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To Väinö and Viola

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ABSTRACT

Selective mutism (SM) is an anxiety disorder that usually onsets during childhood. Its main symptom is inability to speak in some situations despite normal speech in others. Sociodemographic factors are known risk factors for psychiatric disorders, but research on their association with SM is limited. Psychiatric disorders tend to cluster in families, but findings on psychiatric disorders among family members of subjects with SM are not uniform. The aim of the current thesis was to validate the use of the SM diagnosis and to investigate family psychopathology and demographic risk factors associated with SM, along with its long-term outcomes.

The study used a nested register-based case-control setting. Information on subjects, controls and their parents and siblings were obtained from Finnish health registers. Each subject was matched by gender and age with four control subjects. Study I included 860 subjects with SM along with 3,250 controls, and Study II included 658 subjects with 1,661 siblings and 2,029 controls with 4,120 siblings. The validity of the SM diagnosis in use was evaluated by assessing the patient records of a subsample of 53 subjects in Study I. Study I examined parental psychopathology, parental age, maternal socioeconomic status, urbanicity, maternal marital status and parental immigration status. Study II explored sibling psychopathology. A systematic literature review was conducted to investigate the long-term psychiatric outcomes of SM.

The studies found that both parental and sibling psychopathology were associated with SM among the subjects and showed non-specific pattern of clustering of disorders. The validity of SM diagnosis was found to be good. Advanced paternal age, low maternal socioeconomic status and single motherhood at the time of the child's birth were also associated with SM. Among studies included in the review, most children with SM recovered during the follow-up period, but anxiety disorders were common later in life.

Current findings point towards a shared etiology between SM and other psychiatric and neurodevelopmental disorders. In particular, the relationship between the etiology of SM and autism spectrum disorders requires further study. High-quality studies with follow-up times extending to adulthood are warranted.

KEYWORDS: Selective mutism, anxiety disorders, epidemiological studies, register-based studies, child psychiatry

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TIIVISTELMÄ

Valikoiva puhumattomuus (VP) on ahdistuneisuushäiriö, jonka pääasiallinen oire on puhumattomuus tietyssä tilanteessa. Erilaiset väestötieteelliset tekijät on todettu riskitekijöiksi psykiatrisille häiriöille, mutta näitä on tutkittu VP:en suhteen vähäisesti. Psykiatriset häiriöt kasautuvat perheisiin, mutta aiemmat löydökset VP:sta ja perheessä todetuista psykiatrisista häiriöistä eivät ole yhdenmukaisia. Väitöskirjan tavoitteena on arvioida VP diagnoosien luotettavuutta ja tutkia perheen psykiatristen häiriöiden ja väestötieteellisten riskitekijöiden yhteyttä VP:een sekä VP:n psykiatrisia pitkäaikaisvaikutuksia.

Tutkimuksessa käytettiin pesitettyä tapaus-kontrolli asetelmaa ja tiedot tapauksista sekä kontrolleista kerättiin suomalaisista rekistereistä. Yhtä tapausta kohden kerättiin neljä iän ja sukupuolen suhteen kaltaistettua kontrollia. Ensimmäisessä tutkimuksessa oli mukana 860 tapausta sekä 3250 kontrollia, ja toisessa 658 tapausta sekä heidän 1661 sisarustaan ja 2029 kontrollia sekä heidän 4120 sisarustaan. VP diagnoosien luotettavuus arvioitiin käymällä läpi 53 tapauksen potilasasiakirjat. Tutkimuksissa selvitettiin vanhempien ja sisarusten psykiatristen häiriöiden, vanhempien iän, äidin sosioekonomisen aseman, äidin parisuhteen, kaupungissa asumisen sekä maahanmuuton yhteyttä VP:een. VP:en pitkäaikaisvaikutuksia selvitettiin toteuttamalla systemaattinen kirjallisuuskatsaus.

Tutkimuksissa todettiin, että sekä vanhempien että sisarusten psykiatriset häiriöt ovat yhteydessä VP:een, ja yhteys koski laajasti erityyppisiä psykiatrisia häiriöitä. VP diagnoosien luotettavuus arvioitiin hyväksi. Isän korkea ikä, äidin matala sosioekonominen asema sekä se, ettei äiti ollut parisuhteessa lapsen syntyessä olivat yhteydessä VP:een. Systemaattisen kirjallisuuskatsauksen sisältämissä tutkimuksissa lähes kaikkien tapausten oireet väistyivät seurannan aikana, mutta ahdistuneisuushäiriöt ovat yleisiä myöhemmin elämässä.

Tulokset viittaavat yhteiseen etiologiaan VP:en sekä muiden psykiatristen ja kehityksellisten häiriöiden välillä. Erityisesti VP:n yhteyttä autismikirjon häiriöihin tulisi tutkia jatkossa. Laadukkaiden, aikuisuuteen jatkuvien, seurantatutkimusten tarve on ilmeinen.

AVAINSANAT: Valikoiva puhumattomuus, ahdistuneisuushäiriöt, epidemiologinen tutkimus, rekisteritutkimus, lastenpsykiatria

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Abbreviations

ADHD = Attention deficit hyperactivity disorder
ASD = Autism spectrum disorder
CBT = Cognitive behavioral therapy
CI = Confidence interval
DSM = Diagnostic and Statistical Manual of Mental Disorders
FIPS-Anx = The Finnish Prenatal Study of Anxiety disorders
GAD = Generalized anxiety disorder
ICD = International Classification of Diseases
OCD = Obsessive-compulsive disorder
OR = Odds ratio
PRISMA = Preferred Reporting Items of Systematic reviews and Meta-analyses
QuADS = The Quality Assessment with Diverse Studies
RCT = Randomized controlled trial
SES = Socio-economic status
SM = Selective mutism
SP = Social phobia
SSRI = Selective serotonin reuptake inhibitors

List of Original Publications

This dissertation is based on the following original publications, which are referred to in the text by their Roman numerals:

I Koskela, M., Chudal, R., Luntamo, T., Suominen, A. Steinhausen, H-C., Sourander, A. The impact of parental psychopathology and sociodemographic factors in selective mutism - a nationwide population-based study. *BMC Psychiatry* 2020; 20: 221

II Koskela, M., Jokiranta-Olkoniemi, E., Luntamo, T., Suominen, A., Sourander, A., Steinhausen, H-C. Selective mutism and the risk of mental and neurodevelopmental disorders among siblings. *European Child & Adolescent Psychiatry*. 2024; 33: 291-392

III Koskela, M., Ståhlberg, T., Wan Mohd Yunus, W.M.A., Sourander, A. Long-term outcomes of selective mutism: a systematic literature review. *BMC Psychiatry*. 2023; 23: 779.

1 Introduction

Selective mutism (SM) is a psychiatric disorder that usually onsets during childhood. Nowadays, it is considered an anxiety disorder, and is classified as such in the Diagnostic and Statistical Manual of Mental Disorders, fifth edition (DSM-V), and the International Classification of Diseases, eleventh edition (ICD-11) (American Psychiatric Association. 2013; World Health Organization 2019). The main symptom of SM is muteness in certain situations, for example at school, despite speaking normally in other situations.

Prevalence of SM varies between 0.46% and 0.76% in most studies (Viana et al. 2009). Onset of the disorder has been estimated to be around 3–5 years of age (Sharkey and McNicholas 2012; Dogru et al. 2023). There is often a delay after the onset of the symptoms before a diagnosis is made; children with symptoms are usually diagnosed at 6.5–9 years of age (Sharp et al. 2007; Muris and Ollendick 2015). SM is highly comorbid with other anxiety disorders, social phobia (SP) being the most common comorbid diagnosis (Driessen et al. 2020).

Knowledge on the etiology and possible risk factors of SM is limited. Only one genetic study has focused on SM, but it implies that SM does have a genetic background (Stein et al. 2011). There are a few different models that aim to explain the onset of SM (Wong 2010; Muris and Ollendick 2015; Kearney and Rede 2021). The psychodynamic model states that SM could be a way to cope with anger and anxiety that is caused by unresolved problems in the family. The family systems model theorizes that, in families with a child with SM, the relationship between the child and a parent is neurotic and the parent is controlling towards the child. This could lead to phobic behavior that manifests as SM. These two theories lack scientific support as empirical studies on SM are scarce (Wong 2010). It has also been suggested that SM could be a response to a traumatic event, but the latest studies do not support this theory (Muris and Ollendick 2015). Some have argued that SM could be categorized as neurodevelopmental disorder of speech and language because subjects with SM often have speech delay, communication difficulties and sensory issues, and not all subjects have anxiety symptoms (Kearney and Rede 2021). The developmental psychopathology model on the etiology of SM is currently the most supported theory. It states that, instead of one risk factor being a cause of

SM as in previous models, the etiology of SM is a combination of different factors (Muris and Ollendick 2015). Hence, environmental factors, such as immigration and school-related problems, and genes and neurodevelopmental factors together form a risk that anxiety symptoms can develop into SM (Viana et al. 2009; Wong 2010; Muris and Ollendick 2015).

Associations between various sociodemographic risk factors and SM are still largely unknown. Young maternal age and advanced paternal age have been associated with childhood-onset emotional disorders (McGrath et al. 2014). However, only two previous studies have compared the ages of parents of subjects to that of controls, and these did not find a significant difference in parental age (Alyanak et al. 2013; Poole et al. 2021). SM has been observed in all social strata (Kristensen 2000). However, findings on how SM is divided between different socioeconomic status (SES) classes are not uniform (Steinhausen and Juzi 1996; Kristensen 2000; Boneff-Peng et al. 2023). SM is more common in immigrant families (Elizur and Perednik 2003), and bilingualism seems to be a risk factor for SM (Slobodin 2023). Both single motherhood (Guhn et al. 2020; Khanal et al. 2022) and living in a big city (Helenius et al. 2014) have been associated with anxiety disorders among children, and could potentially also increase risk for SM, but no previous studies have analyzed these relationships.

There is existing evidence on the clustering of different psychiatric disorders in families (Steinhausen et al. 2009; Ma et al. 2015). This could be because of shared genetic backgrounds of different psychiatric disorders (Pettersson et al. 2016). However, studies on clustering of SM and other psychiatric disorders in families are limited. Further, previous studies on parental psychopathology and SM are not uniform. Some studies have found high prevalences of psychiatric disorders, especially Social phobia (SP), among both parents of subjects with SM (Remschmidt et al. 2001; Kristensen and Torgersen 2001). In contrast, one study found association only with paternal psychopathology (Alyanak et al. 2013). The only previous epidemiological study on SM that has investigated parental psychopathology did not find a statistically significant association (Elizur and Perednik 2003). Studies on psychiatric disorders among siblings of subjects with SM are scarce. Two studies have found SM symptoms among 20% of the siblings of subjects with SM (Black and Uhde 1995; Remschmidt et al. 2001). SP has also been observed among about 20% of the siblings of subjects with SM (Black and Uhde 1995). There have been no previous register-based studies conducted on family psychopathology and SM. Register-based studies facilitate gathering information on all family members without recall bias, and family members can be identified regardless of the type of relationship, which is helpful in the case of divorced families, for example.

Only a few systematic literature reviews have focused on SM, and most of these have centered around the treatment of SM (Stone et al. 2002; Manassis 2015;

Østergaard 2018; Steains et al. 2021; Hipolito et al. 2023). There have been no systematic literature reviews on the outcomes of SM later in adolescence or adulthood. Duration of SM is considered to be relatively long, around eight years (Remschmidt et al. 2001), but there are no evidence-based conclusions about the recovery rate of SM or about the psychiatric morbidity of the subjects later in life.

Previous studies on SM are based on relatively small numbers of subjects—large, register-based studies are hard to find. Epidemiological studies on SM have been mostly school-based and have focused on the prevalence of the disorder (Elizur and Perednik 2003; Karakaya et al. 2008). Register-based studies enable collecting large samples cost-effectively. Registers can be used to study prevalence, lifetime psychiatric morbidity and different perinatal risk factors for psychiatric disorders. Finnish national health registers have been used widely in research, and the quality of registered diagnoses has been estimated to vary from satisfactory to very good (Sund 2012). In addition to diagnoses, Finnish national registers include information on various sociodemographic variables, pregnancy and birth. Using these registers makes it possible to study sociodemographic risk factors of even rare disorders, such as SM, and to control the findings for several potential cofounders. Knowledge on the risk factors of SM could facilitate earlier psychosocial support and help prevent the onset of the disorder. Recognizing the etiological backgrounds of SM could help in the identification of those at risk for developing SM, as well as in planning treatment and steering future research.

2 Review of the Literature

2.1 Selective mutism

KEY POINTS:

- Selective mutism is a childhood-onset anxiety disorder.
- Age of onset is usually around 3–5 years.
- Occurrence among girls is higher than among boys.
- Selective mutism is often comorbid with other anxiety disorders.
- No previous studies have aimed to validate the use of the SM diagnosis in Finnish health care.

2.1.1 Diagnostic criteria

SM is a disorder that usually onsets during childhood. Its main symptom is the inability to speak in certain situations, despite otherwise speaking normally (Oerbeck et al.). The ICD-10 requires that development of speech is within a normal range and that the symptoms persist for at least four weeks (World Health Organization 1993b). Detailed diagnostic criteria in different diagnostic classifications are presented in **Table 1**. In Finland, it is most common to make diagnoses using criteria according to the ICD-10 manual for research (World Health Organization 1993a). This manual does not mention schizophrenia or transient mutism (i.e., short-lasting muteness) as a part of separation anxiety as exclusion criteria. Otherwise the criteria are identical to ICD-10 criteria for clinicians (World Health Organization 1993a). Overall, the quality of diagnoses registered in Finnish registers have been considered to be good (Sund 2012). However, using the SM diagnosis has not been previously validated in Finnish health care.

The concept of SM was first introduced in 1877 by German doctor Kussmaul as *aphrasia voluntaria* (Kussmaul 1877) and then in 1934 by Swiss child psychiatrist Trames as *elektiver mutismus* (Tramer 1934). DSM-III was the first international diagnostic classification to publish diagnostic criteria for SM (American Psychiatric Association 1980). In the ICD classification, it was first included in the 9th revision

(World Health Organization. 1977). The disorder was called "elective mutism" in the DSM-III and the ICD-10 (American Psychiatric Association 1980; World Health Organization 1993a), but the term was replaced by "selective mutism" in the DSM-IV because the silence among subjects is not considered to be a conscious choice (American Psychiatric Association 2000). Nowadays, SM is classified as an anxiety disorder, first being named as such in the DSM-V and later in the ICD-11 (American Psychiatric Association. 2013; World Health Organization 2019).

Table 1. Diagnostic criteria of SM in the ICD-10 and 11 and in the DSM-V.

Classification	Inclusion criteria	Exclusion criteria
ICD-10 (F94.0)	-Muteness is consistent in certain social situations -Normal or nearly normal comprehension of speech -Symptoms last for at least four weeks	-Symptoms appear only during the first four weeks of school -Child is not familiar with the spoken language -Disorders of speech and language (if there is no clear difference in how the speech is used in certain situations) -Transient mutism during separation anxiety -Pervasive developmental disorders -Schizophrenia
ICD-11 (6B06)	-Consistent failure to speak in certain situations despite speaking normally in others -Symptoms last for at least one month -Interferes with educational achievements or social communication or causes significant impairment in some other area of functioning	-Symptoms appear only during the first four weeks of school -Symptoms are caused by lack of knowledge of, or comfort with, the spoken language -Symptoms are better explained by another mental or neurodevelopmental disorder, such as schizophrenia, transient mutism as part of separation anxiety in young children, or autism spectrum disorder
DSM-V	-Consistent failure to speak in some situations -Normal speech in other situations, for example at home -Duration of the symptoms is at least one month -Symptoms cause impairment in educational or occupational achievements or with social communication	-Symptoms appear only during the first four weeks of school -Symptoms are caused by lack of knowledge of, or comfort with, the spoken language -Symptoms are explained by developmental language disorder -Symptoms occur exclusively during the course of ASD -Symptoms occur exclusively during symptoms of psychotic disorder

2.1.2 Epidemiology

Only a few epidemiological studies have focused on SM. To the best of our knowledge, there are no previous register-based studies on SM besides the ones that were conducted as a part of the current thesis. **Table 2** presents the epidemiological studies on SM.

Table 2. Epidemiological studies on SM.

Authors **Year** **Country**	**Data sources** **Method of data collection**	**Sample size** **Age range** **Diagnostic criteria used**	**Aims**	**Results**	**Other**
Y. Elizur and R. Perednik **2003** **Israel**	Students in obligatory and pre-obligatory state preschools in West Jerusalem Telephone interviews with teachers and questionnaires competed by the mothers of subjects. Controls were recruited from preschools and assessed similarly.	8,475 students 19 controls (10 native, 9 immigrant) 4–6 years DSM-IV	To evaluate prevalence of SM in West Jerusalem preschools, and to evaluate social anxiety, social competence and markers of neurodevelopmental disorders among native and immigrant subjects with SM.	64 (0.76%) children with SM were found among students, of which 31 were immigrants and 33 natives. Incidence for immigrants was 2.2%.	SM was associated with social anxiety, markers of neurodevelopmental disorders (immaturity in motor, cognitive, linguistic and social skills) and poorer social competence.
L. Sharkey and F. McNicholas **2012** **Ireland**	Children in primary school in a pre-defined area in Ireland Survey completed by teachers and a clinical assessment of suspected subjects	10,927 children 4–12 years DSM-IV	Aimed to define prevalence of SM in defined geographic area in Ireland. Additionally, comorbidities and family psychopathology were reported.	20 (0.18%) children had symptoms of SM. Of them, 14 agreed to clinical evaluation, and they all met diagnostic criteria for SM.	50% had a family history of social anxiety disorder, and 43% had family history of autism spectrum disorder.
Bergman et al. **2002** **USA**	Kindergarten, first and second grades in public schools in Los Angeles Survey completed by teachers. Controls were chosen from peers from the same class as subjects.	2,256 students 12 controls 5–7 years DSM-IV	To evaluate prevalence of SM in school-based sample, and to examine characteristics of children with SM.	16 (0.71%) students fulfilled the criteria for SM. Rate of social anxiety and internalizing symptoms were higher among subjects than controls.	Subjects improved during the six-month follow-up but remained symptomatic.

