where parents with custody of children do not give informed consent.
- If the only diagnosis the parent ever had was alcohol or drug abuse.
- Translators are provided to ensure that foreign language families can also participate, but there will be cases where this is not possible.
- Families living in the municipalities of the island of Læsø (in the North Denmark Region) or in Bornholm (in the Capital Region of Denmark)—both islands without a bridge connection.
- Families, where all children are placed in care outside of the home full-time, either in an institution or in professional family care. (The family is not excluded if the children are placed part-time in care outside the home).
- If the child/children are not genetically associated with the parent with mental illness (e.g., children born after egg donation or other forms of assisted fertilization with an unknown donor).
- Families with a stepped care score of 0 are excluded to avoid overtreatment. However, these families can be re-referred if their situation (i.e., the number of risk factors) changes.
- Ongoing intensive, full-time family treatment in the municipality (for example staying at an institution for parental evaluation by the authorities).

Intervention

The VIA *Family 2.0 intervention* is offered to all families who are assigned to it via randomization. The experimental intervention involves child-involving elements adapted to the specific age groups of the children and adolescents.

Each family that is randomized to VIA *Family 2.0 team* intervention will be affiliated with a *case manager*, who is a team member that will coordinate all activities and appointments both within the team and with other stakeholders. The case manager will be available throughout the 2-year intervention period. The case manager is educated in all the elements that are offered to the family, plays a very central role in the intervention and will thus be involved in most activities around the family. The case manager offers sparring, coordination and support throughout the period. The family and the case manager initially formulate and define, on the basis of the age of the child(ren) and the family's individual and specific needs and motivation, which problems or aspects of life

are relevant to work with and are also guided by information from the baseline data collection.

The multidisciplinary VIA *Family 2.0 teams* at each site consist of the following:

- A psychologist with experience from child and adolescent psychiatry.
- A nurse with experience from adult psychiatry.
- A social worker with experience from the primary sector.
- A pedagogue with experience from family work in the primary sector.
- A health nurse with a specialty in family functioning.
- An adult psychiatrist and a child and adolescent psychiatrist will be appointed as consultants and have at least monthly meetings with the team.
- Peer-support workers.

The VIA *Family 2.0 team* in the Capital Region of Denmark (i.e., Copenhagen) consists of ten team members and three peer-support workers due to the doubled number of study participants/families, and some positions are therefore doubled. The team in the North Denmark Region (i.e., Aalborg) consists of five team members and three peer-support workers.

All families start with an introduction with the case manager, where both parents are invited to tell their life story and reflect on being a parent. The focus is on hope and coping mechanisms. This leads to a list of themes that the family finds relevant to work with. Making a safety plan for all family members is often relevant—what to do if a crisis arises in the family—who can help and with what? Each family will have the option to select the elements that best meet their needs from the following in dialog with the case manager:

- *Family-based psychoeducation* with the use of Beardslee's Family Talk method [55], with 6–8 sessions about the impact of mental illness on the family's daily life focuses on family communication and family resources.
- *Parent and youth groups* with integrated peer-support.
- *Children's groups.*
- *Parenting support and parental training* (The Triple P method, Positive Parenting Program [56], different courses for each child age group [47]).
- *Mapping and nurturing of resources* in the social network.
- Access to social counseling from the VIA *Family 2.0 team*'s *social worker.*
- *Early assessment of children's possible mental health problems.*
- Focus on support for *school attendance* including the transition to relevant education plans, leisure time activities, hobbies, sports, and other protective factors.

All the elements are adapted to the age of the children. The first three points are central and will be elaborated below.

Psychoeducation Family-based psychoeducation is considered crucial to help families be able to talk openly about the consequences of the mental illness of the parent. Furthermore, it can often improve communication in the family about other topics, such as emotions, conflicts, or problems in general. We chose the Beardslee's Family Talk program, since it has been widely used globally for more than thirty years and has been proven to have significant and positive long-term effects on children's mental health, especially in families with parental depression but also for other mental health problems [55]. The program is manualized with descriptions of each session, six to eight in total, with at least one meeting with all family members present and with an agenda that has been prepared and agreed upon with the parents. For families with children below the age of six, individual material based on the method of "words and pictures" will be made and used to support the children's ability to learn and talk about the mental illness, for example, a book with photos and symbols that parents and children have agreed on.

Co-led peer groups We have developed manuals that include the participation of peers in groups for adolescents, parents living with a mental illness and parents being co-parent to a parent living with a mental illness (i.e., the "other" parent). The manuals are based on a literature search and a coproduction process. All manuals have eight sessions and in the manual for the youth, there is a booster session as well. Each session has a subject, i.e., the family and the mental illness, coping, empowerment and stigmatization. The groups are co-led, meaning that the group is led by a professional worker and a peer-support worker with lived experiences of either being a parent with a mental illness, being a parent with a co-parent with a mental illness or being a youth with a parent with a mental illness.

