

Cohort profile: The Trondheim Early Secure Study (TESS) – A study of mental health, psychosocial development and health behaviour from preschool to adolescence

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Why was the cohort set up?

Many mental health disorders in childhood and adolescence are already evident by the preschool years (1-3), but there is little empirical research concerning the prevalence and predictors of psychiatric disorders in young children. If left undetected, child problems may deteriorate and, with time, become more resistant to change (4). Identifying risk factors, co-occurrence of difficulties, developmental trajectories and potential causal mechanisms can aid researchers and clinicians in preventing, diagnosing, and treating mental health problems in children. A true community study using structured diagnostic tools, which are the preferred methods for diagnosis in all age groups and corresponds to medical decision making, had not been published when the Trondheim Early Secure Study (TESS) was established in 2007. Of note, other comprehensive longitudinal community studies of mental health problems in young children did exist at that time, such as the Dunedin study (5) and the Stony Brook Temperament Study (6); however, these studies did not apply diagnostic interviews to assess children's psychopathology. Subsequently, other prospective studies using clinical interviews to assess a wide spectrum of psychiatric disorders, beginning in the preschool years, were launched, perhaps most notably the Factors of Vulnerability to Psychopathology (Barcelona; 2010) (7) and the Leipzig Developmental Study (Leipzig; 2010) (8, 9).

Furthermore, to identify disorders and their risk and protective factors, it is imperative that we understand what characterizes typically developing children. As described in ecological models (10), children's development is affected by the interplay between a variety of influences at the (i) individual (e.g., temperament), (ii) interpersonal (e.g., parent-child interaction), and (iii) community (e.g., access to play areas) levels, but the breadth of potential predictors of development has not been thoroughly captured in former studies, and information has often been collected from only single sources. Because children may behave differently in different arenas (e.g., home versus school), there is only modest agreement

among different informants (11); additionally, to reduce common method variance, data should be gathered from several sources. The TESS therefore aims to capture both the *breadth* of factors affecting children's psychological and social development, as well as the *depth*, by applying diagnostic interviews, observations and tests, in addition to standardized questionnaires, gathering information from the child, the parent and the teacher, as well as from register information. Finally, because unhealthy eating, sedentariness and a lack of physical activity is of great concern in Western societies—nearly one in four American children are overweight (12), with corresponding numbers from Europe (13)—identifying predictors and mechanisms related to weight development, eating behaviour, sedentariness and physical activity was also included as an objective of TESS. In sum, the overall aims of TESS are therefore to (1) identify risk factors, co-morbidity, and developmental trajectories of mental health problems; (2) identify individual, interpersonal, and community factors affecting children's psychosocial development; and (3) identify individual, interpersonal, and community factors affecting children's weight and health-related behaviours. The study is also well positioned to examine mediators, moderators and mechanisms of development. TESS is established in Trondheim, the third-largest city in Norway (approximately 200,000 inhabitants), and has primarily been funded by the Research Council of Norway.

Who is in the cohort?

All children born in 2003 and 2004 with their parents living in the city of Trondheim, Norway, were invited to participate in the study. A letter of invitation along with the Strengths and Difficulties Questionnaire (SDQ) version 4-16 (14), a screening assessment for emotional and behavioural problems, was sent to the children's homes. Parents brought the completed SDQ when they attended the well-child clinic for the routine health check for children aged 4. The health nurse informed the parent(s) about the study using procedures approved by the Regional Committee for Medical and Health Research Ethics and obtained written consent to

participate. Parents with insufficient proficiency in Norwegian to fill out the SDQ screening were excluded (n=176). Of those who were asked to participate (n=3,016), 82.2% consented. To increase statistical power, children with emotional or behavioural problems were oversampled; participants were allocated to four strata according to their SDQ scores (cut-offs: 0-4, 5-8, 9-11, and 12-40), and a subsample (n=1,250) was drawn to participate. The drop-out rate after consent at the well-child clinic did not differ across SDQ score ($p=.86$) or gender ($p=.31$). The recruitment procedure and the participation rates are depicted in Figure 1.

Figure 1 here

Table 1 displays baseline characteristics of the sample.

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The sample is comparable to the Norwegian population with regard to the parents' level of education (15), family situation (i.e., parents married, one-parent household, etc.) (16, 17) and children's Body Mass Index (BMI) (18). Parent's occupation were categorized according to the 6-level International Classification of Occupations (1 = leader to 6 = unskilled worker) (19), and information provided by Statistics Norway showed that differences in the rates of occupational categories between the parent sample and the parent population in the city were negligible, and did not exceed 3.6%.

How often have they been followed up?