Karakaya et al. 2008 Turkey	Kindergarten, first, second and third grade students of all public/private schools within the city of Kocaeli Survey completed by teachers. Parents of suspected subjects were interviewed.	64,103 students 5–8 years DSM-IV	To evaluate the prevalence of SM in kindergarten, and first, second and third grades in Kocaeli.	526 (0.82%) students had symptoms of SM, but only 21 were confirmed to have SM after interviewing parents. Prevalence was 0.033%. Male to female ratio was 1.3:1.	Most of the diagnosed subjects (15/21) were in the first grade.
Kumpulainen et al. 1998 Finland	Students attending second grade in elementary school in Kuopio Survey completed by teachers. School nurse assessed suspected subjects.	2,010 students 7–10 DSM-III-R	To investigate prevalence of SM and identify characteristics of the subjects with SM.	38 (1.9%) students met criteria for SM. Symptoms started in elementary school in 53% of the subjects with SM. Duration had been more than 12 months in most cases.	32% were performing lower than average in school, the rest were performing at an average level (49%) or above average (19%).
S. Kopp and C. Gillberg 1997 Sweden	Students in schools in West Central Göteborg Survey completed by teachers. Neuropsychiatric examination for suspected subjects.	2,793 students 7–15 years DSM-IV	To establish prevalence of SM by screening school-aged population in two school districts in Göteborg	5 (0.17%) children fulfilled diagnostic criteria for SM.	25 children were classified as shy or reticent.

2.1.2.1 Incidence and prevalence

Prevalence rates of SM vary between different studies: 0.033% at its lowest (Karakaya et al. 2008) and 1.9% at its highest (Kumpulainen et al. 1998) in previous epidemiological studies. A study by Kumpulainen et al. (1998) has been the only one to use DSM-III-R instead of DSM-IV criteria, which could explain its higher rate. A study by Elizur and Perednik (2003) investigated SM prevalence among immigrants separately, and found it to be 2.2%, whereas the respective figure among the whole study population was 0.76% (Elizur and Perednik 2003). More detailed information on these studies can be found in **Table 2.** Incidence of SM can be expected to be lower in register studies, as not all subjects are recognized and diagnosed clinically (Kumpulainen et al. 1998). Since all epidemiological studies have been based on surveys from schools or kindergarten, existing studies cannot show if incidence of SM has changed over time.

2.1.2.2 Age of onset and duration

Age of onset of SM varies between different studies. A cohort study by Black and Uhde (1995) that aimed to describe psychiatric characteristics of subjects with SM (n=30, aged 5.3–12.8 years) reported the mean age of onset to be 2.7 years. Another study, which recruited subjects with diagnosed or suspected SM (n=230, aged 3.75–12 years) via fliers, similarly reported the mean age of onset as 2.85 years (Boneff-Peng et al. 2023). Most studies report symptoms to most likely onset between the ages of 3 and 5 years (Steinhausen and Juzi 1996; Sharkey and McNicholas 2012; Dogru et al. 2023). A Finnish study by Kumpulainen et al. (1998) (described in **Table 2)** found a higher age of onset, as over 50% of the subjects had an onset of symptoms at the beginning of elementary school (Kumpulainen et al. 1998). The duration of the symptoms is considered to be long, 8–9 years (Remschmidt et al. 2001; Melfsen et al. 2022).

Previous studies have shown that there is usually a delay between the onset of symptoms and clinical diagnosis of SM. Most studies show a delay of almost two years (Kristensen 2000; Dogru et al. 2023; Boneff-Peng et al. 2023).

2.1.2.3 Gender ratio

SM seems to be more common among girls than boys, with a ratio of almost 2:1 (Black and Uhde 1995; Steinhausen and Juzi 1996; Kumpulainen et al. 1998; Dogru et al. 2023; Boneff-Peng et al. 2023). Further, the onset of SM symptoms in most studies seems to be later in girls compared to in boys (Steinhausen and Juzi 1996; Dogru et al. 2023). However, the results are not totally consistent; the previously described study by Boneff-Peng et al. (2023) found a later onset of SM symptoms

among boys. A case-control study with clinical subjects (n=21, ages 6–8 years) found that boys had more persistent symptoms than girls (Kolvin and Fundudis 1981), but there are no consistent findings on whether the severity of SM differs between sexes.

2.1.3 Comorbidity

A summary of the most common comorbid diagnoses with SM is presented in **Table 3**, with other anxiety disorders being at the top of the list (Muris and Ollendick 2015; Driessen et al. 2020). Among other anxiety disorders, the most common is SP (Driessen et al. 2020). Previous studies have even considered whether SM is simply a more extreme manifestation of SP instead of its own disorder (Chavira et al. 2007; Young et al. 2012; Poole et al. 2021). The rate of comorbidity with SP varies from 8.2% (Dogru et al. 2023) to 100% (Chavira et al. 2004; Lang et al. 2016), and a meta-analysis resulted in a rate of 69% (Driessen et al. 2020). In a small study where comorbidity was assessed with a form filled by parents (n=14), none of the subjects with SM (n=19, aged 5–8 years) fulfilled the criteria for SP (Nowakowski et al. 2011). Lower rates of SP are often found in studies that report clinical diagnoses (Dogru et al. 2023). It must be noted that there are no instructions for clinicians on whether SM and SP diagnoses should be used at the same time or not. Other anxiety disorders that are commonly comorbid with SM include specific phobia (19%) and separation anxiety disorder (18%) (Driessen et al. 2020).

Associations between SM and various neurodevelopmental disorders have also been studied widely. Studies show that subjects with SM often have language impairment (Steinhausen and Juzi 1996; Kristensen 2000; Manassis et al. 2003). According to the ICD-10, severe language impairment is an exclusion criterion for SM, but both diagnoses can be used if the language skills allow communication and if there is clear difference in using the language in different settings (World Health Organization 1993a). A study by Kristensen (2000) found that, in a clinical sample of subjects (n=54, aged 3.7–16.8 years), 68.5% had some developmental disorder. Among these, the most common were phonological disorder (42.6%), mixed receptive-expressive language disorder (17.3%) and developmental coordination disorder (17.0%), that is, motor dyspraxia (Kristensen 2000). In a Finnish study by Kumpulainen et al. (1998) (described in **Table 2**), a notable proportion of subjects with SM, 32%, also performed below average in school, which could imply learning disorders. Findings on academic skills and learning among subjects with SM are not consistent. One study that evaluated reports by parents and teachers did not find a difference in academic skills between the subjects (n=52, mean age 7.2 years) and the controls (n=52, mean age 7.0) (Cunningham et al. 2004).

Autism spectrum disorder (ASD) is an exclusion criteria for SM in the ICD-10 and ICD-11 (World Health Organization 1993a; World Health Organization 2019); DSM-V allows using these two diagnoses simultaneously but advise caution when doing so (American Psychiatric Association. 2013; World Health Organization 2019). Co-occurrence of these two disorders have been previously discussed (Muris and Ollendick 2021a). A study by Steffenburg et al. (2018) found that the rate of comorbid ASD among subjects with SM (n=97, mean age at diagnosis 8.8 years) was as high as 63%. However, as the diagnoses were assessed retrospectively from the patient records, and the clinic was specialized in neurodevelopmental disorders, the results should not be generalized (Steffenburg et al. 2018). In a previously mentioned study by Kristensen (2000), 7.5% of the subjects were diagnosed with Asperger's disorder. A study by Muris et al. (2023), conducted with sample of clinical (n=25, mean age 8.1 years) and non-clinical (n=127, mean age 8.69 years) children with SM, found autistic features among 48% of the subjects based on assessment forms filled in by parents. This could at least partly be explained by behavioral inhibition, a temperament trait that is common to subjects with SM as well as subjects with ASD (Muris et al. 2023).

Oppositional defiant disorder is also sometimes diagnosed with SM, but it is not likely that SM would be caused by oppositionality (Muris and Ollendick 2015). Previous studies have found diagnostic criteria of oppositional defiant disorders to be fulfilled among 5–14% of the subjects (Black and Uhde 1995; Steinhausen and Juzi 1996; Dogru et al. 2023). The ICD-11 states that an additional oppositional defiant disorder diagnosis should not be assigned if oppositionality is only present in situations where speech is required and refusal to speak is explained by SM symptoms (World Health Organization 2019).

Table 3. Most common comorbidities among subjects with SM

Previously reported comorbidities among subjects with SM	Prevalence according to previous studies
Anxiety disorders	80%[a]
Social phobia	69%[a]
Language disorders	42[b]–52%[c]
Oppositional defiant disorders	5[d]–14%[b]
ASD	7.5[c]–63%[e]

[a] Driessen et al. 2020
[b] Dogru et al. 2023
[c] Kristensen 2000
[d] Steinhausen and Juzi 1996
[e] Steffenburg et al. 2018

2.2 Current knowledge on etiology of selective mutism

KEY POINTS:

- The etiology of SM is still unknown, but anxiety-related background has the strongest evidence.
- The developmental psychology model suggests that the etiology of SM is a combination of environmental factors, neurodevelopmental factors, genetic vulnerability and anxiety-prone temperament (behavioral inhibition).
- Parenting style might play a role in the onset of SM.
- There is some evidence on neurodevelopmental features, such as delayed language and motor skills and sensory issues, among subjects with SM.

The background of SM is still mostly unknown, but there are a few different models aiming to explain its etiology (Wong 2010; Muris and Ollendick 2015). The oldest models are based on the functioning of the family system or on the psychodynamic background (Wong 2010). The family systems model states that SM symptoms originate from a neurotic relationship with a parent (Wong 2010). The psychodynamic model theorizes that SM is caused by family trauma or a "family secret" and that muteness is a way to cope with anger or anxiety (Wong 2010; Muris and Ollendick 2015). Some previous studies suggest that SM is a fear response, and children do not speak when they are frozen with fear (Vogel et al. 2022).

Several previous literature reviews have suggested that the developmental psychology model best explains the development of SM (Viana et al. 2009; Muris and Ollendick 2015; Rozenek et al. 2020), that is, that different environmental factors (such as immigration, school problems and relationships with parents), neurodevelopmental factors (such as developmental delay or speech and language problems) and genetic and temperamental features (behavioral inhibition, oppositionality) together cause the development of anxiety symptoms into SM (Muris and Ollendick 2015). A review by Rozenek et al. (2020) also supports the developmental psychological model and speculates that there could be some unknown factors that cause SM to sometimes manifest with SP and sometimes without it. This review found evidence from previous studies that female gender, controlling parents and educational difficulties might increase the risk for SM (Rozenek et al. 2020). The developmental psychology model is also supported by previous findings that behavioral inhibition plays an important role among subjects with SM (Muris and Ollendick 2021a).

SM having an anxiety-related background is supported by a high rate of comorbid anxiety disorders among subjects with SM (Driessen et al. 2020) as well as the strong resemblance between SM and SP (Chavira et al. 2007; Poole et al. 2021). Researchers have previously hypothesized that subjects with SM have more severe anxiety symptoms than subjects with SP and are frozen with fear in social situations (Yeganeh et al. 2003), although self-reported levels of anxiety have not differed between subjects with SM and SP in previous studies (Manassis et al. 2003; Yeganeh et al. 2006; Young et al. 2012). However, there is some evidence that non-speaking behavior could be an avoidance mechanism in scary situations (Young et al. 2012; Vogel and Schwenck 2021).

Some reviews suggest that SM might not be an ambiguous anxiety disorder, and that sometimes SM symptoms originate from oppositionality or developmental problems (Kearney and Rede 2021; Muris and Ollendick 2021b). This is supported by the finding that many of the subjects with SM additionally have some neurodevelopmental disorder, such as delayed language or motor development, and that they show a higher rate of non-specific markers of neurodevelopmental disorders than controls (Kristensen 2000; Kristensen 2002). With this in mind, it has been speculated that SM might even benefit from categorization among neurodevelopmental disorders instead of anxiety disorders (Kearney and Rede 2021). One review has also suggested that auditory deficiencies might play a role in the onset of SM (Henkin and Bar-Haim 2015).

2.3 Demographics, family and life event risk factors of selective mutism

KEY POINTS:

- Only one previous study has investigated parental age, without findings.
- Findings on family socioeconomic status and on marital status associated with SM are not consistent.
- Immigration and bilingualism are considered to be risk factors for SM.
- Studies have not found that divorce is a risk factor for SM, but there are no case-control studies on parental marital status and SM.
- There are no previous studies on urbanicity and SM.
- The role of family dynamics on onset and on maintaining SM symptoms requires further study.
- Recent literature does not support the theory that traumatic events play a major role in the onset of SM.

There are gaps in existing research on sociodemographic risk factors and SM. Studies report various risk factors, but many of them lack controls and only report prevalence among the subjects (Dogru et al. 2023; Boneff-Peng et al. 2023). Also, there are no previous register studies on the sociodemographic risk factors of SM.

2.3.1 Parental age

Parental age has been found to be associated with different psychiatric disorders. For example, low parental age was found to be associated with attention deficit hyperactivity disorder (ADHD) (Chudal et al. 2015), advanced maternal age has been associated with obsessive-compulsive disorder (OCD) (Chudal et al. 2017) and advanced paternal age with schizophrenia (Helenius et al. 2012). A register-based study by McGrath et al. (2014) that investigated the relationship between parental age and different psychiatric disorders found that low maternal age and high paternal age were associated with behavioral and emotional disorders of childhood. This category also included SM (McGrath et al. 2014).

Only a few studies have investigated the associations between parental age and SM, or have even reported the parental age of the subjects. A study by Boneff-Peng et al. (2023) reported that the mean age of parents during participation was 39.8 years, while the mean age of the subjects was 7.4 years. In a study with 26 clinical subjects (aged 5–13 years) there was no difference in parental ages between subjects and controls (Alyanak et al. 2013). In a study by Poole et al. (2021), comparing

subjects with SM and social anxiety (n=48, mean age 7.9 years) to subjects with only social anxiety (n=48, mean age 9.8 years) and to controls (n=62, mean age 8.6 years), no statistically significant differences in primary caregivers' age between groups was found. The study did not investigate maternal and paternal ages separately, but the primary caregiver was the mother for approximately 90% of the subjects and controls (Poole et al. 2021).

2.3.2 Maternal socioeconomic status

Low family socioeconomic status (SES) has been found to be associated with childhood mental disorders (Reiss 2013). Some studies have looked at SES among families with a child with SM (Steinhausen and Juzi 1996; Kristensen 2000; Boneff-Peng et al. 2023). However, the definition of SES has varied between studies, some defining it based on family income (Boneff-Peng et al. 2023) and some based on parental occupation (Kristensen 2000). In many Finnish studies, SES is based on maternal occupation because previous research has found it to be the strongest indicator for health inequality in Finland (Rantakallio 1979). Boneff-Peng et al. (2023) found that the majority (75.4%) of the families in their study had high SES when defined by family income. A study by Steinhausen and Adamek (1997) investigated family SES in a case-control setting (38 subjects, mean age 9.0, 31 controls, mean age 6.8 years) but did not describe how SES classes were defined. The study found that there were significantly more families with a child with SM in the middle class and fewer in the lower SES class when compared to controls. This finding could be explained by subjects being collected from self-help groups and controls being the other clinical patients without SM (Steinhausen and Adamek 1997). The previously mentioned study by Kristensen (2000) that used a case-control setting and clinically diagnosed subjects with SM did find that there were more families in lower SES classes and fewer in the highest SES class among subjects when compared to controls, but the finding was not statistically significant and SM was observed among all social strata (Kristensen 2000). As findings on family SES and offspring SM are not uniform, more studies are needed.

2.3.3 Parental marital status

A recent study that retrospectively investigated familiar factors of 49 subjects with SM (aged 7–11 years) found that 73.5% of the subjects lived in nuclear families (Dogru et al. 2023). In addition, a study from the US that recruited subjects mainly via flyers found that 90.4% of the parents who completed the forms were married, but it did not specify if the married family members were part of the nuclear family or the extended family (Boneff-Peng et al. 2023). Unfortunately, neither of these

studies compared subjects to controls. A previously described clinical case-control study from Canada did not find a difference between rates of divorced parents between subjects and controls (Cunningham et al. 2004). This is in line with a case-control study by Melfsen et al. (2022) from Germany, which also included clinical subjects (n=28, mean age 12.7 years). It did not find divorced parents to be more common among subjects with SM than among controls (Melfsen et al. 2022). In contrast to these findings, an epidemiological study by Elizur and Perednik (described in **Table 2**) found that marital conflict could be associated with the onset of SM. There are no studies on single motherhood at the time of the child's birth and SM. As single motherhood might be a risk factor for anxiety disorders (Guhn et al. 2020; Khanal et al. 2022), studies on this are needed.

2.3.4 Immigration and bilingualism

Several studies have found association between immigration and bilingualism and SM, but it is still unclear if the reasons behind this are cultural or lingual. A recent literature review by Slobodin (2023), which included eight studies about SM with a group of subjects with immigrant status, stated that onset of SM might be associated with both minority status and bilingualism. However, current literature does not take into account other sociocultural factors (Slobodin 2023). An epidemiological study from Israel (described in **Table 2)** found that the prevalence of SM might be as much as fourfold (2.2%) among immigrants compared to that of native children (0.5%) (Elizur and Perednik 2003). A long-term outcome study by Steinhausen et al. (2006), including clinical subjects with SM (n=33, mean age at follow-up 21.6 years), found 48% of the subjects to be from immigrant families. Immigration predicted additional phobic disorder diagnosis at the follow-up, but was not found to have association with SM symptom outcome at follow-up (Steinhausen et al. 2006). In a study by Starke et al. (2018), 11 bilingual and 7 monolingual mute subjects (aged 3–5.7 years) were followed up for 9 months. Of these children, eight fulfilled the diagnostic criteria for SM at the beginning of the study and seven at the end of the study. Bilingualism or receptive language skills alone were not associated with onset of SM, but speaking behavior in preschool was best predicted by level of anxiety. The results proposed that how well parents were orientated to the mainstream culture affected the speaking behavior of the child. Good orientation to mainstream culture was associated with lower levels of muteness in preschool (Starke 2018). It should be noted that immigration and bilingualism are factors that should be considered when diagnosing SM (i.e., muteness cannot be explained by the child not knowing a language or not being comfortable with it), and SM should not be mistaken for a nonverbal period that is common in bilingual children (Toppelberg et al. 2005).