Children's groups Children's groups are based on Danish manuals, which have already been tested and used in other relevant contexts. They are based on a clear structure with a mix of playful activities combined with changing topics about family life situations, knowledge about

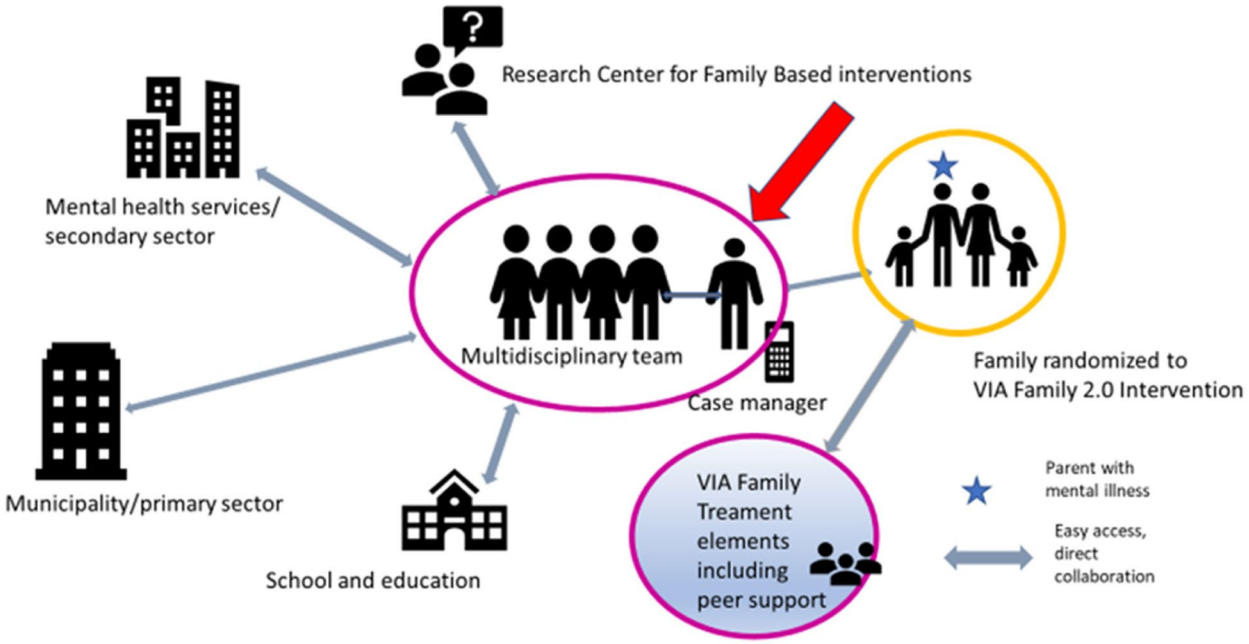

Fig. 1 A graphic overview of the central case manager and the family and the connections and collaboration with relevant institutions in VIA *Family 2.0*

good mental health, coping strategies, etc. Two therapists will be present.

Groups will be conducted simultaneously for adults and children whenever practically possible and will be held in family-friendly locations in the afternoon. After each group session a sandwich is provided to make dinner easy that day for the family.

Parental competence training Parenting has a pervasive influence on child development, given that every parent should have easy access to parental competence building whenever relevant and needed, independent of any mental health problem. We decided to implement the Triple P – Positive Parenting Program by Matts Sanders as part of the intervention offers due to the flexibility of the program, since it has manuals and courses for families with children of all ages and the program can be as intensive or light as needed in each specific family [56]. Furthermore, it is based on widely accepted theories about good parenting and children's needs and development and is always provided according to the principle of least means, meaning that only what is relevant and needed is given. Overall, the key concepts are about having realistic expectations toward the child, using options for learning and stimulation, making clear communication about rules and restrictions, being affectionate and loving when being with the child and knowing and accepting one's own needs and limitations as a parent.

Figure 1 illustrates the team-family working alliance and the connections to other instances. The red arrow shows the case manager's central position between the family and authorized systems.

For the families randomized to the VIA *Family 2.0* intervention, information on selected predefined risk factors from the baseline assessment will be available for the case manager on the intervention team to be able to provide the most relevant elements of the intervention on the basis of the stepped care model.