Data have been gathered biennially from the age of 4 to the age of 12, and the study is currently ongoing. The sixth wave of data collection will be conducted from August 2017 to June 2019 (age 14). For each measurement point, children and one attending parent have come to the University clinic (4-5 hours), information has been obtained from day-care personnel/teachers, and the non-attending parent completed a questionnaire from the second wave of assessment onwards. Families that have relocated to other parts of the country or

abroad are reimbursed for their travel and accommodation expenses. As shown in Figure 1, the attrition rate is low; our analyses show very little selective attrition, as described in detail in several TESS papers (20-26). More specifically, factors such as gender, attachment, social skills, emotion regulation, behavioural functioning, effortful control, parental mental health and socioeconomic status did not affect the level of attrition (20-24, 26). However, some factors do predict attrition, such as word comprehension, teacher-rated social competence and children's percentage of body fat, but this effect is only observed between certain time points (e.g., from T1 to T2, but not from T1 to T3 and T4), and the combined effect of these predictors of attrition have been shown to be modest (20, 27-29).

What has been measured?

As noted above, to cover a substantial range of factors at the individual, interpersonal and community levels, data have been gathered from the participating child and the attending parent via interviews, validated questionnaires, observations, and objective measures and testing. For example, to capture symptoms of psychiatric disorders the Preschool Age Psychiatric Assessment (PAPA) (30) and the Child and Adolescent Psychiatric Assessment (CAPA) (31) have been applied, which are semi-structured psychiatric interviews for parents of preschoolers and parent- and child interviews for school aged children, respectively. Interviews have also been applied to capture the perceived relationship to parents and friends (32), and a range of questionnaires have been used to measure psychosocial functioning (e.g., Self-esteem: Self Description Questionnaire (33)) and health behavior (e.g., eating: Children's Eating Behavior Questionnaire (CEBQ) (34)). We have included objective measures such as actigraphy (Actigraph GT3X accelerometer) to assess physical activity and bioelectrical impedance (Tanita BC420MA) to assess body composition, as well as observational measures and tests to capture attachment (the MCAST) (35), executive functioning (e.g., A Developmental Neuropsychological Assessment (NEPSY) (36);

CANTAB® neuropsychological test battery (37)), and emotion comprehension (the Test of Emotion Comprehension TEC) (38)). Genetic information was also gathered by collecting two millilitres of saliva using the Oragene DNA saliva kit (DNA Genotek, Ottawa, Ontario, United States of America). Genetic loci of interest were sent to Illumina for generation of a Custom Oligo Assay Pool (OPA) and genotyping was performed at the NTNU Genomics Core Facility with Illumina GoldenGate Genotyping Universal-32 assays, following the manufacturer's protocol. We also have access to register information on the child and parents (e.g., children: grades, scores on national and city-wide school tests, student absenteeism; parents: income, social security benefits, and convictions). A description of the primary measures applied at the six measurement points are displayed in Table 2.

Table 2 here

We have aimed to capture the same factors and to apply the same measures at all assessment points; however, when necessary, we have introduced developmentally appropriate adaptations to the assessments.

What has it found? Key findings and publications

The TESS research group has thus far published more than 40 papers. Some key findings from each of the three main areas of research (i.e., the aims of TESS) are presented here.

Psychiatric symptoms and disorders in childhood

Being the first study to assess psychopathology according to the DSM system (39) in a general population sample of young children outside the US, we found the prevalence rate of psychiatric disorders to be 7% (40), which is 2-4 times lower compared to US studies (3, 41). Children whose parents did not live together or who had low SES were at increased risk for emotional and behavioural disorders, and comorbidity was the norm: Children who had one psychiatric diagnosis were more likely than not to have an additional emotional or

behavioural disorder. Built on these initial findings, several TESS papers have examined predictors of mental health problems from preschool to school age, and have shown that both the child's temperamental negative affectivity and parental depression predicted increased depressive symptoms from ages 4 to 6, whereas social skills protected against symptoms of depression at age 6 (29), as did physical activity. The increase in depressive symptoms from age 6 to 10 was lower in TESS participants with previous higher levels of moderate to vigorous physical activity (MVPA) (42). In relation to childhood anxiety, social skills were found to be protective, whereas high scores on behavioural inhibition, attention-deficient/hyperactivity disorder, parental anxiety, and peer victimization predicted increases in symptoms of anxiety from preschool to first grade (43).