2.3.5 Urbanicity

No prior studies have been conducted on the relationship between urbanicity and SM. Levels of urbanization could play a role in the development of some psychiatric disorders. A study by Helenius et al. (2012) found that living in a smaller region than the city of Copenhagen decreased the odds of developing schizophrenia (Helenius et al. 2012). Similarly, living in a big city was found to increase the risk for anxiety disorders and substance use disorders (Helenius et al. 2014; Steinhausen et al. 2017). As SM is classified as an anxiety disorder, similar associations could be expected for it, and studies on this are needed. In previous studies, urbanicity was not associated with bipolar disorder and OCD (Helenius et al. 2013; Steinhausen et al. 2013).

2.3.6 Family dynamics

Associations between SM and family dynamics have also been studied previously. The family systems model and the psychodynamic model both theorize that SM has its origins in family functioning (Wong 2010). Originally, these theories arose from clinical observation that mothers of children with SM often seemed to be over-protective and fathers distant (Knud 1979), and a similar pattern has been observed in one case-control study with clinical subjects (n=45, mean age 8.7 years) (Remschmidt et al. 2001). In a study examining parent-child interaction, compared to controls, primary caregivers (90% mothers) of subjects with SM (n=63, aged 4–13 years) seemed to be more controlling and would take over the situation when the child was required to speak (Edison et al. 2011). This finding is not fully supported, as two previously described studies that compared self-reported parenting styles between parents of subjects and controls did not find differences between groups (Cunningham et al. 2004; Alyanak et al. 2013). Another case-control study mentioned above, by Melfsen et al. (2022), that assessed subjects with SM and their parents did not find a difference in the relationships between the mother and the child when compared to controls. The relationship between the father and the subject was more distant and less supportive, compared to controls (Melfsen et al. 2022). Studying dynamics and relationships inside families requires long-term observation, which is difficult to conduct cost effectively with larger data.

2.3.7 Traumatic life events

Case studies have found SM to be associated with post-traumatic stress disorder (Wong 2010) Therefore, several studies have investigated if traumatic life events play a role in the onset of SM (Black and Uhde 1995; Kopp and Gillberg 1997; Kumpulainen et al. 1998; Remschmidt et al. 2001). However, recent literature does not support this theory (Muris and Ollendick 2015). The study by Kumpulainen et

al. (1998) (described in **Table 2**), which included assessments of teachers, found that, although 47% of the subjects had encountered stressful life events, the event occurred had just before the onset of SM symptoms only in 16%. This is in line with a study that found the onset of SM to have occured after a traumatic event in the family only among 17% (5/30) of the subjects (Black and Uhde 1995). Another study, analyzing 100 subjects with SM (mean age 8.7 years), found that among 32% there had been a stressful life event prior to the onset of SM symptoms (Steinhausen and Juzi 1996). A clinical follow-up study by Remschmidt et al. (2001) found at baseline that, for 28 out of 45 subjects, there had been some conflict inside the family (mean age at baseline 8.7 years). The study did not compare the ratio to that of controls; therefore, the significance of this finding remains unclear (Remschmidt et al. 2001).

2.3.8 Language development

Delays in speech and language development among subjects with SM have been reported in several studies (Steinhausen and Juzi 1996; Kristensen 2000; Manassis et al. 2003). Kristensen (2000) found that 52% of the subjects had delayed language development, which was a significantly higher rate than among controls (11%). Steinhausen and Juzi (1996) found that 38% of the subjects (n=100, mean age 8.7 years) had a language or speech disorder, expressive language disorder being most common one (28%). A study comparing seven subjects with SM (mean age 9.7 years) to seven subjects with SP (mean age 11.1 years) found that the subjects with SM showed normal non-verbal cognitive skills and receptive language skills but had poorer narrative skills than the controls (McInnes et al. 2004). Investigating language skills in a child with SM is difficult and partly relies on parental assessment and non-verbal ways of assessment (McInnes et al. 2004). Previously, the concern that clinicians can misdiagnose SM as a language disorder has been raised (Pereira et al. 2019). It is not known, if language disorders are a risk factor for SM or if persistent SM symptoms disturb the development of speech and language (Manassis et al. 2003). This could be studied, for example, with follow-up studies measuring language skills non-verbally to see if persistent mutism symptoms are associated with poorer language skills at follow-up than at baseline.

2.4 Mental and neurodevelopmental disorders among parents and siblings of subjects with selective mutism

KEY POINTS:

- Psychiatric and neurodevelopmental disorders tend to aggregate in families, but findings on parental psychopathology and SM are not uniform.
- Studies on psychiatric and neurodevelopmental disorders among siblings of subjects with SM are lacking.

There are several studies that report psychopathology among family members with SM. Many of these studies report only parental psychopathology (Kristensen and Torgersen 2001; Elizur and Perednik 2003; Chavira et al. 2007; Alyanak et al. 2013; Capozzi et al. 2018), and siblings' psychopathology is only an additional finding in some papers (Kristensen 2000; Elizur and Perednik 2003). Some studies report the prevalence of specific psychiatric disorders, such as anxiety and depression (Alyanak et al. 2013) or SM and SP (Black and Uhde 1995). Some studies report psychopathology in general instead of individual diagnoses (Kristensen 2000; Elizur and Perednik 2003). There are no register-based studies on family psychopathology and SM. Studies on family psychopathology and SM are presented in **Table 4**.

Table 4. Studies on psychopathology among family members of subjects with SM.

Authors Year Country	Study type Data source	Sample size Age range	Aims	Results	Other
Alyanak et al. **2013** **Turkey**	Case-control study Clinical sample	26 subjects, 32 controls and their parents 5–13 years (mean age 8.11 for subjects and 8.18 for controls)	To study if subjects present more internalizing behavior compared to controls, if parents report increased rates of psychopathology and if there is correlation between these two findings.	Rates of paternal anxiety and depression were higher among parents of subjects than among parents of controls.	Maternal psychopathology was not associated with offspring SM, but it was correlated with severity of emotional and behavioral problems of children. This was not observed for paternal psychopathology.
Black and Uhde **1995** **USA**	Cohort study School-based sample	30 subjects 5.3–12.8 years	To assess characteristics of children with SM by using structured clinical interviews and to study if SM and SP are common among family members.	44% of the parents had a history of SP or avoidant disorder and 15% had a history of SM. Among siblings, 21% had a history of SP or avoidant disorder and 19% had a history of SM.	
Capozzi et al. **2018** **Italy**	Case-control study Clinical sample	26 subjects and 32 controls with generalized anxiety disorder (GAD) 2.3–5.8 years among subjects, 2.7–5.8 years among controls	To evaluate psychological characteristics among subjects with SM, controls with GAD and their parents.	There was no significant association between psychiatric diagnoses among parents or family members of subjects with SM. Both mothers and fathers of subjects with SM scored higher in a global severity index of symptom assessment, and fathers of subjects with SM scored higher in phobic anxiety scores compared to parents of children with GAD.	Mothers of subjects with SM scored higher in obsessive-compulsive symptoms, but the finding was not statistically significant.

Chavira et al. **2007** **USA**	Case-control study Sample from internet survey	70 subjects with their parents and 31 controls with their parents Mean age was 6.4 years for subjects and 7.12 years for controls	To assess personality traits and psychiatric disorders among parents of children with SM.	Parents of children with SM had higher rates of generalized SP and avoidant disorder than parents of controls. The rate of non-generalized SP or other psychiatric disorders did not differ between parents of subjects and parents of controls.	More severe form of SM predicted parental generalized SP.
Y. Elizur and R. Perednik **2003** **Israel**	Cohort study School-based sample	8,475 children (64 subjects with SM and 19 controls) 4–6 years	To evaluate prevalence of SM in school-based sample, and to examine characteristics of children with SM. Additionally, association of maternal psychological adjustment and offspring SM was examined.	There was no significant difference between maternal mental health scores among subjects and controls, neither between mental health scores of mothers of immigrant nor non-immigrant subjects with SM.	
H. Kristensen **2000** **Norway**	Case-control study Clinical sample	54 subjects with 108 controls 3.7–16.8 years (mean 9.0 years)	To study developmental disorders, anxiety disorders and elimination disorders among subjects with SM. Additionally, overall rate of parental and sibling psychiatric disorders (reported by parents) was reported.	Rate of psychiatric disorders did not differ between parents of subjects and controls. 16% of the siblings had psychiatric disorders, which was a significantly higher than rate 4.9% among controls.	
H. Kristensen and S. Torgensen **2001** **Norway**	Case-control study Clinical sample	54 subjects with 108 controls Mean age 9.0 years among subjects, 9.1 years among controls	To evaluate personality features and symptom rates among parents of subjects with SM.	There was statistically significant association between maternal schizoid, schizotypal and avoidant features and SM, and paternal schizoid and anxiety features and SM. There was a significantly higher rate of shyness/social anxiety among parents of children with SM than parents of controls.	As avoidant and schizotypal features are associated with social anxiety, results imply that social anxiety among subjects with SM is a familial phenomenon.

Remschmidt et al. **2001** **Germany**	Case-control study/cohort study Clinical subjects	45 subjects (41 at follow-up) and 46 controls Mean age at time at referral 8.7 years and at follow-up 20.5 years	To follow up on subjects with SM, evaluate its course and evaluate different predictive factors.	Among 18/45 mothers of subjects, there were mild psychiatric symptoms, and among 9/45 there were severe psychiatric symptoms. Among fathers, 12/44 had minor psychopathology and 16/44 had remarkable symptoms. 13/44 had characteristics that could be categorized as “abnormal”, as shyness, irritability, and aggressive behavior.	18% of the mothers, 9% of the fathers and 18% of the siblings had a history of SM symptoms.
L. Sharkey and F. McNicholas **2012** **Ireland**	Cohort study School-based sample	10,927 (of which 20 had SM based on assessment form and 14 attended clinical evaluation) 4–12 years	Aimed to evaluate the prevalence of SM in a defined geographic area in Ireland. Additionally, comorbidities and family psychopathology were reported.	Among 9/14 of the families, there were language disorders in first-degree family members. In 2/14 families there was SP among siblings and 7/14 of the parents had received treatment for SP or SM. In 6/14 families there was ASD among first-degree relatives.	
H.C. Steinhausen and R. Adamek **1997** **Switzerland**	Case-control study Cohort study (partly clinical, partly from self-help group)	38 subjects and 31 controls (with emotional disorder and language disorder) Mean age for subjects was 9.0 years (SD 2.9 years) and for controls 6.8 years (SD 2.6 years)	To systematically assess familial factors among subjects with SM.	There were significantly more psychiatric disorders among mothers (15.8%) of subjects than mothers of controls (0%). There was no significant difference between the rate of psychiatric disorders among fathers or siblings of subjects and controls.	

2.4.1 Parental psychopathology

Several studies have explored parental psychopathology and psychological traits and symptoms among parents of subjects with SM. These studies are described in **Table 4.** No register-based studies on parental psychopathology and SM have been previously conducted. The numbers of subjects therefore remain small, as the largest study includes 70 subjects (Chavira et al. 2007). Most studies focused on anxiety disorders in the family, and none of the studies collected parental diagnoses from patient records. The ways of measuring parental mental health varied between different studies, as some assessed symptoms and some psychiatric diagnoses among parents, which makes results difficult to compare.

Results of these studies are not uniform. The studies reported psychopathology among 15.8–60% of the mothers and among 5.3–91% of the fathers of subjects with SM (Steinhausen and Adamek 1997; Remschmidt et al. 2001; Chavira et al. 2007; Capozzi et al. 2018). Some studies found high rates of psychiatric symptoms or disorders among parents of subjects with SM (Remschmidt et al. 2001; Capozzi et al. 2018). However, some studies found no statistically significant difference among the rates of psychiatric disorders or symptoms among parents of subjects and controls (Kristensen 2000; Elizur and Perednik 2003). A case-control study by Alyanak et al. (2013) only found association between paternal psychopathology and SM. Another study found that maternal psychopathology predicted a higher rate of emotional and behavioral problems among subjects with SM (Alyanak et al. 2013). The only association that Steinhausen and Adamek (1997) found with SM was with maternal psychiatric disorders. It should be noted that the study included controls who had diagnosed emotional disorders and language disorders (Steinhausen and Adamek 1997).

Some studies (described in **Table 4**) reported especially high rates of social anxiety among parents of subjects with SM (Black and Uhde 1995; Kristensen and Torgersen 2001; Chavira et al. 2007; Sharkey and McNicholas 2012). In a study by Black and Uhde, 44% of the parents reported having a history of SP. In an epidemiological study by Sharkey and McNicholas (2012), 50% of the parents reported that they had received treatment for SP or SM, but the study did not define which one was being treated. Chavira et al. (2007) used systematic assessments to evaluate for lifetime psychiatric disorders among parents of subjects with SM. They found that 37% of the parents of subjects fulfilled the criteria for generalized SP and 24% for avoidant disorder, while the rates were 14.1% and 4.7% among parents of controls, respectively (Chavira et al. 2007). Kristensen and Torgensen (2001) found significantly more shyness and social anxiety among the parents of subjects than the parents of controls.

Many of these studies reported rates of SM among the parents (Black and Uhde 1995; Steinhausen and Adamek 1997; Remschmidt et al. 2001; Kristensen and

Torgersen 2001; Chavira et al. 2007; Sharkey and McNicholas 2012). Most of the rates were so low that it was not possible to form statistically significant results (Steinhausen and Adamek 1997; Kristensen and Torgersen 2001; Chavira et al. 2007). Among studies described in **Table 4**, the majority of parents with a history of SM were parents of subjects with SM, and 3.9–9.3% of the children with SM had at least one parent with SM (Steinhausen and Adamek 1997; Kristensen and Torgersen 2001; Chavira et al. 2007). Black and Uhde (1995) found a history of mutism among 15% of the parents with SM but did not compare these results to controls. Reported rates of SM among parents of subjects with SM are notably higher than its prevalence in the general population, which is mostly reported to vary between 0.46–0.76% (Viana et al. 2009; Muris and Ollendick 2015).

Only a few studies reported parental psychopathology broadly among different diagnostic categories (Remschmidt et al. 2001; Chavira et al. 2007; Sharkey and McNicholas 2012). These studies found high rates of depression, neurotic disorders, personality disorders, substance use disorders (Remschmidt et al. 2001), ASD (Sharkey and McNicholas 2012) and social anxiety disorders (Chavira et al. 2007) among parents of subjects with SM. Among these studies, only one compared subjects to controls, and only found a statistically significant association with social anxiety disorders (Chavira et al. 2007).

2.4.2 Sibling psychopathology

As most family studies (described in **Table 4)** focused on parental psychopathology, only a few reported psychiatric disorders or symptoms among siblings of subjects with SM (Black and Uhde 1995; Steinhausen and Adamek 1997; Kristensen 2000; Remschmidt et al. 2001; Sharkey and McNicholas 2012). No register-based studies have yet focused on SM and sibling psychopathology. Studies on this possible association have included only small samples, and there have been no case-control studies focusing on it either. None of the existing studies have investigated the siblings directly or have collected the information from the siblings' patient records—most based the findings on parental interviews (Black and Uhde 1995; Steinhausen and Adamek 1997; Kristensen 2000; Sharkey and McNicholas 2012). This may have caused recall bias, and with older siblings, there could be diagnoses that are not known to parents.

Kristensen (2000) reported psychiatric illness among 16% of the siblings of subjects and among 4.9% of siblings of controls, and the finding was statistically significant. In contrast, Steinhausen and Adamek (1997) found no significant difference between the rate of psychopathology between the siblings of the subjects and those of the controls.

Two of the studies described in **Table 4**, only reported rates of SM and/or SP among siblings of subjects (Black and Uhde 1995; Remschmidt et al. 2001). In their school-based cohort study, Black and Uhde (1995) found that 21% of the siblings had a history of SP or avoidant disorder and 19% had a history of SM. The study collected information on sibling psychopathology from parents (Black and Uhde 1995). Remschmidt et al. (2001) found that 18% of the siblings of the subjects had a history of mutistic reactions. They collected information on sibling psychopathology from patient records of the subjects with SM (Remschmidt et al. 2001).

Sharkey and McNicholas (2012) found speech and language disorders among 64.3% of the families and ASD among 43% of the families but did not report if these were diagnoses of the parents or of the siblings. They also reported that there was SP among siblings in two families (14.2%). It should be noted that the study only included 14 families, and only collected information from parents, not directly from siblings (Sharkey and McNicholas 2012).

2.5 Literature reviews on selective mutism

KEY POINTS:

- Most systematic literature reviews focus on the treatment of SM.
- There have only been a few RCTs focusing on the treatment of SM, with low numbers of subjects.
- Treatment studies are unsystematic in reporting outcomes.
- One systematic literature review studied anxiety disorders among subjects with SM and found that 80% of the subjects had comorbid anxiety disorder.
- One systematic literature review found that immigration is most likely a risk factor for SM.
- No reviews have been conducted on the long-term outcomes of SM.

There are not many systematic literature reviews or meta-analyses about SM. This most likely reflects the overall lack of studies on SM. Most of the systematic literature reviews focus on the treatment of SM (Manassis 2015; Østergaard 2018; Steains et al. 2021; Hipolito et al. 2023). However, there are some non-systematic literature reviews have aimed to pull together recent literature on SM (Muris and Ollendick 2015; Hua and Major 2016), and some to bring up recent issues on diagnosing SM (Muris and Ollendick 2021b; Rodrigues Pereira et al. 2021). Systematic literature reviews on SM are presented in **Table 5.**

Table 5: Systematic literature reviews on SM.