The stepped care model is presented in Fig. 2. Each risk factor is weighted equally, and the families' risk factors are simply summed after baseline evaluation to inform and guide the intervention team about the level of support needed. Families with one to three risk factors, who are randomized to the VIA *Family 2.0* intervention, will receive "the small package" which consists of case management with monthly contacts, family-based psychoeducation (Family Talk) and parents' and children's groups with integrated peer-support. Families with four to seven risk factors are assigned to "the medium package," which adds parenting support and parental training to the small package. Finally, families with eight or more risk factors are offered individual support, social workers' advice and weekly case management meetings. Since the number of current risk factors can change during the two-year period, the stepped care model is only meant to be a guideline to ensure that the information from the

Parental health-related factors	Cut-off
Hospitalization at psychiatric hospital within previous three years (biological parents)	Yes
Substance or alcohol abuse - *within the last 12 months*	Yes
Family functioning (FAD)	Low
Daily functioning, PSP	≤60
Single parent	Yes
Social network (SPS) - *at least one parent living with the child*	Low

Child factors	Cut-off
Current diagnoses based on DAWBA	≥1 diagnosis
Alcohol or substance abuse	Yes
SDQ age 2-5 years	SDQ ≥13
CGAS from age 6 years	≤60
ADBB until age 25 months	≥5
Bayley-4 scale scores	<8
HOME	<39 or <32 depending on child's age
Absence from school or daycare	*Worrying absence*

Fig. 2 Stepped care model—number of risk factors on the basis of the baseline assessment. Each risk factor is typically given as a score of 1 point. Parents may each contribute 1 point per risk factor, except for the FAD, which contributes a maximum of 1 point per family. Children contribute 1 point per risk factor individually; e.g., multiple children below the CGAS cutoff each add to the total score

baseline data collection is used to inform the intervention team and to ensure that no families receive irrelevant or unneeded intervention elements. The intervention can thus change during the two-year period if the family's situation changes. The intervention team reevaluates the relevant risk factors nine months after inclusion and after 20 months. The principle of least means is always fundamental for all interventions provided.

Intervention fidelity

All staff in the intervention team undergo comprehensive training in all the provided elements, including Beardslee's Family Talk [55] and the Triple P, Positive Parenting Program [56], and they receive supervision during treatment delivery. Fidelity assessments ensure that the intervention is carried out according to the described model and manual. Assessors will monitor fidelity to the model 18 months after study initiation and at least once more during the inclusion period. Fidelity will be monitored via a specifically developed VIA *Family 2.0* fidelity scale. To improve implementation, an action plan will be developed on the basis of the outcome of the fidelity assessments. Furthermore, the intervention team registers every component administered to a family for subsequent analysis in the data entry program REDCap [57].

Treatment as usual (TAU)

The treatment as usual differs slightly between the two regions, but at both sites, it consists of one to three family consultations involving parents and all children above the age of six. In the North Denmark Region, consultations are delivered at the Center for Relatives, whereas in the Capital Region of Denmark, a clinical "key person" with special training in talking to children and families with parental mental illness is employed at the clinical wards or departments. Extra resources have been assigned in the Capital Region of Denmark to assist each family in obtaining access to this offer, since we know from our clinical experience that this is not always implemented as systematically as it is in the Northern Region of Denmark. At both sites, children from age six can be referred to participate in psychoeducational groups conducted by mental health services at various hospitals in the Capital Region or in the Center for Relatives, depending on geography. In these groups, children meet with peers, who also have a parent with a mental illness. In both regions, these groups are run by two therapists with broad experience working with groups such as this for different age groups. Participation in groups is voluntary, and not all children continue in a group after family consultations. For families with children aged zero to five, the intervention is much less systemized and more random in both regions, meaning that there are no fixed recommendations or standards in terms of what the families can expect. There are no national guidelines or legal regulations governing the support provided.

In the trial setup, we assigned resources to ensure that the standard treatment was comparable and similar at the two sites. A specific person will assist families who are randomized to the TAU to ensure access to the treatment offers if the family would like that.

Data collection

Data collection takes place in the families' homes by two researchers, and if needed, supplementary telephone or online contacts can be made. At baseline, intellectual level among children from age 3 was assessed with the Reynolds Intellectual Screening Test (RIST [58]), which was used only descriptively; all other instruments were administered again at the two-year follow-up.

Outcomes

All outcomes, measured at the 24-month follow-up except Bayley-4 (Bayley Scales of Infant and Toddler Development) [59] for infants as described below, are listed in Table 1.

The choice of assessment tools for measuring outcomes after the intervention is informed by findings from two key studies, the Danish High Risk and Resilience Study - VIA 7 [9] and the VIA Family 1.0 study [38, 40], both of which were led by the last author.

All the outcome measures were pilot tested, and a literature search was conducted to ensure the relevance and usability of the intervention and measurement of change over time.

Primary outcomes The main study has three co-primary outcomes. One for the children and adolescents aged 3–17 years, one for the parents, and one for the domain of the entire family. A separate substudy with a sole primary outcome is planned for infants and toddlers aged 0–2 years at inclusion, since these have not been targeted in previous studies.

Children: The primary outcome for children and adolescents aged 3–17 years is development and well-being measured by the SDQ [60]. This 26-item questionnaire is a brief emotional and behavioral screening that includes both problems and social resources. It is widely used and user friendly, and Danish norms are available.