Childhood psychiatric symptoms evince both within-disorder (homotypic) and between-disorder (heterotypic) continuity (44). However, one may ask why this is the case – do prior symptoms cause later symptoms, or do the same causal factors simply operate at different ages? Using TESS data from ages 4, 6, 8 and 10, we found that symptoms of oppositional defiant disorder (ODD) increase the risk for emerging symptoms of conduct disorder (CD) (45). However, in a recent study where a novel data analytic approach (the dynamic panel model) (46, 47) was applied, we showed that most of the observed homotypic and heterotypic continuities in symptoms of psychiatric disorders in childhood are not due to the effect of earlier symptoms on later symptoms, but rather to the effect of unmeasured time-invariant factors (e.g., genetics and stable parenting practices) (27). However, symptoms of ODD/CD did affect later symptoms of such disorders and of ADHD, and ADHD was observed to increase the risk of later anxiety. These findings indicate that interventions which aim to reduce the risk of specific disorders may also protect against the development of other disorders, even if the interventions do not alter basic aetiological factors.

Children's psychosocial development

Children spend most of their waking hours in day-care or in school; therefore it is important to study how aspects of these environments can affect children's development and functioning. In a series of papers, we have examined how organizational and relational characteristics of children's day-care environment can impact their social and behavioural development. In one study, we revealed that time in childcare and the size of the peer group were unrelated to externalizing problems and social competence but were positively related to more caregiver-child conflict (48). Building on these findings, we found that children from open-group centres experienced less teacher-child closeness in preschool and more teacher-child conflict in first grade, and that high levels of preschool problem behaviour predicted high levels of future teacher-child conflict, but only for children from open-group centres (49). Extending these findings and using TESS data collected when children were 4, 6, and 8 years old, we showed that aggression and rule-breaking behaviour were important contributors to future conflicted teacher-student relationships (50). Thus, children's development is affected by an interplay between the organizational aspects of the day-care facility, the quality of the teacher-child relationship and the characteristics of the child. Relationships to peers, or lack thereof, are also influential. We have documented that social exclusion in preschool amplifies aggressive behaviour among children who already behave aggressively (51), and this negatively impacts children's development of self-regulation from preschool to first grade (52).

Acknowledging the bidirectionality of children's social interactions, we examined reciprocal relations in several of our studies. We demonstrated the existence of a reciprocal relation between child-teacher conflict and behavioural problems from preschool to first grade (22) and between social exclusion and self-regulation; lower levels of self-regulation forecast, but were also prospectively predicted, by social exclusion (52). In the same line of research, we have shown that ADHD symptoms at age 4 predict more peer rejection at age 6 and that peer

rejection at age 4 predicts more symptoms of ADHD at age 6 (24). Moving beyond simply establishing prospective relations between potential predictors and their outcomes, the longitudinal design of TESS and the breadth of factors captured have enabled us to examine moderators, mediators and interaction effects. In several papers, we have tested the differential susceptibility model of child development, which states that putatively vulnerable children (e.g., genetic-wise) are also more susceptible to supportive or positive experiences and are thus more developmentally plastic, ‘for better and for worse’ (53). In accordance with this theoretical framework, we have shown that increased attachment security (from ages 4 to 6) predicted improved emotion regulation (from age 6 to 8) and that this effect was most pronounced among children who were homozygous for the 5-HTTLPR-S allele (20). Additionally, val homozygotes (Catechol-Omethyltransferase Val158Met (COMT), a common, functional polymorphism that has been implicated in aggression (54)) are more susceptible to the effects of serious life events on aggression, and when parenting changed for the worse, so did the children’s relationships with teachers, whereas when parenting changed for the better, the teacher–child relationships improved accordingly, but only for children who were homozygous for the A allele of rs53576 (AA carriers) (a polymorphism related to the child’s oxytocin receptor gene (OXTR)) (55). Thus, genetic susceptibility is ‘for better and for worse’.

Eating behaviour, physical activity and weight

Aiming to identify potential predictors of overweight and unhealthy eating behaviours which can be addressed with preventive efforts, TESS has produced several interesting findings. Children whose eating is particularly triggered by the sight and smell of food (‘food responsiveness’) have a steeper increase in BMI SDS (Body Mass Index Standard Deviation Score) than those children whose eating is less externally driven (56). Unsurprisingly, children with a genetic risk for obesity gained weight and fat more rapidly compared to their