Authors **Year** **Country**	**Databases searched** **Type of review**	**Aims**	**Papers included (N)** **Publication years** **Sample sizes (range)**	**Results**	**Other**
Stone and Kratochwill 2002 **USA**	Exhaustive search of literature (searching references from major texts) and databases: Psych Lit, ERIC, Dissertation Abstracts, Social Sciences Citation Abstracts, Biological Abstracts Meta-analysis	Examined treatment outcomes and quality of methods used in different studies. Aimed to form evidence-based procedures for treating SM.	114 (effect size was calculated for 20 articles) N/A N/A	Behavioral treatment was better than no treatment, and there were no differences between different behavioral methods.	Broader reporting of outcome variables, especially academic variables is needed.
Manassis et al. **2015** **Canada**	Medline, Embase, PsycINFO, Web of Science and Cochrane Systematic literature review	To review existing evidence on using medication in treatment of SM.	10 1994–2012 3-21	Symptoms improved in a major proportion of the subjects that used SSRIs (83.5%). Study designs were heterogenous, and there were only three studies with unmedicated controls.	Medication used was SSRIs in 9/10 studies and Phenelzine in one study.
Østergaard **2018** **Denmark**	PubMed, Embase and PsycINFO Systematic literature review	To test if there is evidence in the literature to support if psychosocial or medical interventions, or a combination of these, is effective in treating SM.	15 1994–2015 3–33	In the included studies, 60 children were treated with CBT, 67 with pharmacological treatment and seven with a combination of both. 53 of the children receiving CBT, 55 with pharmacological treatment and 6 with a combination of both had fewer SM symptoms at the end of the of the treatment.	More studies for using combination therapy are needed. Studies had heterogenous study designs, small numbers of subjects and short follow-up periods.

Driessen et al. **2020** **Neatherlands**	Web of science, PubMed, PsycINFO, Embase, Picarta Meta-analysis	To find out prevalence of anxiety disorders among subjects with SM.	22 1995–2016 9–142	80% of the subjects with SM were diagnosed with some additional anxiety disorder. The most common diagnoses were social phobia (69%), specific phobia (19%) and separation anxiety (18%).	Presence of comorbid anxiety disorders had to be validated in some way, for example by using a semi-structured interview.
Pereira et al. **2021** **Neatherlands**	Embase, Medline (Ovid), PsycINFO, Web of Science, Cochrane Central and Google Scholar Systematic literature review	To identify assessment tools that have been used to measure symptoms of SM among studies during the last ten years.	91 (of which 56 used standardized measures and were described in more detail) 2010–2021 1–860	38% of the studies did not report using any standardized assessments. The most common instruments used were The Selective Mutism Questionnaire, the Anxiety Disorders Interview Schedule and the School Speech Questionnaire.	Using standardized assessments is important so that results between different studies are comparable.
Steains et al. **2021** **Australia**	ProQuest, Cochrane, Web of Science, EBSCO, SAGE, Scopus, PubMed, and Clinicaltrials.gov Meta-analysis	To combine results from randomized controlled trials on psychological intervention for SM.	5 2013–2019 21–138	Psychological interventions were more effective than no treatment. The effect was similar whether the outcome was reported as SM symptoms or non-SM symptoms, as anxiety or global functioning.	
White and Bond **2022** **UK**	PsycINFO, British Education Index, Education Resources Information Center, British Library EThOS and Google Scholar Systematic literature review	To evaluate if schools meet the needs of children and adolescents with SM.	24 2003-2018 N/A	Schools play an important role in early identification of SM, planning the treatment of SM and offering support for children with SM.	It is important to educate teachers on SM. Collaboration between parents and the school is essential in treating SM.

Hipolito et al. **2023** **UK**	Medline, EMBASE, PsycINFO, Web of Science, The Cochrane Controlled Trials Register, ICTRP (WHO), CINAHL, ProQuest Dissertation and Theses Global, Educational Resources Information Centre, British Education Index, Education Research Complete, EMCARE and Child Development & Adolescent Studies Meta-analysis	What are the outcomes when SM is treated with nonpharmacological interventions, how are the results measured and is there difference between different treatment methods used?	25 (5 studies included in the meta-analysis) 2000–2021 3–166	Using behavioral interventions and combined methods showed promising results when measuring SM remission and speaking behavior. Study methods were improved over time, but still showed inconsistency.	Outcomes were reported mostly by evaluating speaking behavior, but some also reported level of anxiety, and a few, overall wellbeing and academic impact.
Slobodin **2023** **Israel**	PubMed, PsycNET, Web of Science, and Cochrane Systematic literature review	To review research on SM among linguistically or culturally diverse children.	8 1975–2020 18–860	Included studies show that bilingualism and minority status might be associated with onset of SM, but studies did not examine other sociocultural factors or how bilingualism affected persistence of the disorder.	

2.5.1 Reviews on comorbidities

Although there are non-systematic reviews on comorbidities of SM (Muris and Ollendick 2015; Muris and Ollendick 2021a), only one systematic literature review on this subject was found, and it is described in detail in **Table 5** (Driessen et al. 2020). The study aimed to combine the results of studies investigating the comorbidity rate of SM and anxiety disorders by conducting a meta-analysis. The researchers included 22 studies in the review. Of the subjects, 80% had been diagnosed with an additional anxiety disorder, with social phobia (69%) being the most common one. The other 20% did not have anxiety disorders, but it was unclear if those subjects had any anxiety symptoms (Driessen et al. 2020).

No systematic literature reviews or meta-analyses have focused on other comorbidities among subjects with SM, but some non-systematic reviews discuss, for example, neurodevelopmental and oppositional disorders among subjects with SM (Muris and Ollendick 2015; Muris and Ollendick 2021a). There is some evidence that neurodevelopmental disorders, such as speech and language disorders or general developmental delay, are associated with SM (Muris and Ollendick 2015). Further, there may be similarities between SM and ASD regarding social difficulties, but as current diagnostic criteria advise against diagnosing these disorders simultaneously, studies are lacking (Muris and Ollendick 2021a). Especially because several non-systematic reviews point out the possibility of a heterogenous background of SM, more studies, particularly systematic reviews on comorbidities of SM other than anxiety, are warranted (Rozenek et al. 2020; Kearney and Rede 2021; Muris and Ollendick 2021a).

2.5.2 Reviews on risk factors

Systematic reviews on the etiology and risk factors of SM are lacking. One systematic review by Slobodin (2023) investigates role of immigration and bilingualism in the development of SM; this study is described in **Table 5**. Slobodin found eight articles and summarized that bilingualism and being in a minority may play a role in the onset of SM, but existing studies have not taken other cultural factors into account (Slobodin 2023). No other systematic literature reviews on the risk factors of SM were found.

2.5.3 Reviews on treatment

There are five systematic literature reviews on the treatment of SM, and these are described in **Table 5** (Stone et al. 2002; Manassis 2015; Østergaard 2018; Steains et al. 2021; Hipolito et al. 2023) Of these, three also include a meta-analysis (Stone et al. 2002; Steains et al. 2021; Hipolito et al. 2023). All of these reviews are relatively

new, the oldest one having been published in 2002 (Stone et al. 2002) and the newest in 2023 (Hipolito et al. 2023).

In the oldest systematic literature review, Stone et al. (2002) included studies that had all used psychosocial treatment, behavioral interventions in most studies. This provided evidence that, for SM, treatment is better than no treatment. As most studies used behavioral interventions, a comparison between the different methods could not be done (Stone et al. 2002).

A review by Manassis (2015) aimed to investigate whether medication is an effective treatment for SM. They found that there were ten studies that investigated medication as a treatment for SM, and in most of the studies the medication of choice was selective serotonin reuptake inhibitors (SSRIs), mainly fluoxetine. The majority of the subjects included in the reviewed studies benefitted from SSRIs. The review found that three studies were randomized controlled trials (RCTs), but among these, the numbers of subjects were low, between 4 and 15 (Manassis 2015). A review by Østergaard (2018) aimed to study which treatment, that is, which psychosocial intervention, medication or combination of these two, is most effective in treating SM. There was evidence that both medication and psychosocial interventions, cognitive behavioral therapy (CBT) in particular, were effective in treating SM, with CBT having a slightly better effect. There were not enough studies that used the combination of medication and psychosocial treatment to draw conclusions, but 6/7 of the subjects who received this combination of treatment had fewer SM symptoms at the end of the follow-up, compared to baseline (Østergaard 2018).

A meta-analysis by Steains et al. (2021) aimed to combine the results from RCTs that used psychosocial interventions to treat SM. It included five studies that had all used some kind of behavioral interventions. The controls in most of these studies were assigned to a waitlist or received psychoeducation. The study did not include or review studies with other treatment methods. Results showed that psychosocial interventions were effective in treating SM symptoms and comorbid anxiety symptoms among subjects when compared to no treatment (Steains et al. 2021). In their latest study, Hipolito et al. (2023) conducted both a systematic literature review and a meta-analysis and aimed to compare different nonpharmacological interventions. There were 25 studies included in the synthesis, and they found six RCTs, of which five were included in the meta-analysis. Among the RCTs, all used behavioral methods as exposure and rewarding. One used online CBT treatment, one used psychomotor therapy, one used app-based treatment, one used intensive group behavioral treatment and behavioral therapy at home or at school. The studies using combined behavioral treatments showed promising results when measuring remission rates and speaking behavior. Due to the low number of RCTs, it was not possible to test the effect of specific treatment methods (Hipolito et al. 2023). When Hipolito et al. (2023) compared their results to the results from a review by Stone et

al. (2002), they found that the newer studies included improved study methods. There had been more experimental studies during the last two decades, and almost all studies had used manualized treatments (Stone et al. 2002; Hipolito et al. 2023).

In conclusion, all reviews showed promising results for both psychological interventions and medication in treating SM, the best evidence observed with CBT-based interventions. As CBT-based therapies are mainly studied among subjects with SM, there were no comparisons between CBT and other psychosocial methods. There has been no meta-analysis on pharmacological interventions for SM. Even though the latest review found that study methods have improved (Hipolito et al. 2023), all of the reviews reported that the included studies were heterogenous and that systematic good-quality studies are warranted in the future.

2.5.4 Reviews on long-term outcomes

There are no systematic reviews on the long-term outcomes of SM. None of the systematic reviews on the treatment of SM have aimed to report long-term outcomes, that is, whether subjects develop other psychiatric disorders or if the effect of the treatment persists.

There are some systematic literature reviews on long-term psychiatric outcomes of anxiety disorders other than SM. One systematic literature review on SP found that, among clinical subjects, the recovery rate after 5 years was only 27%. The recovery rate was better among a community-based sample: 77% after three years. Remission rates were 36–100% among studies that used CBT (Steinert et al. 2013). A meta-analysis on childhood anxiety and its long-term outcomes found that childhood anxiety disorders were associated with anxiety, mood disorders, behavioral disorders and substance use disorders later in life. They also found association between childhood anxiety disorders and higher economic costs, although the follow-up time among those studies was only up to two years (Pollard et al. 2023).

2.5.5 Other reviews

Two systematic literature reviews did not fall into the scope of any previous categories. These reviews are also reported in **Table 5**. A review by Pereira et al. (2021) aimed to assess systematic measures for SM symptoms that are used in clinical practice and research. Even though the majority of the studies used some kind of quantified measures to assess SM symptoms, 38% of the studies did not use any diagnostic instruments. The review found that the most common assessments were the Selective Mutism Questionnaire and its version for teachers, the School Speech Questionnaire. These questionnaires are widely used but are studied mostly

with young children. The review emphasizes the importance of using standardized measures in research on SM so that results can be compared (Rodrigues Pereira et al. 2021).

A systematic literature review by White and Bond (2022) investigated the kind of role school has in identifying and supporting children with SM. It found that school has three main roles in supporting children with SM: early identification, planning of treatment together with parents and implementation of the treatment. The review states that it is important that teachers and school staff understand the symptoms of SM so that they can recognize it (White 2023).

2.6 Relevant gaps in research

KEY POINTS:

- Previous epidemiological studies have small numbers of subjects, and there are no previous register-based studies.
- There are no previous validation studies on the SM diagnosis.
- There are no larger population-based studies on parental psychopathology and SM.
- The overall number of studies on sibling psychopathology and SM is low.
- There are no systematic literature reviews on the long-term outcomes of SM.

Studies on SM are lacking, considering the chronicity and psychosocial impairment the disorder causes. There are no previous register-based studies on SM. Register-based studies would add important information to our current knowledge on this disorder by cost-effectively enabling larger sample sizes. This would allow the study of incidence, comorbid diagnoses during lifetime and sociodemographic risk factors, for example. Registers enable matched subjects and controls from the same population, and they can be used to gather information over longer time periods. There are no studies connecting information from different databases, which would be needed to study how SM is related to sociodemographic risk factors such as parental age, maternal SES, immigration and urbanicity. Combining information from different registers would allow researchers to study several risk factors at once, and it would enable them to get more reliable results by controlling for the results with several confounding factors. Some epidemiological studies do exist, but as SM is a relatively rare disorder, the number of detected subjects remains small in these studies (Kopp and Gillberg 1997; Kumpulainen et al. 1998; Elizur and Perednik 2003; Sharkey and McNicholas 2012).

No previous studies have aimed to validate the use of the SM diagnosis in Finnish national health care registers. As Finnish national registers are not originally created for research, it is important to evaluate whether diagnoses are being made according to international diagnostic classifications. Validating registered diagnoses is vital groundwork for register studies, as it makes the studied subjects more reliable.

Literature on the association between parental psychopathology and SM is not uniform. There are no larger population-based studies on parental psychopathology and SM. Most studies on parental psychopathology have focused on anxiety disorders, and only few studies have investigated the broad spectrum of different psychiatric disorders (Chavira et al. 2007; Sharkey and McNicholas 2012). Studies on sibling psychopathology are scarce, and no studies have assessed siblings directly or have factored in siblings' clinical information. Only using information reported by parents can lead to reporting bias. Methods in reporting psychopathology among family members of subjects with SM varies between different studies: some measure symptoms and some disorders. This makes results less comparable to each other. Further studies on family psychopathology and SM could reveal if there are shared backgrounds with other psychiatric disorders. This could be studied from registers by combining information of different family members and their diagnoses.

There are only a few systematic literature reviews on SM and no systematic literature reviews on the long-term outcomes of SM. Evidence-based conclusions about the duration and future psychiatric problems of SM could help clinicians better plan the treatment of SM and the follow-up. Register studies could also be used to study psychiatric diagnoses among subjects with SM later in life.

3 Aims

The aims of the current thesis were to study the risk factors of SM using nationwide register-based data and to validate the use of the SM diagnosis in Finnish national registers. The aim was also to investigate long-term outcomes of SM through a systematic literature review. Detailed aims were as follows:

- The first aim was to evaluate if the ICD-10 diagnostic criteria of SM are fulfilled among a cohort of subjects and, by doing this, to validate the use of the SM diagnosis in Finnish health care (Study I). This was done to lay the groundwork for further studies, to improve reliability of the subjects. The hypothesis was that the validity of the SM diagnosis would be good, as previous studies have found the quality of the Finnish Hospital Discharge Register to be good (Sund 2012).
- The second aim was to examine several potential risk factors for SM in a large nationwide cohort (Study I). The hypothesis was that both advanced and young parental age would be associated with SM, along with lower maternal SES, single motherhood, immigration and living in an urban environment.
- The third aim was to examine the association between mental and neurodevelopmental disorders among parents (Study I) and SM. The hypothesis was that parents of subjects with SM have a higher rate of various disorders than parents of controls.
- The fourth aim was to examine the association between mental and neurodevelopmental disorders among siblings (Study II) and SM among subjects. The hypothesis was that siblings of subjects with SM have a higher rate of mental and neurodevelopmental disorders than siblings of controls, and that the finding would not be restricted to anxiety disorders.
- The fifth aim was to address the lack of evidence regarding the long-term outcomes of SM by systematically reviewing existing follow-up studies that have explored the psychiatric outcomes of SM (Study III). The aim was also to examine the chronicity and psychiatric comorbidity of SM later in life.

4 Materials and Methods

4.1 Register studies (Studies I and II)

Studies I and II were based on a nationwide register-based sample. The data used in the studies was part of the Finnish Prenatal Study of Anxiety Disorders (FIPS-Anx), which is a register study that uses a nationwide population-based sample and examines the association between early developmental factors and family histories of various anxiety disorders (https://www.utu.fi/en/university/faculty-of-medicine/research-centre-for-child-psychiatry/research Accessed: 18.1.2024).

Studies I and II were based on the same sample of subjects and controls. Subjects included only singleton births. All the subjects had received an SM diagnosis (ICD-10: F94.0) in specialized health services in Finland. Subjects were identified from the Care Register for Health Care (Care Register). All the information on controls, parents and siblings and on possible covariates was collected from the Care Register, the Finnish Central Population Register (Population Register) and the Finnish Medical Birth Register (Birth Register). Study I included register information on parents of subjects and controls, and Study II included information on siblings of subjects and controls. In study I, subsample of the subjects diagnosed in the Hospital District of Southwest Finland was obtained to evaluate validity of given SM diagnoses. A more detailed description of the study design can be found in **Figure 1**.