The primary outcome for infants and toddlers aged zero and up to two years at inclusion is cognitive, language and motor development, which is based on scores from the Bayley-4 [59]. Assessments are conducted by trained researchers every 6 months because of the rapid pace of development during early childhood. Therefore, owing to the age span of the instrument, the final follow-up was after 18 months.

Parents: The primary outcome for parents is perceived parental stress measured with the questionnaire Parental Stress Scale (PSS) [61].

Family: The primary outcome for the domain of the entire family is family functioning measured by the questionnaire Family Assessment Device (FAD) [62], which is rated by the primary child informant. However, this instrument is not suitable and is therefore not used for single parents with minor children.

Secondary outcomes The secondary outcomes focus on domains where improvement, positive changes or strengthening of resilience factors can be expected due to specific elements of the intervention and our theory of change (Appendix 2).

Children: For children aged 3–17 years, the secondary outcome is the child's general daily functioning during the previous month measured by the Children's Global Assessment Scale (CGAS), a semi-structured interview with both the caregiver and the child by the researchers [63].

Development and Well-Being Assessment (DAWBA) [64] is a structured, online questionnaire used for child psychopathology assessment and is filled out digitally at baseline by the primary caregiver prior to the clinical assessment and potential diagnoses are subsequently evaluated by a child and adolescent psychiatrist.

Parents: For the parents, the secondary outcomes are measures of perceived stress via the Perceived Stress Scale [65] along with the Client Satisfaction Questionnaire [66] to assess the user's opinions about the services.

Family: For the family context, the secondary outcomes are measures of the quality of the home environment in which the child grows up on the basis of the semi-structured interview Home Observation for Measurement of the Environment (HOME Inventory) [67], which measures the level of stimulation, structure and support provided in the home while the parenting practices, parental adjustment, and family relationships are measured by the Parenting and Family Adjustment Scales (PAFAS questionnaire) [68].

Exploratory outcomes Children: For children aged 7–17 years, the exploratory outcomes are children's stress (Daily Life Stressor Scale (DLSS)) [69], and children's resilience (Child and Youth Resilience Measure (CYRM-R)) [70].

For children aged 0–2 years (at inclusion) the exploratory outcomes are infant social withdrawal (Alarm Distress Baby Scale (ADBB)) [71], and infant social and emotional development (Ages and Stages Questionnaire:SE-2, up to age 60 months) [72].

Parents: For parents, the exploratory outcomes are personal and social functioning according to a semi-structured interview (Personal and Social Performance Scale (PSP)) [73], parental mental well-being (only those without mental illness) (Warwick Edinburgh Mental Wellbeing Scale (WEMWBS)) [74], parental level of psychiatric symptoms according to an interview (Global Assessment of Function – Symptoms (GAF-S)) [75], parental

Table 1 Adapted SPIRIT Figure including outcome measures

	Study period				
	Enrolment	Post-allocation			
Timepoint	$-t_1$	24 months follow up	36 month follow up	Other	Type of assessment
Enrolment					
Eligibility screen	X				
Informed consent	X				
Assessment scales					
Primary outcomes					
Children aged 3–17 years: Strength and Difficulties Questionnaire (SDQ)	X	X	X		QC age 11–17 years QA
Parents: Parental Stress Scale	X	X	X		QA
Family: Family Assessment Device 12 (FAD)	X	X	X		QC age 12–17 years QA
Children aged 0–2 years: Bayley Scales of Infant and Toddler Development (Bayley-4)	X	X *18 months*		Every sixth month	T
Secondary outcomes					
Parents, about the child					
Children's Global Assessment Scale (CGAS)	X	X	X		SI child aged 6–17 years
Children					
Children's Global Assessment Scale (CGAS)	X	X	X		SI child aged 6–17 years
Development and Well-Being Assessment (DAWBA)	X				QC age 11–17 years QA
Parents, about self					
Perceived Stress Scale (PSS)	X	X	X		QA
Client Satisfactory Questionnaire (CSQ)		X			
The family					
Home Observation for Measurement of the Environment (HOME)	X	X	X		SI child and parent together
Parenting and Family Adjustment Scales (PAFAS)	X	X	X		QA
Explorative outcomes					
Children					
Ages and Stages Questionnaire:SE-2	X			Every sixth month	QA
Daily Life Stressor Scale (DLSS)	X	X	X		QC age 7–17 years
Child and Youth Resilience Measure (CYRM)	X	X	X		QC age 7–17 years
Reynolds Intellectual Screening Test (RIST)	X				T age 3–17 years
Alarm Distress BaBy Scale (ADBB)	X			Every sixth month	T age 2 weeks – 24 months
Parents, about self and family					
Personal and Social Performance Scale (PSP)	X	X	X		SI
Warwick Edinburgh Mental Wellbeing Scale (WEMWBS)	X	X	X		QA
Global Assessment of Function – Symptoms (GAF-S)	X	X	X		SI
Kessler Psychological Distress Scale (K10)	X	X	X		QA
General Self-Efficacy Scale (GSE)	X	X	X		QA
Social Provision Scale (SPS-10)	X	X	X		QA
Quality-adjusted life year (EQ5D)	X	X	X		QA
Self-Stigma of Mental Illness Scale – short form (SSMIS-SF)	X	X	X		QA
The Questionnaire about the process of Recovery (QPR)	X	X	X		QA