peers with a lower genetic risk (57). Although eating behaviour is a candidate mechanism for explaining the link between the genetic risk for obesity and accelerated weight gain in childhood, eating behaviour did not mediate genetic associations with weight gain (57). Nevertheless, since unhealthy eating behavior is related to overweight and may be involved in the development of eating disorders (58-60), it is of great importance to identify factors which affect the development of such behavior. Because parents play a crucial role in shaping their children's eating (61, 62), we examined how the parent's feeding practices affected the development of children's eating behavior in middle childhood. Our research revealed that parental use of food as a reward promotes food responsiveness (i.e., eating is triggered by the sight and smell of food) and emotional eating (63), two eating behaviours that have been shown to be associated with overweight and eating disturbances (58-60). Emotional eating is also predicted by emotional feeding (i.e., using food to soothe the child) (64). Our eating- and weight-related studies have also examined reciprocal relations, revealing a bidirectional relation between emotional feeding and emotional eating, i.e., children who emotionally overeat are more likely to do so over time if their parents use emotional feeding, and parents are more likely to emotionally feed their child if the child is prone to emotional eating) (64). We have also shown that eating behaviour not only predicts, but is also predicted by, children's weight status (56). In summary, these and other TESS studies of children's eating behaviour and weight-development (28, 65-67) have yielded new knowledge upon which to build future preventive interventions.

What are the main strengths and weaknesses?

The main strengths of TESS are 1) the combined use of objective measures, tests, interviews and questionnaires; 2) capturing factors at the individual, interpersonal and community levels; 3) the use of multiple informants and access to register information; and 4) the biennial data collections capturing the years from preschool to adolescence. Furthermore, the

sample is fairly large and representative (e.g., SES, BMI), and the dropout rate is low (Figure 1) and, to a limited extent, selective by study variables. As in most cohort studies on children's psychosocial development (5, 68, 69), parent informants are primarily mothers (84.4%) but their reports are to some extent corroborated by information from the second parental figure (if applicable). In addition, TESS utilized self- and teacher reports to further reduce the risk of relying on a single informant, avoiding the common methodological problems with which it is associated. The application of a semi-structured psychiatric interview (PAPA/CAPA) (30, 31) to capture mental health problems also strengthens the data, as the interviewer probes until he/she can be sure whether a symptom is present; it is not up to the parent to decide. In recent TESS papers (27, 70), we have used a Dynamic Panel Model/fixed effects approach that accounts for time-invariant unmeasured confounders, thus narrowing the gap between mere predictions and causality (46, 47). The application of advanced statistical methods that are rarely used in psychological research is an additional strength of our work.

In the majority of our studies on children's psychopathology, we use symptom counts rather than disorders, which could be considered a limitation. Although there is no convincing evidence that psychopathology is categorical in nature (71), the use of symptom counts indicates that our findings cannot be generalized to diagnosed disorders. Generalization of the findings may also be limited by the fact that our study is carried out in Norway, which we have shown is a country with low rates of psychiatric disorders in childhood (40). Regarding TESS studies of children's psychosocial development, only validated questionnaires are applied, but some of the measures do display moderate internal consistency in our sample (21, 66). In our studies of social exclusion, student-teacher relations, and feeding practices and eating behaviours, we have noted that observational measures would have been an advantage but are too time- and cost-consuming to be applied to large samples, such as the

TESS cohort. A notable limitation in our studies that tested the differential susceptibility theory is that the applied measures do not always encompass both negative and positive aspects of the environment or the measured outcome (e.g., child aggression), which affords the best test of differential susceptibility theorizing.

Can I get hold of the data? Where can I find out more?

The TESS research group collaborates with a number of national and international researchers and welcomes potential collaborators to contact the principal investigator Lars Wichstrøm (lars.wichstrom@ntnu.no) or co-PI Silje Steinsbekk (silje.steinsbekk@ntnu.no). However, the data cannot be made available because the study is still ongoing and consent restrictions from the participants apply. More information regarding the study and the research group, along with a complete list of publications, can be found at <https://tidligtrygg.no/Pages/Hjem.aspx>.

Profile in a nutshell

- TESS is a study of individual, interpersonal and community factors affecting children's mental health, psychosocial development and health behaviour from preschool to adolescence.
- All children born in 2003 and 2004 living in Trondheim, Norway and their parents were invited, and a subsample of 1250 was drawn to participate.
- The first wave of data was collected in 2007/2008 (n=997) when the children were 4 years of age. The fifth data collection was completed in October 2017, and the sixth wave of data (age 14) is being gathered from August 2017 to June 2019.
- The data set comprises information on a huge range of individual (e.g., temperament, genetics), interpersonal (e.g., parent-child interaction, parental mental health) and community factors (e.g., availability of play areas) affecting children's mental health, psychosocial development and health behaviour.
- Information is gathered from participating children, their parents and teachers by means of interviews, tests, observations and questionnaires. TESS also has access to register information.
- Others cannot get hold of these data due to restrictions related to participant consent and because the study is still ongoing, but potential collaborators are welcome to contact the PI or the co-PI of the study.

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