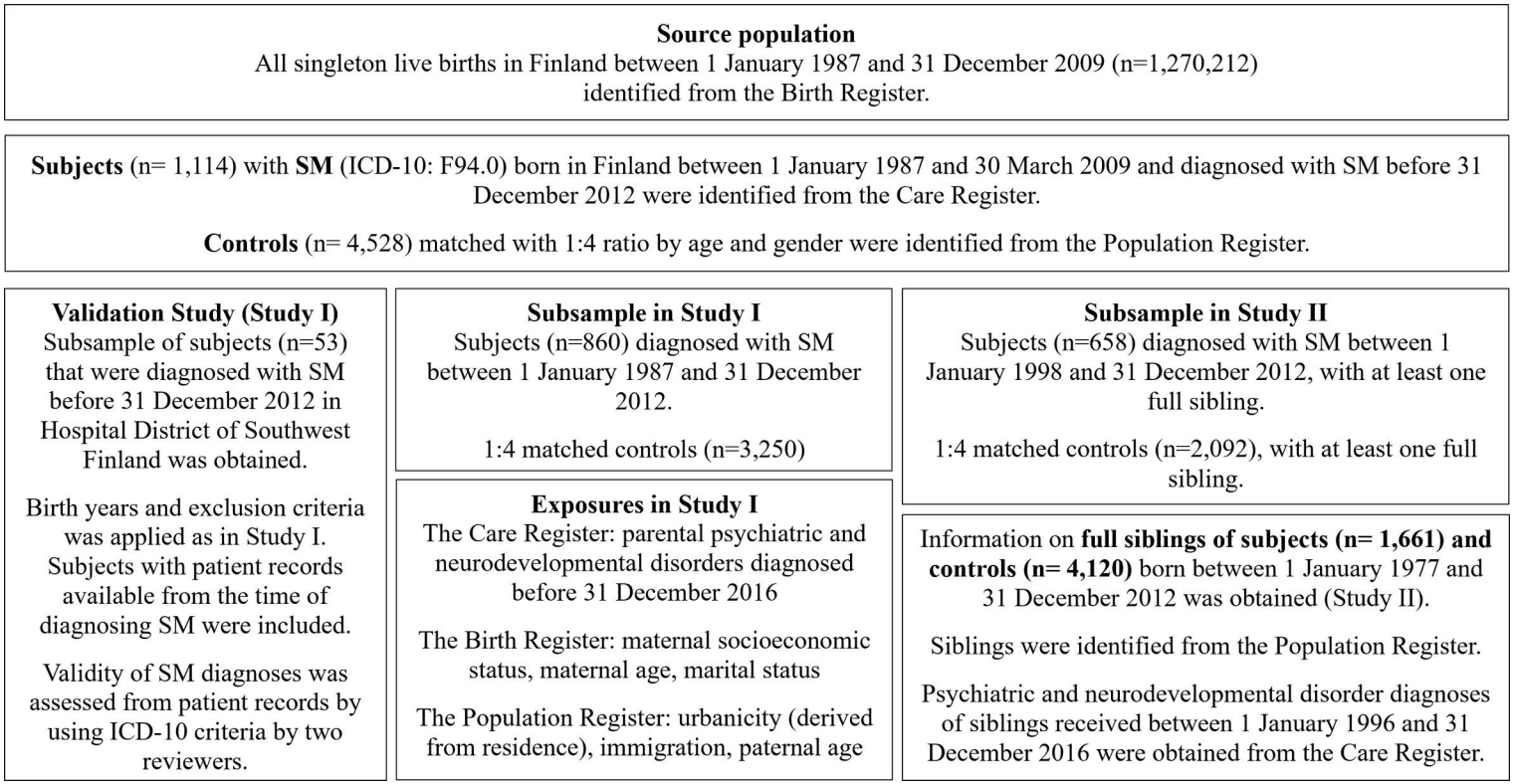

Figure 1. Study design for Studies I and II.

4.1.1 National registers

The data was collected from three registers (the Care Register, the Birth Register and the Population Register). The data collected was linked using the personal identity codes that are issued to all Finnish residents at birth or when they become permanent citizens after immigration.

The Care Register (formerly known as The Finnish Hospital Discharge Register) was established in 1967, and it includes information on the use of health services since 1969. It is maintained by the Finnish Institute for Health and Welfare. It contains information on all diagnoses given in specialized health care services in public health care. It includes information on all inpatient visits since 1969 and information on outpatient visits in specialized health care since 1998. Diagnoses in Finland were registered based on the ICD-9 (World Health Organization. 1977) from 1987 to 1995 and on the ICD-10 (World Health Organization 1993a) since 1996. There is no previous research on how well outpatient visits were recorded in the Care Register during the study period, but coverage for inpatient treatment is considered to be good (Sund 2012). The quality of the Care Register has been shown to vary from good to satisfactory, depending on the diagnosis (Sund 2012). Validation studies have been conducted on various psychiatric diagnoses, and the validity has been shown to be good for ADHD (Leivonen et al. 2014), ASD (Joelsson et al. 2016) and Tourette's syndrome (Lampi et al. 2010). The Care Register was used to identify subjects and to collect information on all mental and neurodevelopmental disorder diagnoses given to subjects and controls and their parents and siblings.

The Birth Register collects information on pregnancy and birth and is maintained by the Finnish Institute for Health and Welfare. It was established in 1987. It contains information on previous pregnancies and deliveries, personal information of the mother, information on pregnancy monitoring, delivery, and information about the infant, such as birth characteristics and data at discharge or by the age of seven days. Maternal SES and maternal marital status have been included in the register since 1991. If the information is for some reason not added to the register during pregnancy and labor, it is completed afterwards; therefore, its coverage is estimated to be near 100% (Gissler, M 2015). This register was used to obtain information on maternal SES, maternal age and marital status during delivery.

The Population Register is maintained by The Finnish Population Register Centre (a government agency), along with local register offices. The Population Register was established in 1969 and contains information on all Finnish citizens and permanent residents living in Finland, including their name, personal identity code, address, native language, citizenship, date of birth and, after passing away, date of death. This register was used to identify controls, as well as the siblings and fathers of the subjects and controls, the age of fathers, controls and siblings, and to

obtain information on residence, which was used to define urbanicity and immigration.

Using register-based data does not require ethical approval in Finland. Despite that, approval for the study was applied for and received from the Ethical Committee of the Hospital District of Southwest Finland.

4.1.2 Validity of selective mutism diagnoses

4.1.2.1 Diagnosing childhood-onset mental disorders in Finnish healthcare

In Finland, health care for children is free of charge. Public health care services are publicly financed in Finland. Growth and development are closely monitored, and there are 15 general health check-ups before children go to school at the age of seven. During the years of school, health check-ups are annual. Practically all children participate in these check-ups (99.5%) (Gissler, M 2015), which are conducted by registered nurses and doctors. Since 2011, it has been required by law to conduct a broad assessment of psychosocial well-being at the ages of 4, 7, 11 and 14 years (Hakulinen-Viitanen et al. 2012). If a concern arises in a health check-up, the situation is first evaluated by a doctor in primary health care; then, if needed, the child is referred to specialized health care. In Finland, 12.9% of children are referred to specialized health care due to a psychiatric or neurodevelopmental issue by the age of 14 (Gyllenberg et al. 2014). Diagnoses in Finland are made based on the ICD criteria and registered in the Discharge Register.

4.1.2.2 Validation of the SM diagnosis used in Finnish healthcare (Study I)

To validate the SM diagnosis in Finnish specialized health services, patient records of the Hospital District of Southwest Finland were searched (Study I) for subjects with SM diagnosed before 31 December 2012. Same inclusion and exclusion criteria as in Study I was used to obtain the same subjects that are included in the register data. This search identified 53 children diagnosed with SM with ICD-10 code F94.0 whose patient records were available at Turku University Hospital. Two reviewers (Petteri Joelsson, Miina Koskela) performed chart assessments for all 53 subjects. The chart assessments were based on the ICD-10 diagnostic criteria for SM and listed all the inclusion and exclusion criteria based on the classification (World Health Organization 1993a). Both reviewers independently went through each subject's patient records thoroughly and recorded in the chart if inclusion or exclusion criteria were fulfilled. It was also written down if there was suspicion of misdiagnosis or

insufficient diagnostic methods, even if criteria according to the chart were fulfilled. Two experienced specialists in child and adolescent psychiatry (Andre Sourander, Terhi Luntamo) supervised the process. To determine if the subjects were correctly diagnosed, the detailed recordings from each reviewer were compared and reviewed by a senior researcher (Terhi Luntamo). Approval from Turku University Hospitals ethics committee was received for the validation study.

4.1.3 Subjects and controls

4.1.3.1 Study I

The sample for Study I included all singleton children born in Finland between 1 January 1987 and 30 March 2009 who had been diagnosed with SM before 31 December 2012, resulting in 1,114 subjects. Subjects diagnosed before age 3 or after age 15 were excluded, as the age range SM most commonly occurs is 3–15. All registered psychiatric and neurodevelopmental diagnoses of subjects and controls and their parents were observed until 31 December 2016; the observation period was thus from 1 January 1987 to 31 December 2016.

All subjects were matched with four controls—who had no anxiety disorders—by their birth date (±30 days) and sex. Subjects and controls with ASD (ICD-10 F84.0–.9, ICD-9229), moderate or severe intellectual disability (ICD-10 F72–73, ICD-9318) or psychotic disorders diagnosed before or concurrently with SM (ICD-10 F20–25, F28–29, ICD-9295, 297, 2989X and 3012C) were excluded, according to ICD-10 exclusion criteria. Due to the predefined inclusion criteria of the FIPS-Anx study, controls with anxiety disorders (ICD-10 codes F40–42, F43.0, F43.1, F43.22, F43.23 and F93–94) diagnosed during the observation period were excluded to make sure that controls did not have any of the disorders that were being studied. After exclusions, 860 subjects and 3,250 controls were included in the final analyses.

4.1.3.2 Study II

The sample for Study II included all singleton children born in Finland between 1 January 1987 and 30 March 2009 who had been diagnosed with SM between 1 January 1998 and 31 December 2012. Subjects that had been diagnosed with SM before 1998 were excluded, as only inpatient diagnoses were registered until 1998. Subjects diagnosed before age 3 or after age 15 were excluded. All subjects were matched with four controls by age (± 30 days) and sex. Subjects and controls diagnosed with ASD (ICD-10 F84.0-0.9, ICD-9 229), psychotic disorders (ICD-10 F20-25, F28-29, ICD-9 295, 297, 2989X, 3012C) or a moderate or severe intellectual disability (ICD-10 F72-73, ICD-9: 318) were excluded, according to the ICD-10

exclusion criteria. As in Study I, all anxiety disorders during observation period were excluded from controls. All registered psychiatric and neurodevelopmental diagnoses of subjects and controls were observed until 31 December 2016; thus, the observation period was from 1 January 1998 to 31 December 2016 for subjects and controls.

Full siblings of both subjects and controls were identified from the Population Register. Siblings born between 1 January 1977 and 31 December 2012 were included. All psychiatric and neurodevelopmental diagnoses given to the siblings were observed between 1 January 1996 and 31 December 2016. Siblings were excluded if they had died or emigrated before the age of 3 as they would not have had the opportunity to have their diagnosis registered. Also, siblings who had immigrated after age 3 were excluded, as they could have had diagnoses given in other countries that were not registered in Finland.

A set of subjects and controls were included in the analyses, if a subject and at least one control had at least one full sibling. Therefore, 658 subjects with SM along with their 1,697 siblings and 2,092 controls along with their 4,211 siblings were included in the study.

4.1.3.3 Diagnostic categories

For the studies, different psychiatric diagnoses were divided into categories based on ICD-10 classification. Two different categorizations were used as adulthood diagnoses were the main interest in Study I, which investigated parental psychopathology. For parental diagnoses in Study I, ICD-10 and -9 diagnoses were divided into categories: SM, ADHD, ASD, conduct disorders, learning and coordination disorders, intellectual disabilities, schizophrenia and schizoaffective disorders, other non-affective psychoses, bipolar disorders, unipolar mood disorders, anxiety disorders, personality disorders, alcohol and drug addiction/abuse and other psychiatric disorders.

Study II focused more on childhood-onset categories. The classification used in Study II is presented in **Table 6**. The same categorization was used to study comorbid diagnoses among subjects with SM in Study I.

Additionally, in Study II, anxiety disorders among siblings were investigated separately in smaller subcategories. This was done to see what kind of anxiety disorders the siblings of subjects with SM had. The classification used for anxiety disorders is presented in **Table 7.**

Table 6. Diagnostic categories used in Study II and for comorbidity in Study I. Modified from Studies I and II.

	ICD-10	ICD-9
1.Any mental or neurodevelopmental disorder	F10–F99	291–319, excluding 316
Schizophrenia spectrum disorders	F20, F21, F22, F23, F24, F25, F28, F29	295, 297, 2989X, 3012C
Affective disorders	F30, F31, F32, F33, F34, F38, F39	296, 3004A, 2988A
Bipolar disorders	*F30, F31*	*2962A-G, 2963A-G, 2964A-G, 2967A*
Unipolar disorders	*F32, F33, F34, F38, F39*	*2961A-G, 2968A, 3004A, 2988A*
Anxiety disorders	F40, F41 (excluding F41.2), F42	3000A, 3000B, 3000C, 3002B, 3002C, 3002D, 3002X, 3003A
Other neurotic and personality disorders	F41.2, F43, F44, F45, F48, F50, F51 (excluding F51.3; F51.4), F52, F53, F54, F55, F59, F60, F61, F62, F63, F64, F65, F66, F68, F69, F99	300–302 (excluding 3000A, 3000B, 3000C, 3002B, 3002C, 3002D, 3002X, 3003A, 3004A and 3012C), 3071A, 3074A, 3074F, 3074H, 3075A, 3075B, 3075C, 3075E, 3078A, 3079X, 309 (excluding 3092A and 3092B), 312 (excluding 3120A, 3123C and 3123D)
Substance abuse disorder	F10, F11, F12, F13, F14, F15, F16, F17, F18, F19	303–305, 291–292
2. Childhood-onset disorders		
Autism spectrum disorders	F84	299
Attention deficit hyperactivity disorder	F90	314
Intellectual disability	F70–F79	317–319
Childhood emotional disorders	F93, F94	3092A, 3092B, 3133A, 3132C, 3138C
Conduct and oppositional disorders	F91–F92	3120A, 3123C, 3123D, 3138A
Tic disorders	F95	3072A, 3072B, 3072C, 3072D
Learning and coordination disorders	F80–F83	315

Table 7. Diagnostic categories for anxiety disorders (Study II). Modified from Study II.

	ICD-10
Generalized anxiety disorder	F41.1, F93.80
Panic disorder and/or agoraphobia	F40.00, F40.01, F41.00, F41.01, F41.08, F41.09
Separation anxiety disorder	F93.0
Social phobia	F40.1, F93.2
Specific phobia	F40.2, F93.1
Unspecific anxiety disorders	F40.8, F40.9, F41.2, F41.3, F41.8, F41.9, F93.89, F93.9
Selective mutism	F94.0

In Study I, a hierarchical model was used, meaning that, if a parent was diagnosed with schizophrenia or a schizoaffective disorder, they would not be assigned to any other additional adolescent or adult-onset category because these are distinctively severe and chronic disorders. With subsequent studies, it was decided that the hierarchical model would be left out. Study II focused more on childhood-onset disorders, and schizophrenia during adulthood cannot be seen as an exclusion criterion for psychiatric disorders during childhood.

4.1.3.4 Other risk factors and covariates

Other variables that were studied as risk factors and used as covariates were maternal and paternal age, maternal SES, parental immigration status, maternal marital status and urbanicity. For Study I, maternal and paternal age were divided into categories as described in **Table 8**. In Study II, parental age was used as a continuous variable because it suited the chosen model best. Maternal age and SES have only been recorded since 1991 in the Birth Register, and because of that, some information is missing. The categories used for maternal SES in Study I can be found in **Table 8**. In Study II, instead of forming a "missing" category, the analyses were only conducted on complete data, as this was seen as a more accurate way to deal with missing data. Maternal SES was missing from 94 subjects (14.3%) and 322 controls (15.4%). This included 7.8% and 7.7%, respectively, who had been born before 1991. The categorization of maternal SES is based on a study by Gissler et al. (2003).

Maternal marital status is registered in the Birth Register at the time of birth. It was classified as married/in a relationship or single. Immigration status was obtained from the Population Register. "Immigrant" was defined as a person who had been born abroad and was not a native speaker of Finnish. Those who had been born in Finland and/or whose native language was one of Finland's official languages (Finnish, Swedish or Sami) were defined as native Finnish. The classification of

immigration status is described in **Table 8**. Urbanicity was also obtained from the Population Register. It was based on density of the population in the area. Towns where ≥90% of the population were living in densely populated areas (i.e., area of 250m^2 with >200 population) were classified as urban, if the figure was 60%–89%, as semiurban, and if <60%, as rural (Gyllenberg et al. 2016).

Table 8. Classification of potential risk factors in Study I

Maternal and paternal age	**Maternal marital status**
• *Under 20* • *20–24* • *25–29* • *30–34* • *35–39* • *40+*	• *Married/in a relationship* • *Single* **Urbanicity** • *Urban* • *Semiurban* • *Rural*
Maternal SES	**Immigration status**
• *Upper white collar* • *Lower white collar* • *Blue collar* • *Other* • *Missing*	• *Both parents Finnish* • *Mother immigrant* • *Father immigrant* • *Both parents immigrants*

4.1.4 Statistical methods

Frequencies of subjects, controls, parents, siblings and covariates were calculated separately for each study (Studies I and II). Pearson's chi-square test was used to test for association between the risk factor and potential covariates in Study I, and between diagnoses among siblings and potential covariates in Study II. P-values less than 0.1 were considered statistically significant. Conditional logistic regression was used to test for association between the outcome and potential covariates in Study I, and between risk factor (i.e., SM among subject) and potential covariates in Study II. Additionally, in Study II, results were adjusted with comorbidities among subjects with SM in the final model. The statistical analyses were performed with SAS software version 9.4 (SAS Institute Inc, Cary, NC, USA).

4.1.4.1 Study I

The outcome in the analysis was an SM diagnosis. The associations between various risk factors and SM were tested using conditional logistic regression, first with an unadjusted model and then adjusting with covariates. The results were reported as

odds ratios (OR) with 95% confidence intervals (CI), together with p-values. P-values less than 0.05 were considered statistically significant. Additionally, similar analyses were conducted by two subgroups: one with subjects with comorbid psychiatric disorders and one without any comorbid diagnoses.

As diagnoses given prior to 1998 only included inpatient diagnoses, sensitivity analyses were conducted on data after excluding subjects with SM diagnosed before 1998, then after excluding parental diagnoses given prior to 1998, and then after excluding these both. Unadjusted results of these subgroups were compared to the results from the complete data.

4.1.4.2 Study II

The numbers of siblings were compared between subjects and controls with Fisher's exact test, using a Monte Carlo simulation approach. A joint test was used to see if there was an interaction between the sex of the subjects and the outcome. The unit of the analyses was the sibling; the exposure was SM in the subject, and the outcome was sibling mental disorders. Each stratum included the siblings of a subject with SM and siblings of their matched controls. Generalized estimating equations (GEE) for logistic regression models were used to test for association between the exposure and the outcome. Observation years were used as an offset in all models. Results were reported as ORs with 95% CIs. P-values were calculated using Pearson's chi-square test, and P-values less than 0.05 were considered statistically significant. The first model was unadjusted, the second model was adjusted with significant covariates and the third model was adjusted with these covariates and comorbid disorders among the subjects with SM.