SI semi-structured interview, *QA* questionnaire adult, *QC* questionnaire child, *T* test

psychological distress (Kessler Psychological Distress Scale (K10)) [76], parental general belief in own capabilities (General Self-Efficacy Scale (GSE)) [77], parents' perceived social network (Social Provision Scale-short form (SPS)) [78], parents' quality of life (quality-adjusted life year (EQ5D)) [79], and parents with a mental illness, mental health self-stigma (Self-Stigma of Mental Illness Scale – short form (SSMIS-SF)) [80] and process of recovery (The Questionnaire of the Process of Recovery (QPR)) [81].

Sample size

Sample sizes are estimated via the formula in Hemming et al. [82].

Level of power and significance: We target a power of at least 90% after adjustment for multiple testing in the main study, implying that the nominal level of significance for the sample size estimation was set to 0.05/3 = 0.0167 because of the three co-primary outcomes (Bonferroni adjustment). In the substudy on infants and toddlers, we target a power of at least 80%.

- SDQ: The VIA Family 1.0 pilot study included 95 families with a mean number of 1.70 children per family and a coefficient of variation (CV) of 0.50 [40]. After baseline adjustment, the residual SD for the SDQ at follow-up was 3.89, with an intraclass correlation coefficient of 0.33. Hence, to detect a clinically relevant difference of 1.5 points, data from 228 families are needed.
- PSS: The mean number of parents participating per family in the pilot study, VIA Family 1.0 was 1.87 with a CV of 0.18. In the VIA Family 1.0, the PSS is measured on an 18-item scale, which is also used in the current study; scores range from 18 to 90, with the lower scores indicating a lower level of stress. After baseline adjustment, the residual SD for PSS at follow-up was 7.38 with an intraclass correlation less than 0.05. Hence, to detect a clinically relevant difference of 4 points, data from 104 families are needed.
- The long version (60 items) of FAD was in the VIA Family 1.0 study, making the SD at follow-up incomparable with that of the current VIA Family 2.0 study, where the short version is used (12 items, measured once per family). However, we expect that our study population will resemble that in The Danish High Risk and Resilience Study, VIA 11 [83], which displayed an SD of 0.51 on the 12-item scale. Expecting a correlation of 0.67 between the baseline and follow-up measurements as in VIA1, we estimate that the residual SD after baseline adjustment will be sqrt (1–0.67^2)*0.51 = 0.38. Please note that similar correlations are to be expected since they are invariant under transformations of scale. Thus, 198 families are needed to detect a clinically relevant difference of 0.2 points.
- Bayley-4: We expect that each family will contribute at most one infant and toddler due to the limited recruitment period. On the basis of data from Rosario et al. [84], we expect that the SD at baseline and follow-up will be 15.0. Hence, if the correlation between the baseline and follow-up measurements is at least 0.50, the residual SD after baseline adjustment will be at most 13.0 and 128 infants and toddlers are needed to detect a clinically relevant difference of 6.5.

To accommodate an attrition rate of up to 25% (as in the pilot study VIA Family 1.0) and support rigorous sensitivity analyses for the missing data, we will include at least 304 children aged 3–17 years and 128 children aged 0–2 years in the entire study.

Allocation

After the baseline assessment is finalized, all families receive verbal feedback about the results of the randomization from the team member, who provides information about participation at the first meeting. If a family has any urgent needs or problems, the researchers will provide the necessary help in terms of e.g., referring to mental health services or making a notification to the municipality. Families are informed about this at the information meeting.

Randomization is conducted digitally by the intervention team leaders via a computer algorithm integrated in REDCap [57]. The allocation concealment mechanism is executed autonomously by a computer algorithm. Neither the individual conducting the randomization, nor any other personnel can influence this process. The randomization sequence follows a predetermined concealed block size order with an allocation ratio of 1:1. The randomization is stratified on the following: site (the North Denmark Region or Capital Region of Denmark), age of the youngest child (0–2 vs. 3–17 years), and dichotomized parental PSP score [73] above or below 60, indicating good/poor daily functioning, and has been shown to correlate with the quality of the home environment and level of child psychopathology [25].

Blinding

Furthermore, researchers are blinded to the block size and frequency. While it is not possible to blind participants or intervention providers, the VIA *Family 2.0* intervention will be situated at a location separate from assessors, data analysts, and researchers. Additionally,

minimal interaction and communication between the intervention team and assessors aims to mitigate the risk of unblinding. In the event of unblinding, this will be documented, and another assessor, unaware of the revealed treatment allocation, will conduct the follow-up outcome assessment for that specific family.