Additionally, unadjusted analyses were conducted for a subgroup of subjects who were born between 1 January 1995 and 31 December 2009, and for a subgroup that had not been diagnosed with anxiety disorders or childhood emotional disorders. A sensitivity analysis was performed by comparing the results to the results from the complete data.

To control for bias caused by excluding subjects with psychotic disorders or moderate or severe mental disorder, a drop-out analysis was conducted. The characteristics of the excluded group were compared with the complete data by calculating the p-values using Pearson's chi-square test.

4.2 Systematic literature review

Study III was a systematic literature review on the long-term psychiatric outcomes of SM. During the process, the guidelines of the Preferred Reporting Items of Systematic Reviews and Meta-Analyses 2020 (PRISMA) were followed (Page et al.

2021). The study plan was registered in the Open Science register on 12 May 2022 and updated on 28 October 2022 (Koskela et al. 2022). The search terms "selective mutism*" and "elective mutism*" were applied. The search terms were approved by an information specialist from the university library, and the same search terms were used in a meta-analysis conducted by Driessen et al. (2020). Databases were first searched 31 May 2022, and the search was updated 11 September 2023. The search included PubMed, PsycINFO, Web of Science, the Cochrane Library and Embase databases. Reference lists of included papers were searched for relevant papers.

Inclusion criteria were that there should be at least two subjects with diagnosed SM and the follow-up period should be at least two years after the baseline. Studies that had unclear diagnostics or timing or an unclear follow-up time, and articles in other languages than English were excluded. Studies with no original data (editorials, comments, reviews, etc.) were excluded. As case series studies were not seen as presentative, they were left out from the synthesis, and the results of these were only summarized shortly in the manuscript.

The search was conducted individually by two authors (MK and TS). The results from each database were exported to a reference manager, and duplicates were removed. After an abstract screening, the results were cross-checked between the two reviewers. The remaining articles were full-text reviewed to see if they fulfilled the inclusion criteria. Included articles were assessed with the Quality Assessment with Diverse Studies tool (QuADS) (Harrison et al. 2021). This tool was chosen as it fits assessing several types of studies with the same tool. QuADS includes 13 questions that are graded from 0 to 3. Questions were graded 0 if study did not fulfill the criteria at all and 3 if it fulfilled the criteria perfectly. The tool instructs that points should be used as directional and the quality of each study should be discussed point by point (Harrison et al. 2021).

Data was collected by the first author (MK) into a shared spreadsheet, and data extraction was verified by one of the co-authors (TS).

5 Results

5.1 Validation study (Study I)

The validation study included 53 subjects that were identified from patient records. One did not have sufficient information for evaluation; therefore, 52 subjects were evaluated. A total of 87% of the subjects fulfilled the ICD-10 diagnostic criteria for SM. Seven subjects (13%) were not considered to fulfill the diagnostic criteria: Two subjects did not have mutism symptoms and had been falsely diagnosed (4%), among four subjects (8%) speech and language development was not within the normal range, and one subject (2%) was diagnosed with Asperger's syndrome.

5.2 Descriptive results of Studies I and II

Study I included 860 children with 3,250 controls. Of them, 59.1% of the subjects and 58.9% of the controls were females. In Study I, the mean age at first SM diagnosis was 8.1 ± 3.1 years for girls (3–15 years) and 7.9 ± 3.0 for boys (3–15 years). The prevalence of SM at the end of the observation period in Study I was 6.2 per 10,000. In Study I, information on the father was missing in 9 subjects of SM (2.2%) and 31 controls (1.0%), urbanicity was missing in 3 subjects (0.4%) and 28 controls (0.9%) and marital status was missing in 63 subjects (7.3%) and 245 controls (7.5%).

In Study II, there were 658 subjects (59.4% girls) with 2,092 controls (59.2% girls). Additionally, there were 1,661 siblings of subjects (48.9% girls) and 4,120 siblings of controls (48.9% girls) included. The mean number of siblings was 2.5 for subjects and 2.0 for controls. At the end of the observation period, the mean age of siblings of subjects was 15.6 years (SD 7.3, range 0.3–35.7 years), and the mean age of siblings of controls was 15.3 years (SD 7.5, range 0.008–35.9 years). The mean age difference was -0.15 (SD 5.7) between subjects and their siblings and -0.4 (SD 5.8) between controls and their siblings. In Study II, information on maternal SES was missing for 94 subjects (14.3%) and 322 controls (15.4%), and information on maternal marital status was missing for 37 subjects (5.6%) and 145 controls (6.9%).

5.3 Comorbidity (Study I)

Among the subjects in Study I, 69.1% received an additional psychiatric or neurodevelopmental disorder diagnosis during the observation period, when only 11.3% of the controls were diagnosed during this time. The most common comorbid diagnoses among subjects were learning and coordination disorders (33.1%) and childhood emotional disorders (23.0%). As anxiety disorders were excluded among controls, it was not possible to conduct any further statistical analyses on the rates of comorbidity for them. Percentages of comorbid diagnoses among subjects and controls are presented in **Figure 2.**

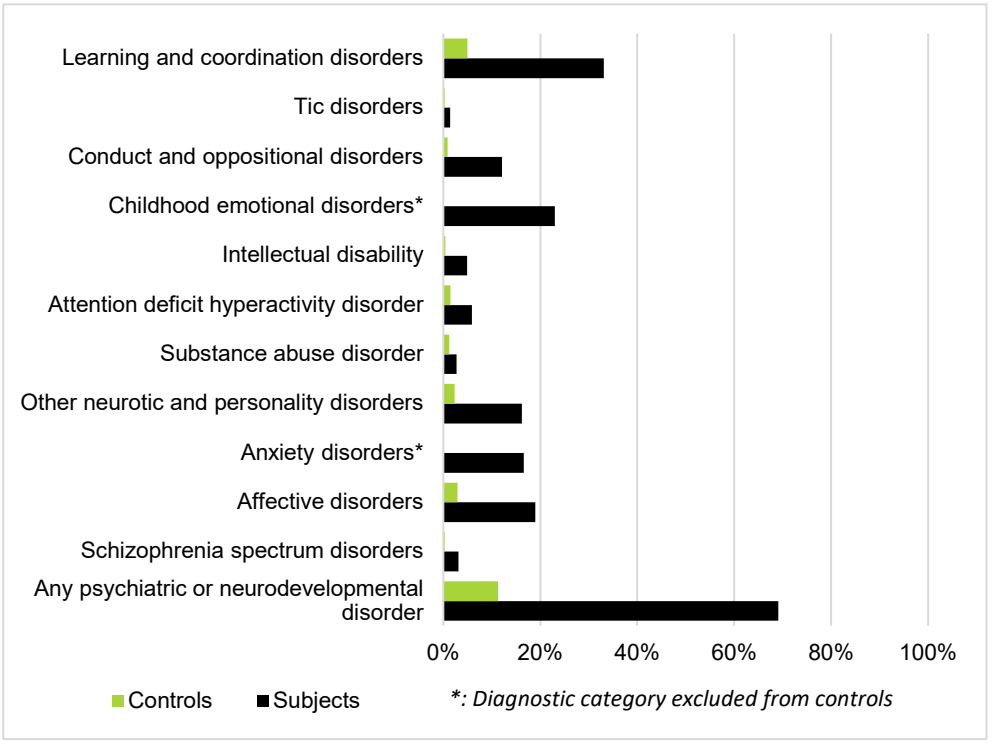

Figure 2. Comorbidity rates among subjects with SM and their controls. Based on Study I.

5.4 Risk factors of selective mutism (Study I)

Results regarding the risk factors of SM that were statistically significant are presented in **Table 9.** Maternal age was not associated with SM among offspring in adjusted analyses. Having an older father was significantly associated with offspring SM. The odds for SM were 1.4-fold for fathers aged 35–39 years and 1.8-fold for fathers over 40 years at the time the child was born.

All maternal SES groups were statistically significantly associated with offspring SM when upper white collar was used as a reference. The highest odds to have a child with SM were seen when the mother was a blue-collar worker and if maternal SES was classified as "other".

Being a single mother at the time of the child's birth showed significantly raised odds for offspring SM, when mother being married or in a relationship was used as a reference. Immigration status or urbanicity were not associated with offspring SM.

Table 9. Sociodemographic risk factors associated with SM. Modified from Study I.

Risk factor	Subjects N (%)	Controls N (%)	Adjusted OR (95% CI)
Paternal age[a]			
35–39	178 (21.2)	578 (18.0)	1.4 (1.1–1.8)*
≥40	123 (14.6)	308 (9.6)	1.8 (1.4–2.4)**
Maternal socioeconomic status[b]			
Lower white collar	296 (34.4)	1183 (36.4)	2.0 (1.5–2.7)***
Blue collar	188 (21.9)	518 (15.9)	2.8 (2.0–4.0)***
Other	166 (19.3)	508 (15.6)	2.4 (1.7–3.4)***
Missing	143 (16.6)	546 (16.8)	2.4 (1.5–3.6)***
Marital status[c]			
Single	55 (6.9)	94 (3.1)	2.0 (1.4–3.0)**

Paternal age missing in 19 cases (2.2%) and 31 controls (1.0%).
Marital status missing in 63 cases (7.3%) and 245 controls (7.5%).
[A] OR adjusted for maternal socioeconomic status (SES), maternal and paternal psychopathology.
[B] OR adjusted for paternal age, marital status, maternal and paternal psychopathology.
[C] OR adjusted for paternal age, maternal SES, and maternal and paternal psychopathology.
* P-value≤0.05 **P-value≤0.001 *** P-value< 0.0001

5.5 Parental psychopathology (Study I)

Having a mother, a father or both parents with at least one psychiatric disorder diagnoses raised the odds of SM in the offspring. In adjusted analyses, results were adjusted with maternal SES, maternal and paternal age and psychopathology of the other parent. The highest odds in the adjusted analyses were seen when both parents had psychiatric diagnoses (OR 2.8, 95% CI 2.0–4.0), and the odds were significantly higher than having only a father (P=0.0077) or only a mother (P=0.042) with psychiatric diagnosis.

There were significant associations between SM and almost all maternal diagnostic categories **(Figure 3)**. The frequencies for various diagnostic categories

are presented in **Table 10**. The highest odds were seen for maternal intellectual disability (OR 7.9, 95% CI 1.4–43.2), schizophrenia and schizoaffective disorders (OR 4.4, 95% CI 2.0–10.1) and for other psychoses (OR 4.2, 95% CI 2.4–7.2). Only maternal ADHD and learning and coordination disorders were not associated with offspring SM. Rates of maternal SM, ASD and conduct and oppositional disorders were so low that analyses could not be performed.

For paternal diagnoses, only other psychoses, unipolar mood disorders, personality disorders, alcohol and drug abuse and learning and coordination disorders were found to be associated with offspring SM in adjusted analyses. The highest odds were seen for learning and coordination disorders (OR 5.6, 95% CI 1.3–25.0), other psychoses (OR 2.1, 95% CI 1.1–4.1) and personality disorders (OR 1.9, 95% CI 1.3–2.8). Due to low rates of paternal SM and ASD, analyses could not be performed.

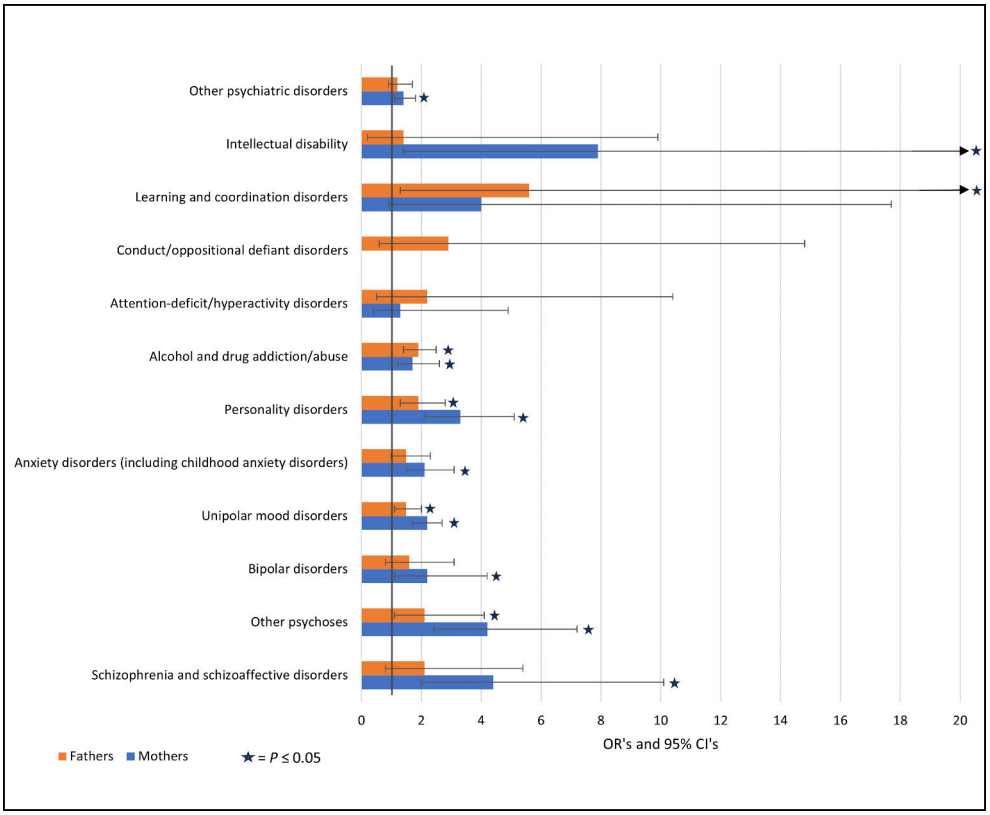

Figure 3. Associations of maternal and paternal psychiatric diagnoses and offspring SM. Results based on Study I.

Table 10. Frequencies of maternal and paternal psychiatric diagnoses by different diagnostic groups. Modified from Study I.

Diagnostic category	Mothers		Fathers	
	Subjects (n=860) n (%)	Controls (n=3,250) n (%)	Subjects (n=841) n (%)	Controls (n=3,219) n (%)
Schizophrenia and schizoaffective disorders	18 (2.1)	14 (0.4)	8 (1.0)	11 (0.3)
Selective mutism	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Other psychoses	35 (4.1)	28 (0.9)	17 (2.0)	27 (0.8)
Bipolar disorders	17 (2.0)	24 (0.7)	14 (1.7)	35 (1.1)
Unipolar mood disorders	158 (18.4)	276 (8.5)	68 (8.1)	153 (4.8)
Anxiety disorders (including childhood anxiety disorders)	66 (7.7)	112 (3.5)	37 (4.4)	81 (2.5)
Personality disorders	48 (5.6)	51 (1.6)	43 (5.1)	77 (2.4)
Alcohol and drug addiction/abuse	43 (5.0)	84 (2.6)	79 (9.4)	143 (4.4)
Attention-deficit hyperactivity disorders	3 (0.4)	11 (0.3)	3 (0.4)	4 (0.1)
Autism spectrum disorders	0 (0.0)	1 (0.03)	3 (0.4)	1 (0.03)
Conduct/oppositional defiant disorders	1 (0.1)	3 (0.1)	3 (0.4)	3 (0.1)
Learning and coordination disorders	5 (0.6)	3 (0.1)	5 (0.6)	3 (0.1)
Intellectual Disability	5 (0.6)	2 (0.1)	2 (0.2)	3 (0.1)

5.6 Sibling psychopathology (Study II)

To illustrate the association between sibling psychopathology and SM, ORs for different diagnostic categories are presented in **Figure 4** and frequencies in **Table 11**. Siblings of subjects had significantly more psychiatric and neurodevelopmental diagnoses than siblings of controls (OR 1.5, 95% CI 1.2–1.8). In Model 2, the covariates, based on covariate analyses, were maternal SES, maternal marital status and maternal psychopathology, and in Model 3, results were adjusted with these same covariates and comorbid diagnoses of the subjects. All the same diagnostic

categories remained significant in unadjusted analyses and after adjusting with covariates in Models 2 and 3. The highest ORs in the final model (Model 3) were found for childhood emotional disorders (OR 4.7, 95% CI 2.9–7.7), ASD (OR 2.9, 95% CI 1.3–6.6) and ADHD (OR 2.3, 95% CI 1.2–4.5). Schizophrenia spectrum disorders, other neurotic and personality disorders, substance abuse disorders, intellectual disability and tic disorders among siblings were not statistically significant. The number of siblings with bipolar disorder were too low for adjusted analyses to be conducted.

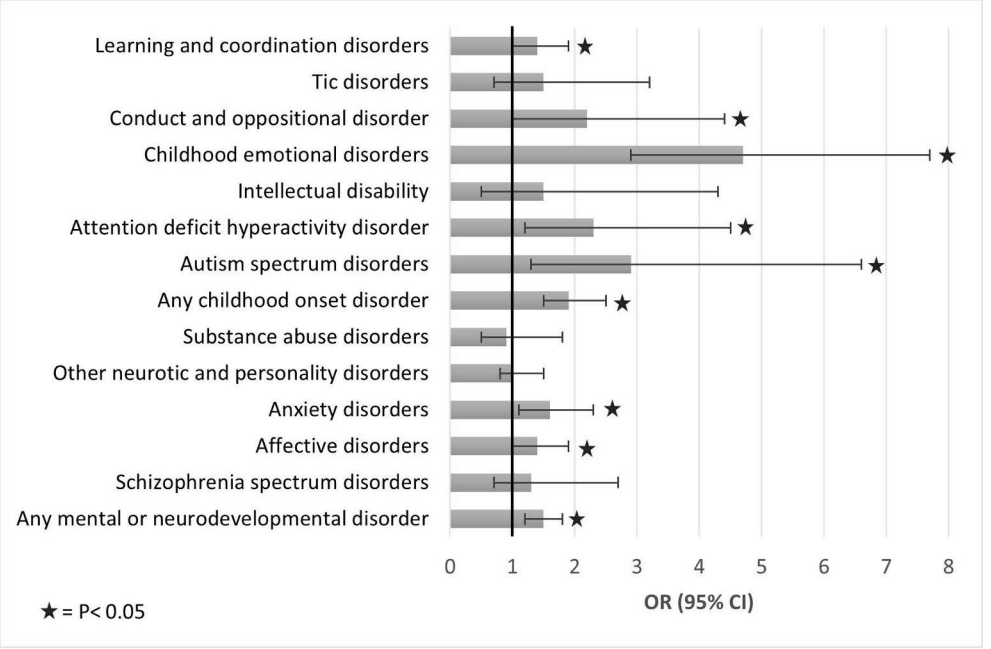

Figure 4. Odds ratios (ORs) of psychiatric and neurodevelopmental disorders among siblings by diagnostic categories. Results based on Study II.

Table 11. Frequencies of psychiatric and neurodevelopmental disorders among siblings of subjects and controls by diagnostic categories. Modified from Study II.

Diagnostic category	Subjects (n=658) n (%)	Controls (n=2,092) n (%)
Any mental or neurodevelopmental disorder	271 (41.2)	435 (20.8)
Schizophrenia spectrum disorders	16 (2.4)	25 (1.2)
Affective disorders	100 (15.2)	165 (7.9)
Bipolar disorders	2 (0.3)	16 (0.8)
Unipolar disorders	99 (15.1)	158 (7.6)
Anxiety disorders	76 (11.6)	110 (5.3)
Other neurotic and personality disorders	74 (11.3)	159 (7.6)
Substance abuse disorders	18 (2.7)	42 (2.0)
Any childhood-onset disorder	198 (30.1)	222 (10.6)
Autism spectrum disorders	23 (3.5)	20 (1.0)
Attention deficit hyperactivity disorder	38 (5.8)	41 (2.0)
Intellectual disability	12 (1.8)	19 (0.9)
Childhood emotional disorders	95 (14.4)	39 (1.9)
Conduct and oppositional disorder	35 (5.3)	40 (1.9)
Tic disorders	7 (1.1)	14 (0.7)
Learning and coordination disorders	104 (15.8)	136 (6.5)

5.7 Subcategories of anxiety disorders among siblings (Study II)

When anxiety disorder diagnoses among siblings were divided into subcategories, specific phobia, panic disorder and/or agoraphobia and separation anxiety disorder among siblings were not associated with SM among subjects. The highest ORs were found for SM, generalized anxiety disorder and social phobia among the siblings of subjects with SM. Adjusted ORs of different anxiety disorder categories are presented in **Table 12**.

Table 12. Different anxiety disorders among siblings. Modified from Study II.

Category	Subjects (N=658) n (%)	Controls (N=2092) n (%)	Adjusted OR[a] (95% CI)
Generalized anxiety disorder	20 (3.0)	17 (0.8)	3.9 (1.6-9.7)*
Panic disorder and/or agoraphobia	19 (2.9)	30 (1.4)	N/A
Separation anxiety disorder	3 (0.5)	3 (0.1)	N/A
Social phobia	31 (4.7)	19 (0.9)	3.2 (1.5-6.7)*
Specific phobia	13 (2.0)	19 (0.9)	1.01 (0.3-3.4)
Unspecific anxiety disorders	82 (12.5)	99 (4.7)	1.7 (1.2-2.5)*
Selective mutism	48 (7.3)	3 (0.1)	27.9 (8.6-90.9)***

*:<0.05 **:<0.001 ***:<0.0001

[A]Model 3, adjusted for maternal mental disorder history, maternal socioeconomic status, maternal marital status and comorbidities of each subject with SM

5.8 Systematic literature review of long-term outcomes of selective mutism (Study III)

There were total of 2,432 titles found from the five databases during the searches between 31 May 2022 and 11 September 2023. After exclusions, 18 papers were reviewed. The study selection is shown in detail in **Figure 5**.

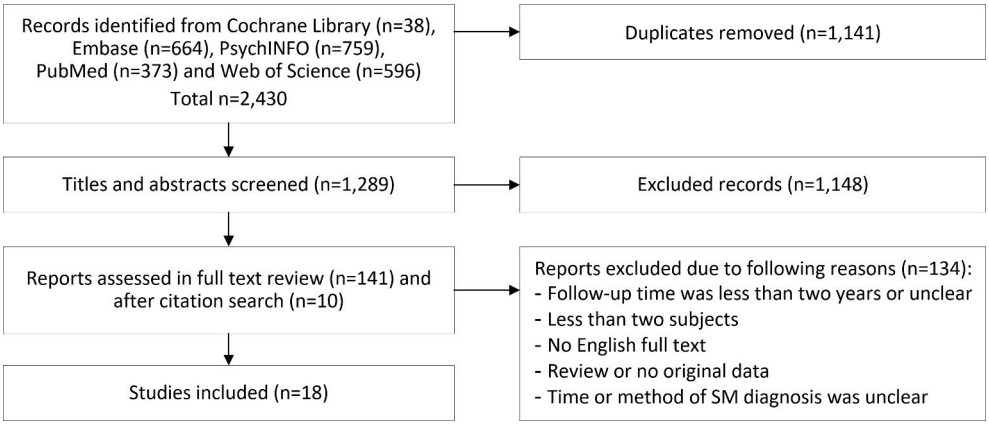

Figure 5. Flow diagram of study selection. Modified from Study III.

Of the studies included after a full text review, nine were clinical cohort studies (Arajärvi 1965; Wergeland 1979; Lowenstein 1979; Sluckin et al. 1991; Lang et al. 2016; Oerbeck et al. 2018; Kamani and Monga 2020; Dogru et al. 2023), two were case-control studies (Kolvin and Fundudis 1981; Steinhausen et al. 2006) and seven were case series (Reed 1963; Elson et al. 1965; Segal 2003; Omdal and Galloway 2008; Çöpür et al. 2012; Albrigtsen et al. 2016; Arigliani et al. 2020). As numbers of subjects in case series studies are low, and the results are not generalizable into population, these studies are described separately and not in the main tables. Publication years and countries are presented in **Figure 6.**

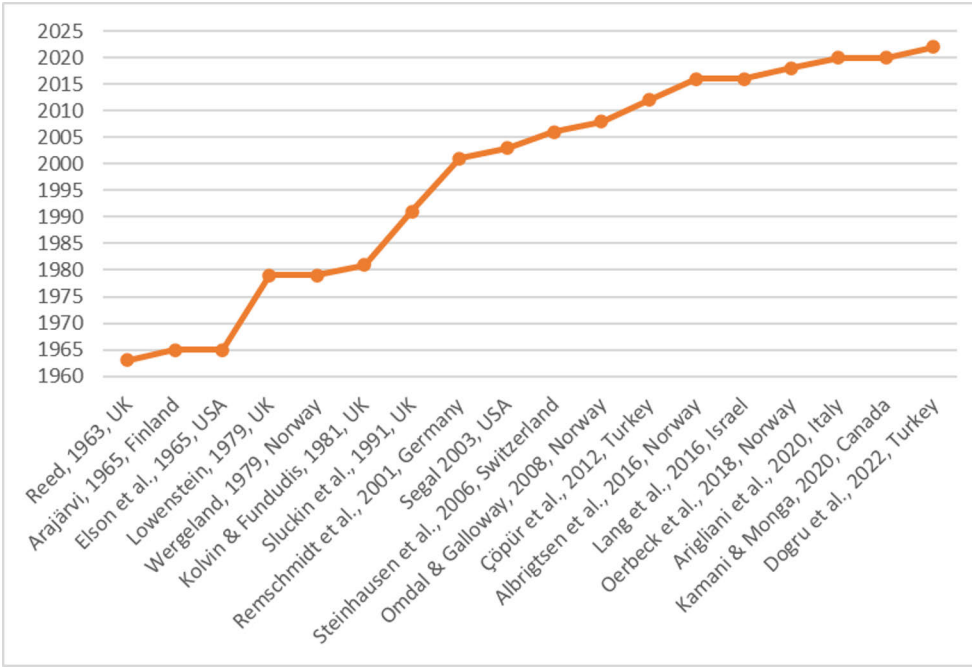

Figure 6. Publication years and countries in cohort, case-control and case series studies that follow-up subjects with SM.

5.8.1 Quality assessment

None of the studies were excluded based on their quality, but most studies were assessed to be of moderate quality. Recruitment of the subjects was described poorly in many studies, and some studies did not discuss their limitations. There were either no analytic methods or the methods were poorly justified in most studies. The mean total score on the QuADS was 23/39 points.

5.8.2 Case series studies

Basic information on the case series studies is summarized in **Table 13.** Treatment or support measures reported in the studies included psychosocial treatments (Reed 1963; Elson et al. 1965; Omdal and Galloway 2008; Arigliani et al. 2020), combined psychosocial and pharmacological treatment (Albrigtsen et al. 2016), pharmacological treatment (Çöpür et al. 2012) and support in school (Segal 2003). In most of the studies, the kind of psychosocial treatment method used was not mentioned (Omdal and Galloway 2008; Albrigtsen et al. 2016; Arigliani et al. 2020), or it was just stated that subjects received psychotherapy (Reed 1963; Elson et al. 1965). In a study by Omdal and Galloway (2008), 3/5 of the subjects remained symptomatic until the end of the follow-up, but in all others, the subjects had fewer SM symptoms at the end of the follow-up. Only two studies also reported other psychiatric symptoms as outcomes (Elson et al. 1965; Arigliani et al. 2020). Arigliani et al. (2020) found that one subject had depressive conduct disorder and the other had anxious depressive disorder and limited oppositional behavior toward family at follow-up. Elson et al. (1965) found symptoms of "thinking disorder" among one subject, and none of the subjects had anxiety or depression.

Table 13. Summary of case series studies.

Study, year, coutry	**Sample size** ***Age at baseline***	**Length of follow-up**	**SM symptoms improved n (%)**
Albrigtsen et al., 2016, Norway	n=2 *7 years*	7 years	2 (100%)
Arigliani et al., 2020, Italy	n=2 *3 years*	11 years	2 (100%)
Çöpür et al., 2012, Turkey	n=4 *5–9 years*	3–6 years	4 (100%)
Elson et al., 1965, USA	n=4 *7–10 years*	0.5–5 years	4 (100%)
Omdal & Galloway, 2008, Norway	n=5 *4-13 years*	1 year (the DSM-IV criteria had fulfilled at least 18 months before the study + 1y. follow-up)	2 (40%)
Reed, 1963, UK	n=4 *12–13 years*	Not reported, ages were 21–23 at the follow-up.	4 (100%)
Segal, 2003, USA	n=2 *5 years*	3 years	2 (100%)

5.8.3 Cohort and case-control studies

Information on included studies can be found in **Table 14.** There were 292 subjects in all cohort and case-control studies, with cohort sizes ranging from 11 (Wergeland 1979) to 49 (Dogru et al. 2023). Follow-up time was two years at the lowest (Kamani and Monga 2020) and 17 years at the highest (Remschmidt et al. 2001). Seven studies used structured instruments or interviews at follow-up (Sluckin et al. 1991; Remschmidt et al. 2001; Steinhausen et al. 2006; Lang et al. 2016; Oerbeck et al. 2018; Kamani and Monga 2020; Dogru et al. 2023), while the rest only used nical interviews. Two studies did not specify if subjects received any treatment (Kolvin and Fundudis 1981; Steinhausen et al. 2006), and two studies reported using both psychosocial treatment (CBT) and pharmacotherapy (SSRIs) (Kamani and Monga 2020; Dogru et al. 2023). Other studies reported using only psychosocial treatments, which included individual or school-based CBT, family counselling or inpatient treatment (Arajärvi 1965; Wergeland 1979; Lowenstein 1979; Sluckin et al. 1991; Remschmidt et al. 2001; Lang et al. 2016; Oerbeck et al. 2018).

Table 14. Summary of cohort and case-control studies. Modified from Study III.

Study ***Country*** **Study design**	**Sample size** ***Age at Baseline*** **Treatment (if any)**	**Length of follow-up** ***Outcome***	**Results at follow-up**
Arajärvi, 1965 ***Finland*** **Clinical cohort**	n=12 *4–8 years* Psychosocial, in-patient treatment	1–10 years *SM symptoms*	11/12 spoke in school after treatment but one still had SM symptoms.
Dogru, 2022 ***Turkey*** **Clinical cohort**	n=49 *5-13 years* Psychotherapy and/or pharmacotherapy	N/A Duration of SM was 2.22 ± 1.35 years *SM symptoms*	Mean duration of SM was 2.2 years. Duration of SM did not differ between males and females. The study did not report recovery rate.
Kamani & Monga, 2020 ***Canada*** **Clinical cohort**	n=31, 22 with SM and 9 with only SP *4–14 years* Psychosocial (CBT) and/or pharmacological (SSRIs).	2–6 years, mean=4.2 years *SM and SP symptoms*	2/31 only had SM, 11/31 only had social anxiety disorder, 9/31 had both and 9/31 had neither.

Lang et al., 2016 ***Israel*** **Clinical cohort**	n=24 *6.40 ± 3.06 years* Psychosocial (CBT)	2.90 ± 3.23 years *SM symptoms and psychiatric comorbidity*	The recovery rate for SM was 84.2%. A significant decrease was observed in the levels of social phobias and specific anxiety disorders. No statistically significant improvement in other comorbidities after the follow-up period.
Lowenstein, 1979 ***UK*** **Clinical cohort**	n=21 *3–8 years* Psychosocial	7 years *SM symptoms*	13/21 spoke normally. 6/21 had some symptoms left. 2/21 had SM.
Oerbeck et al., 2018 ***Norway*** **Clinical cohort**	n=30 *3–9 years* Psychosocial (School-based CBT)	5 years *SM symptoms and psychiatric comorbidity*	21/30 in full remission. 5/30 in partial remission. 4/30 fulfilled diagnostic criteria for SM. 7/30 children (23%) fulfilled criteria for social phobia, and 2/30 had separation anxiety disorder, 3/30 had specific phobia and 1/30 had enuresis nocturna.
Remschmidt et al., 2001 ***Germany*** **Clinical cohort**	n=41 *8.7 ± 3.6 years* Psychosocial (In-patient treatment, family counselling)	12.0 ± 5.2 years *SM symptoms, psychopathology symptoms, family psychopathology*	16/41 cases in remission. 12/41 remarkable improvement. 8/41 mild improvement. 5/41 symptomatology remained unchanged. 10% had dysphoric mood. 19% had depression. 48% had impulsivity. 42% had severe psychopathological disturbances.
Sluckin et al., 1991 ***UK*** **Clinical cohort**	n=25 *4–8 years* Psychosocial (Individual behavioral therapy or school-based program)	2–10 years *SM symptoms*	9/11 in the behavioral group improved, 5/14 in the standard program improved. (Difference in the groups was significant, $p < .05$)
Wergeland, 1979 ***Norway*** **Clinical cohort**	n=11 *6–12 years* Psychotherapy, inpatient treatment or no treatment	8–16 years *SM symptoms and psychiatric comorbidity*	11/11 in remission from selective mutism. Two of four children who had received in-patient treatment were diagnosed with a neurotic disorder, and one of those four was diagnosed with a psychotic disorder at follow-up.

Kolvin & Fundudis, 1981 ***UK*** **Case-control**	n=24 *6–8 years* Not specified ("best treatment available")	5–10 years *SM symptoms*	11/24 had improved: 3/24 had markedly improved, 8/24 had moderately improved and 13/24 had slightly or not improved.
Steinhausen et al., 2006 ***Switzerland*** **Case-control**	n=33 *8.5 ± 3.1 years* Not specified	Not reported, mean age at follow-up was 21.6 ± 3.3 years *SM symptoms and any DSM-IV psychiatric diagnoses*	All displayed some improvement. 6/33 were slightly improved, 8/33 were markedly improved and 19/33 were totally improved. Subjects with SM had significantly more phobic disorders (p<0.001) than healthy controls, but no more than controls with anxiety disorders. 14/33 had phobic disorders. 19/33 had a psychiatric diagnosis. More diagnoses than in healthy controls (p=0.005).

5.8.4 Results on mutism symptoms

Recovery rate from SM symptoms varied from 46% (Kolvin and Fundudis 1981) to 100% (Wergeland 1979). One study only reported the duration of the SM symptoms, which was 2.22 ± 1.35 years (Dogru et al. 2023). Among other studies, 78% of all subjects (190/243) were moderately or totally improved from SM symptoms. Only three studies followed subjects until early adulthood (Wergeland 1979; Remschmidt et al. 2001; Steinhausen et al. 2006). The rate of subjects who recovered moderately or totally from SM among these studies varied from 68% (Remschmidt et al. 2001) to 100% (Wergeland 1979). Follow-up times of all included studies and main results can be found in **Table 14.** Among the studies with the best scores in quality assessment, recovery rates were good: Remschmidt et al. (2001) found that only 12% (5/41) showed no improvement of SM symptoms, Steinhausen et al. (2006) found that all subjects improved at least slightly and that 81.8% improved moderately or completely, and Oerbeck et al. (2018) found that only 13.3% (4/30) still had an SM diagnosis at the end of the five-year follow-up. Three studies were published before DMS-III (Arajärvi 1965; Wergeland 1979; Lowenstein 1979) and showed improvement of SM symptoms among 90% (Lowenstein 1979) to 100% (Wergeland 1979) of the subjects.

5.8.5 Results on other psychiatric outcomes

Only six studies included other mental disorders at follow-up as a finding (Wergeland 1979; Remschmidt et al. 2001; Steinhausen et al. 2006; Lang et al. 2016;

Oerbeck et al. 2018; Kamani and Monga 2020). **Table 14** includes detailed information on these studies. The study by Remschmidt et al. (2001) only reported psychiatric symptoms, but others reported psychiatric diagnoses (Wergeland 1979; Steinhausen et al. 2006; Lang et al. 2016; Oerbeck et al. 2018; Kamani and Monga 2020). Four studies reported SP (Steinhausen et al. 2006; Lang et al. 2016; Oerbeck et al. 2018; Kamani and Monga 2020), five studies reported other anxiety disorders or symptoms (Wergeland 1979; Remschmidt et al. 2001; Steinhausen et al. 2006; Lang et al. 2016; Oerbeck et al. 2018), two reported depression (Remschmidt et al. 2001; Steinhausen et al. 2006), two reported psychotic symptoms or disorders (Wergeland 1979; Steinhausen et al. 2006) and two reported other symptoms or disorders (Remschmidt et al. 2001; Steinhausen et al. 2006) among subjects with SM at the end of the follow-up. The rate of anxiety disorders at follow-up varied from 6% (Remschmidt et al. 2001) to 54% (Lang et al. 2016). Only one of the studies was a case-control study; it found that subjects had more phobic disorders than healthy controls, but not more than subjects with other anxiety disorders (Steinhausen et al. 2006). A study by Kamani and Monga (2020) included subjects with SM, SP or comorbid SM and SP, and the findings implied that the diagnosis of some of the SM subjects was changed to SP after follow-up. Unfortunately, the study did not report how many of the subjects with SM had SP, or how many had recovered by the end of the follow-up (Kamani and Monga 2020).