Data collection, management, and analysis

Data collection methods At baseline and at the 24-month follow-up, each family undergoes a comprehensive assessment comprising a brief neurocognitive test (children), interviews including an anamnestic interview with information on socioeconomic characteristics, among others, and questionnaires. The baseline assessment requires approximately seven hours of data collection in total for a family consisting of two adults and two children, mainly one or two home visits and an additional phone call if needed.

To enhance follow-up among families randomized to the TAU, a single booster session will be offered after completion of the follow-up assessment. This amendment has recently been incorporated into the protocol and is pending final ethical approval.

To ensure data quality, assessors hold certifications in administering Bayley-4 [59], RIST [58], and HOME Inventory [67] assessments, conducting regular co-ratings of videotaped interviews and clinical case descriptions. They are also trained in administering the semi-structured interviews PSP [73] and the CGAS [63], which are always scored at regular consensus ratings conducted in an expert group setting. Interrater reliability tests will be performed on the PSP, GAF-S, and CGAS among all the data-collecting research assistants.

Data management All data, including personal information of potential and enrolled participants, are directly entered into the REDCap data entry system [57] by onsite assessors, except for a neurocognitive test that is conducted on paper. The questionnaires for parents are either completed electronically onsite or at home and are completed only in rare cases on paper (e.g., for families without internet access). Paper surveys are subsequently entered into REDCap via double data entry.

For surveys intended for children, questionnaires are read aloud to the child whenever needed. This approach is adapted to maintain standard procedures, minimize variability in assessors' interpretations of children's reading abilities, and ensure consistency across age groups.

To maintain data quality, range checks for data values have been implemented within the REDCap data-entry systems.

Statistical methods Analysis of population and objectives:

All analyses will be conducted in the intention-to-treat population including all study participants who are randomized, regardless of study discontinuation or adherence to the intervention. To provide proof-of-concept, the primary analyses will target a hypothetical estimand corresponding to the effect that would be observed if all families had completed follow-up. To minimize missing data, we will continue to collect data from families who choose to discontinue the intervention as much as possible. However, in the case of higher-than-expected discontinuation rates (> 25%) or differential discontinuation between the intervention groups, supplementary sensitivity analyses, i.e., the difference between the intervention groups that would be found if de facto outcomes could be obtained from the families who were unable to complete the study, will be performed to target the treatment policy.

Primary analysis:

Main study: The effects of the intervention on the SDQ and PSS will be evaluated via a constrained linear mixed model with inherent baseline adjustments including time (baseline vs. follow-up) [85], the constrained intervention*time interaction, and the three stratification variables as fixed effects with a blocked compound symmetry covariance pattern to account for the clustering of family members and repeated measurements on each family member over time. The effect of the intervention on the FAD will be evaluated via a constrained linear mixed model including time, the constrained intervention*time interaction, and the three stratification variables as fixed effects with an unstructured covariance to account for repeated measurements within each family over time. The estimated effects of the intervention will be presented with 98.33% confidence intervals and Bonferroni-adjusted p-values. An adjusted p-value < 0.05 will be considered statistically significant.

Substudy on infants and toddlers: The effect of the intervention on the Bayley-4 score will be evaluated via a constrained linear mixed model including time, the constrained intervention*time interaction, and the three stratification variables as fixed effects with unstructured covariance to account for repeated measurements on each child. The estimated effects of the intervention will be presented with a 95% confidence interval. A p-value < 0.05 will be considered statistically significant.

Secondary and exploratory analyses:

The secondary and exploratory outcomes will be analyzed via linear mixed models similar to those used for the primary analyses. The estimated effects of the intervention will be presented with 95% confidence intervals and p-values adjusted for multiple testing via the

method of Benjamini and Hochberg which controls the false discovery rate [86]. The *p*-values from the secondary and exploratory analyses and from the children aged 3–17, the parents, the family-domain, and the substudy on infants and toddlers will be adjusted separately. An adjusted p-value < 0.05 will be considered statistically significant.

Handling of missing data:

The numbers and reasons for study discontinuation will be tabulated, and descriptive tables will be used to compare the characteristics of completers and non-completers within each intervention group. In the case of a less than 25% discontinuation rate, missing data are handled implicitly via maximum likelihood estimation within the linear mixed models. In the case of higher-than-expected discontinuation rates (> 25%) or differential discontinuation between the intervention groups, sensitivity analyses for the primary outcomes will be performed via penalized controlled imputations to anticipate that families who discontinue the study potentially have worse outcomes than those who complete the study with treatment as usual, although very high functioning families may also do so. Additional sensitivity analyses, e.g., for secondary outcomes, may be performed if they are deemed relevant by investigators or reviewers.

Monitoring

The study operates without a data monitoring committee. The participants assigned to the VIA *Family 2.0* intervention are monitored for adverse events by the intervention team. In cases of hospitalization, monitoring is carried out by a general practitioner or a physician from the Mental Health Center. Should termination of the trial be deemed necessary, the steering committee retains final decision-making authority. At the 24-month follow-up, all participants will be encouraged to voluntarily report any adverse events or unintended effects stemming from the trial. Weekly audits of the study will be conducted by the principal investigator group, individuals uninvolved in the study's day-to-day operations and independent of the sponsors.

Ethics and dissemination

Research ethics approval The study has received approval from the Regional Committee on Health Research Ethics (H-23067714). Prior to enrollment, the VIA *Family 2.0 team* will secure both oral and written informed consent from all adult participants. Additionally, consent for a child's participation will be obtained from their legal guardians. In cases of shared custody, consent from both parents is needed. Adolescents aged 15–17 years are required to provide oral and written informed consent for their participation in the study, in addition to consent from their guardians. When they turn 18 years of age, they will be contacted again for renewed consent for participation.

Protocol amendments Any modification to this protocol will be submitted for approval to the Regional Committee on Health Research, and all changes will be promptly communicated to sponsors and other relevant stakeholders.

The study is registered at ClinicalTrials.Gov (NCT06312410), where any modifications will be promptly recorded.

Declaration of interests The authors declare that they have no competing interests.

Access to data Not applicable.

Dissemination policy All trial results will be disseminated to health-care professionals, the public, and other pertinent groups, irrespective of the outcomes. Within 3 years following the assessment of the final family at the 24-month follow-up, a fully deidentified dataset will be submitted to a suitable data repository for sharing purposes.

Discussion

The VIA *Family 2.0 study* is a randomized clinical trial that aims to evaluate the efficacy of a multidisciplinary team-based preventive intervention compared with standard treatment for families with recent mental illness in parents and children of all ages. This trial design is considered the gold standard for evaluating the potential effects of interventions on disease processes and improving outcomes.

The VIA *Family 2.0* study addresses a critical gap in the knowledge of effective preventive interventions for children in families with parental mental illness. The expectation is that this intervention will contribute to mitigating adverse outcomes for infants, children and adolescents at familial high risk such as preventing or reducing the severity of later or current mental illness and other negative life outcomes.

The inclusion of families with children aged 0–17 years strengthens the pragmatic relevance of the trial by mirroring the heterogeneity of families encountered in routine services. The intervention is designed to be developmentally adaptable, with parent-focused components for younger children and optional, age-appropriate involvement for older children and adolescents. This

broad inclusion supports external validity and enables evaluation of the model as a comprehensive family-based preventive approach.

The study includes parents with all psychiatric diagnoses, acknowledging that mental illnesses are neither stable nor constant. Numerous studies have demonstrated that even individuals diagnosed with traditionally viewed "chronic" conditions such as schizophrenia may experience partial or complete remission after some years, or their clinical presentation may shift into or be influenced by comorbidities such as an eating disorder, social anxiety, or depression [26, 27]. For example, among young individuals with unipolar depression, the absolute risks of progression to bipolar disorder and psychotic disorders are 7.3% and 13.8%, respectively [28]. Additionally, polygenic risk scores (PRSs) for bipolar disorder and schizophrenia are associated with an increased risk of progression to these conditions among individuals diagnosed with depression; however, these genetic effects are relatively small compared with the influence of parental history, particularly concerning bipolar disorder [28]. This approach—"paying more attention to the person than the diagnosis"—is also part of the destigmatization aim of the project, which again may positively affect the person's self-esteem.

Prevention is not the same as treatment; thus, motivation for engaging in preventive activities may vary over time. When urgent problems or crises arise in life—as they often do in families with parental mental illness—prevention tends to be less important, which is natural and understandable. Therefore, the intervention is offered over a two-year period, which may seem long, but experiences from the pilot study showed that this is needed if a family should be able to work with their relationships, communication and self-understanding. First, for many adults it takes time to build a trustful working alliance with the case manager, and second, it takes time to become accustomed to preventive ways of thinking and working.

Strengths

The VIA *Family 2.0 study* is preceded by the VIA Family 1.0 study [38, 40], a pilot study that has provided valuable knowledge for the development and design of the VIA *Family 2.0*. The longer intervention period of 24 months—6 months longer than that in the pilot study—may allow for the detection of differences that were not captured by the pilot study.

As recommended in prevention theory, our selection of primary and secondary outcomes for the research questions is based on our theory of change, which was made as a cocreation process with many different sources of information, i.e., researchers, clinicians, people with lived experiences and other stakeholders.

The assessment battery is comprehensive and covers several areas of interest with validated tests. For many of the tests we have Danish norms, e.g., the primary outcome for the children, the SDQ [60]. We intend to include approximately 600 families in the study on the basis of power calculations of our primary outcomes. The number of participants in this study is several times greater than that in the pilot study and, to the best of our knowledge, any other study in the world.

Limitations

Attrition, particularly from the control group, poses a significant challenge in intervention studies. We anticipate that the initial feedback provided by the researchers, and the emphasis placed on the importance of research participation will incentivize families to remain engaged throughout the study and intermediate contact for all participants. Furthermore, the fact that all families will receive some kind of help and support will make them more positive toward the research program, and all families will be reminded of the follow-up data collection during the study by the staff (VIA Family and TAU), and we will send all participating families a digital postcard after 12 months to keep them in the study (no data collected).

The intensive nature of the VIA *Family 2.0* intervention offers promising opportunities for flexible and comprehensive support. However, we must acknowledge potential weaknesses. While some participants may benefit from the depth and breadth of the intervention, others may find it overwhelming or overly intrusive. This underscores the importance of tailoring interventions to individual needs and preferences. We therefore make an extra effort to ensure that all families are aware of the purpose of the study and are willing and motivated to work preventively before entering the study.

Given the pragmatic and flexible design of our study, isolating the specific efficacy of each treatment element may prove challenging. Our intervention is multifaceted, encompassing various components aimed at addressing the complex needs of families affected by parental mental illness. While this holistic approach aligns with real-world clinical practice, it complicates the attribution of treatment effects to specific intervention components.

Furthermore, the timing of a 24-month follow-up raises questions about the adequacy of the timeframe for observing meaningful differences given the preventive nature of this intervention. Mental health outcomes, particularly in the context of familial risk factors, may evolve gradually over time, necessitating longer follow-up periods to capture sustained changes.

Trial status

Protocol version

The current protocol is Version 9, October 2, 2025. Recruitment will take place from April 2024 to Spring 2026.

The study is registered at ClinicalTrials.Gov (NCT06312410) on March 15, 2024.

Abbreviations

ADBB	Alarm Distress Baby Scale
CGAS	Children's Global Assessment Scale
CYRM	Child and Youth Resilience Measure
DAWBA	Development and Well-Being Assessment
DLSS	Daily Life Stressor Scale
EQ5D	Quality-adjusted life year
FAD	Family Assessment Device
GAF-S	Global Assessment of Function – Symptoms
GSE	General Self-Efficacy Scale
GP	General practitioner
HOME	Home Observation for Measurement of the Environment
ICD-10	International Classification of Diseases version 10
K10	Kessler Psychological Distress Scale
PAFAS	Parenting and Family Adjustment Scales
PSP	Personal and Social Performance Scale
PSS	Parental Stress Scale
RIST	Reynolds Intellectual Screening Test
SD	Standard deviation
SDQ	Strengths and Difficulties Questionnaire
SPS	Social Provision Scale
SSMIS-SF	Self-Stigma of Mental Illness Scale – short form
TAU	Treatment as usual
WEMWBS	Warwick Edinburgh Mental Wellbeing Scale
QPR	The Questionnaire of the Process of Recovery

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s13063-026-09792-3.

Supplementary Material 1.

Acknowledgements

Student Emma Frostholm, postdoc, psychologist Ida CT Gjøde, data manager Michella Heinrichsen, financial controller Pia Schnedler-Meyer, the intervention teams at both sites, all TAU-coworkers and the steering committee. We also thank all the pilot families who gave us sparring and ideas and all those who are or will be involved in the study for their participation. We thank all the families who are and will be involved in the study for their positive participation.

Authors' contributions

AAET obtained funding for the study, designed the VIA *Family 2.0* intervention, designed the trial, and drafted the manuscript. SH contributed to the design, the writing of this manuscript, and to the design of the trial. AR, MBL, LFE, MN, JS, RV, EMB, MM, JF, JSK, ADM, CH, SI, SH, and AAET contributed to the development and design and provided knowledge from their professional experiences through the process. All co-authors critically read the manuscript and approved the final version.

Funding

Open access funding provided by Copenhagen University. The VIA *Family 2.0 study* received funding from the following Danish funds and companies: TrygFonden, Ole Kirk's Fond, KV Fonden, Liljeborgfonden, Ebbefos Fonden, Novo Nordisk Foundation, The Lundbeck Foundation, Independent Research Fund Denmark, Østifterne, Olga og Peter Dudeks Fond and Danish Regions' Prevention Fund.

Data availability

Not applicable.

Declarations

Ethics approval and consent to participate

The study has been approved by the Regional Committee on Health Research Ethics (DNVK) for the Capital Region of Denmark January 25, 2024 (H-23067714).

The VIA Family 2.0 team will obtain oral and written informed consent to participate in the study from all adult participants before enrollment. Each child's guardians will give consent for the child to participate (i.e., if custody is shared, both parents need to give their informed consent). Further, informed consent is ensured by adolescents aged 15–17 years along with their parents.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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Received: 26 October 2025 Accepted: 10 May 2026
Published online: 27 May 2026

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