Studies with follow-ups reaching early adulthood were the only studies to report other disorders than anxiety disorders at follow-up (Wergeland 1979; Remschmidt et al. 2001; Steinhausen et al. 2006). The rate of depression varied from 9.1% (Steinhausen et al. 2006) to 19% (Remschmidt et al. 2001), and the rate of psychotic disorders varied from 6% (Steinhausen et al. 2006) to 9% (Wergeland 1979) among subjects at follow-up. The case-control study by Steinhausen et al. (2006) found a statistically significant difference between subjects and controls only when comparing rates of any psychiatric disorders and phobic disorders at follow-up.

There were two studies that compared rates of psychiatric disorders from baseline to the end of the follow-up. One had a mean follow-up time of 12 years, and it found the general rate of psychiatric symptoms to decrease from 58% to 42% (Remschmidt et al. 2001). The other study found a decrease in the rate of SP from 100% to 37.5% and in the rate of specific phobia from 45.8% to 16.7% during a mean follow-up time of 2.9 years, and these findings were statistically significant (Lang et al. 2016).

5.8.6 Treatment results

Different kinds of treatment methods were used across studies. In studies that used only psychosocial treatments, recovery rates varied from 56% (Sluckin et al. 1991)

to 86% (Oerbeck et al. 2018). Three studies used CBT-based psychosocial treatment, and among these studies, a recovery rate of 85% (55/65) was reported (Sluckin et al. 1991; Lang et al. 2016; Oerbeck et al. 2018). One study that used inpatient treatment found a recovery rate of 92%, but did not describe the treatment methods (Arajärvi 1965). Only two studies reported using medication. Another did not report a recovery rate or the effectiveness of the treatment (Dogru et al. 2023). Another reported that there were no statistically significant differences between using medication and CBT (Kamani and Monga 2020). **Table 14** includes detailed information on these studies.

5.8.7 Prognostic factors

Six of the studies reported factors that were associated with recovery from SM symptoms. Studies found that a poorer outcome of SM symptoms was associated with older age at first diagnosis (Oerbeck et al. 2018), symptom severity at baseline (Oerbeck et al. 2018; Dogru et al. 2023), male gender (Kolvin and Fundudis 1981), depressive symptoms at baseline (Remschmidt et al. 2001), parental personality problems (Kolvin and Fundudis 1981) and if there was SM (Remschmidt et al. 2001; Oerbeck et al. 2018) or another psychopathology in the family (Sluckin et al. 1991; Remschmidt et al. 2001). Two studies found predictors for other psychiatric outcomes. Personality traits of taciturnity (being reserved or reticent in conversation) among family members were associated with a higher overall rate of psychiatric comorbidity at follow-up, and immigrant status of the family was associated with higher rates of phobic disorders at follow-up (Steinhausen et al. 2006). Severe symptoms of SM at baseline predicted higher rates of comorbid psychiatric disorders (Dogru et al. 2023).

6 Discussion

6.1 Main findings

The aims of the current thesis were to examine the association of different risk factors, such as parental age, maternal SES, maternal marital status, immigration, urbanicity and SM, and the risk for psychiatric and neurodevelopmental disorders among parents and siblings of subjects with SM. Additionally, it aimed to systematically review and summarize current knowledge on the long-term outcomes of SM.

The first main finding was that the quality of SM diagnoses registered in the Discharge Register was considered satisfactory. Developmental disorders of speech and language were the most common causes of misdiagnosis (n=4).

The second main finding was that higher paternal age raised the odds for a child to have SM. Also, being a single mother and having lower maternal SES were associated with SM in children.

Thirdly, both maternal and paternal psychopathology were associated with offspring SM. When looking into specific diagnostic categories, a wider range of maternal diagnostic categories were associated with offspring SM than paternal.

The fourth main finding was that there was a significantly higher rate of psychiatric and neurodevelopmental disorders among the siblings of subjects compared to the siblings of controls. The association was not limited to anxiety disorders but was also seen with many other diagnostic categories. The results were statistically significant after adjusting them for comorbid diagnoses of the subject. When different anxiety disorders among the siblings of subjects with SM were examined, significantly higher rates of SM were seen among the siblings of subjects than among the siblings of controls.

The fifth main finding was that recovery rates from SM symptoms have been good in previous studies. However, there is some evidence that problems with anxiety disorders later in life are common. Some factors, such as older age at first diagnosis and psychopathology, especially SM, in the family might predict poorer recovery from SM symptoms.

Finally, most of the long-term follow-up studies on SM have had a small number of subjects and have lacked controls. Overall, the quality of the studies was found to be moderate, and in the most studies the follow-up ended before adulthood.

6.2 Discussion of the main findings

6.2.1 Validation of the selective mutism diagnosis (Study I)

The validity of the SM diagnosis, according to the ICD-10 classification, was found to be good in the current study population. This is in line with Finnish studies about ADHD, ASD and Tourette's syndrome that found very good accuracy of the diagnoses given in the Finnish population (Lampi et al. 2010; Leivonen et al. 2014; Joelsson et al. 2016). A previous systematic literature review by Sund et al. (2012) of the quality of the Discharge Register found that the accuracy of common diagnoses varied from 75 to 99% depending on the diagnosis. The most common reason for misdiagnosing SM was developmental disorders of speech and language. Even among these subjects, there could have been SM symptoms, even though these were identified as misdiagnosed subjects due to the ICD-10 exclusion criteria. It must be noted that some subjects with less severe symptoms may never get diagnosed in specialized health care. Therefore, these results can be generalized only to the validity of subjects with moderate to severe SM symptoms.

6.2.2 Risk factors of selective mutism (Study I)

This study found that, even after adjusting the results with covariates, a higher paternal age, low maternal socioeconomic status and being a single mother at the time of the child's birth were associated with SM in the child. Immigration and urbanicity were not associated with SM.

6.2.2.1 Parental age

The finding on high paternal age being associated with SM is in line with previous findings that high paternal age is a risk factor for emotional disorders in childhood (McGrath et al. 2014). Associations between advanced paternal age and offspring psychopathology have been seen previously, for example with ASD, ADHD and schizophrenia (Gabis et al. 2010; Helenius et al. 2012; Chudal et al. 2015). Previous studies have not found association with paternal age and anxiety disorders (Helenius et al. 2014) or phobic disorders (Steinhausen et al. 2016). There are several possible explanations why advanced paternal age is associated with offspring SM. It has been previously found that when age of the father advances, the rate of de novo mutations

(new mutations in the germline) in the child raises (Kong et al. 2012; Wood and Goriely 2022). The effect of paternal age is greater than the effect of maternal age, when considering de novo mutations (Kong et al. 2012). De novo mutations have been associated with several disorders, for example ASD and intellectual disability (Acuna-Hidalgo et al. 2016). As genetic studies on SM are scarce, the role of de novo mutations in the development of SM is unknown. Another possible explanation is that advanced paternal age could affect epigenetic regulation by interfering with DNA methylation, histone alterations, and chromatin remodeling. This could be a risk factor for psychiatric disorders like schizophrenia, for example (Perrin et al. 2006). A previous review concluded that the role of paternal age in epigenetic regulation is still somewhat unclear, as epigenetic regulation seems to be more affected by diet or exposure to toxins than paternal age alone (Kaltsas et al. 2023). A third possible explanation is that those who become fathers at an older age may have certain personality traits, or poor social skills, that can make it more difficult to find a partner (Hare and Moran 1979). Although this theory on parental personality traits and advanced paternal age is mostly associated with schizophrenia (Hare and Moran 1979), similar factors could play a role in SM. Previous studies have found that parents of children with SM are more quiet and shy than parents of controls (Steinhausen and Adamek 1997; Kristensen and Torgersen 2001).

In the current thesis, low maternal age was found to be associated with offspring SM in unadjusted analyses, but after adjusting the results with covariates, significance was lost. This could imply that the association seen in the unadjusted analyses could be explained with cofounders, for example maternal SES.

6.2.2.2 Maternal SES

As in previous studies, in this study SM was seen in all SES classes (Steinhausen and Juzi 1996; Kristensen 2000). The highest ORs for offspring SM were seen among families in the lowest SES classes. This finding is in line with a previous study that found an excess of families with low SES among children with SM, although the finding was not statistically significant (Kristensen 2000). However, the current results conflict with studies on children with SM that have found more families to be in high (Boneff-Peng et al. 2023) or middle SES classes (Steinhausen and Juzi 1996). This could be explained by recruitment methods, as one of these studies recruited subjects (n=230) with electronic flyers through social media and different SM organizations (Boneff-Peng et al. 2023) and another recruited subjects (n=100, mean age 8.7 years) from self-help groups (Steinhausen and Juzi 1996). These recruitment channels may have favored families with good resources to gather information on SM.

Low family SES has been associated with childhood mental disorders (Reiss 2013; Guhn et al. 2020), including anxiety disorders (Guhn et al. 2020), in previous studies. Low family SES may be associated with higher levels of stressful or uncontrollable events in life, which can affect the child directly or affect parenting strategies by causing distress (Bradley and Corwyn 2002). As in previous studies, low income has been associated with poorer mental health (Thomson et al. 2022), so it could be assumed that in families with lower SES parental psychiatric problems are also more common. However, a recent Finnish register study on mental health and socioeconomic inequality, which included the entire Finnish population, found that parental mental disorders did not explain socioeconomic disparities (Vaalavuo et al. 2022). They did find interaction showing that risk for mental health problems could be higher for boys with mothers with low education or a parent with mental disorders. That could imply that families with higher SES could have more resources to protect their children from the effects of their mental health problems (Vaalavuo et al. 2022).

6.2.2.3 Maternal marital status

In this study, being a single mother at the time of the child's birth was associated with offspring SM, when being married or in a relationship was used as a reference. This contrasts with a study by Melfsen et al. (2022), which found that the rate of divorced parents did not differ between subjects with SM (n=28, aged 7–18 years) and controls (n=33, aged 7–18 years). Also, a study by Cunningham et al. (2004) found no difference in the rate of single parents between subjects with SM (n=52, mean age 7.2 years) and controls (n=52, mean age 7.0). It must be noted that register-based data does not recognize if parents of the child divorce later, and it does not include information on if the mother is in a relationship with child's biological parent or with someone else. Being a single parent has been associated with offspring anxiety disorders (Guhn et al. 2020; Khanal et al. 2022). Single motherhood has been associated with lower income and education level, and lower social support (Crosier et al. 2007), all of which could affect the relationship with the child by causing stress. Results of the current study were adjusted with maternal SES and parental psychopathology, with statistically significant findings remaining. It must be noted that the association between single motherhood and childhood mental health is ambiguous. A previous longitudinal study did not find differences in maternal mental health, mother-child relationships or children's emotional and behavioral problems between families with a single mother by choice and families with a partnered mother (Golombok et al. 2021). A poor partner relationship could be a risk factor for mental health problems, which could also affect the child. Women in relationships

with poor support from partners were at a higher risk of depression after the child's birth than single mothers (Bilszta et al. 2008).

6.2.2.4 Immigration

The current finding of no association between immigration and SM is in contrast with previous studies that have found that SM is associated with immigration and bilingualism (Slobodin 2023). One possible explanation of this is that the overall level of immigrants in Finland was so low at the time of the study that analyses may have lacked the power to gain statistical significance. The immigration rate in Finland during the study period was lower than in other European countries, and in 2005 the immigration rate in Finland was 2.2% (Tiilikainen 2007). If analyses were repeated with a Finnish cohort from the last ten years, results could be different. It is also possible that SM symptoms among immigrants are not always recognized in school or in health care.

The previously seen association between immigration or bilingualism and SM could be caused by insecurity with the second language (Elizur and Perednik 2003). A study by Starke et al. (2018) followed up bi- and monolingual mute children (n=30) for nine months and found that neither bilingualism nor receptive language skills alone had an effect on speaking behavior. It has been suggested that cultural adaptation could play a bigger role than bilingualism in the development of SM among immigrant children (Slobodin 2023).

6.2.3 Family psychopathology and selective mutism (Studies I and II)

This study is the first to investigate a range of psychiatric and neurodevelopmental diagnoses among parents and siblings of subjects with SM, by using a register-based sample. It compared the overall rate of psychopathology between parents and siblings of subjects and controls and individual diagnostic groups. The hypothesis was that both parents and siblings of subjects with SM would have higher rates of psychiatric disorders compared to controls, and the current findings support this hypothesis.

6.2.3.1 Parental psychopathology (Study I)

When the total rate of psychopathology was investigated, mothers and fathers of the subjects had more diagnosed psychiatric disorders than the parents of controls. The results remained significant when they were adjusted with maternal SES, maternal age and paternal age. The association with offspring SM was strongest when both

parents were diagnosed with a psychiatric or neurodevelopmental disorder. This is in line with previously mentioned studies (described in **Table 4**) that found that both parents of subjects with SM had higher rates of psychiatric symptoms than parents of controls (Remschmidt et al. 2001; Kristensen and Torgersen 2001; Capozzi et al. 2018). This is also in line with previous findings that several other childhood-onset psychiatric disorders, for example OCD, ADHD and Tourette's syndrome, are associated with parental psychiatric morbidity (Steinhausen et al. 2013; Leivonen et al. 2017; Joelsson et al. 2017). However, previous findings on parental psychopathology and SM are conflicted. Kristensen (2000) found no association between parental psychopathology and SM. The study by Alyanak et al. (2013) only found association between SM and paternal psychopathology, and the study by Steinhausen et al. (1997) only found association between SM and maternal psychopathology. Studies on SM and family psychopathology are described in detail in **Table 4**.

Previous research suggests that psychiatric disorders tend to aggregate in families (Steinhausen et al. 2009; Helenius et al. 2014). This aggregation is most likely partly genetic and partly environmental, but it is somewhat difficult to extract these two factors from one another (Jami et al. 2021). A previous systematic literature review by Jami et al. (2021) found that there is evidence on genetic transmission for depression and substance use, for example. However, parental psychiatric traits were associated with offspring internalizing and externalizing problems through environmental pathways (Jami et al. 2021). One hypothesis is that, instead of psychiatric disorders being individual entities, they could be considered as a continuum with a shared background (Caspi et al. 2014).

Another important finding of this study was that a wide range of different kinds of maternal psychiatric disorders were associated with SM among offspring. Almost all maternal diagnoses were associated, whereas among fathers, only other psychotic disorders, unipolar mood disorders, personality disorders, substance use disorders and learning and coordination disorders were associated with offspring SM. This finding of relatively stronger maternal psychopathology is partly in line with a previous finding in a study by Steinhausen and Adamek (1997), where only maternal psychopathology was associated with offspring SM. The study by Alyanak et al. (2013) found that the severity of emotional problems among subjects with SM correlated with maternal psychopathology. This could partly explain the current findings, as subjects treated in specialized health services most likely represent subjects with moderate to severe symptoms of SM. In the current study, paternal anxiety disorders were not associated with offspring SM. SM diagnoses were not found among parents of subjects. This is in contrast to previous studies (described in **Table 4**) that found high rates of SP among parents of children with SM (Black and Uhde 1995; Kristensen and Torgersen 2001; Chavira et al. 2007). The reason behind

this could be that SM might not have been very well recognized during the years when the parents of the children in the current data were young. Diagnoses before 1998 were made as inpatient diagnoses, and in most cases SM does not require inpatient treatment. Therefore, there could have been some SM diagnoses that were not registered.

Maternal psychopathology could affect the child in other ways than through genetic pathways. Maternal psychiatric disorders could affect maternal caregiving behavior. The study by Edison et al. (2011) (n=63, aged 4–13 years) on parenting styles and SM found that parents of children with SM might be more controlling in social situations compared to parents of controls. Anxiety symptoms among parents and subjects predicted controlling behavior in parents. However, the study did not address if the controlling behavior existed before the onset of SM symptoms, or only after (Edison et al. 2011). In two studies, when parenting attitudes and strategies were measured by reports from parents, differences between parents of subjects and controls were not found (Cunningham et al. 2004; Alyanak et al. 2013).

Prenatal factors, such as medication use, substance use, nutrition, obstetric complications and maternal stress, could play a role in future psychiatric problems of the child. There is only one previous study on perinatal risk factors and SM (Steinhausen and Juzi 1996). The study by Steinhausen and Juzi (1996) found that one-third of the subjects (n=100) with SM were exposed to at least one risk factor during pregnancy, complicated delivery was reported among 43% of the subjects, and 20% had some complications during neonatal period. A systematic literature review investigating pre- and perinatal risk factors of anxiety disorders found that preterm birth might be a risk factor for anxiety disorders later in life (Ståhlberg et al. 2020). Also unplanned cesarean sections were associated with anxiety disorders during childhood and adolescence (Ståhlberg et al. 2022).

There are no studies on the association between maternal medication use during pregnancy and SM. However, there is some evidence that maternal SSRI use during pregnancy might elevate the risk for depression and anxiety during childhood, but results are conflicted, and further research is required (Upadhyaya et al. 2023). In this study, odds for maternal substance abuse disorders were higher among mothers of subjects than mothers of controls. A previous meta-analysis found that prenatal alcohol exposure is a risk factor for internalizing problems (for example, anxiety and depression) of the child, and the risk for these problems seemed to increase later in childhood (Khoury et al. 2018). Based on the results of this study, no conclusions on the matter can be drawn because maternal alcohol or medication use during pregnancy was not investigated.

6.2.3.2 Sibling psychopathology (Study II)

This study found that siblings of subjects had significantly more psychiatric and neurodevelopmental disorders than siblings of controls. This is in line with a previous case-control study that also found higher rates of psychiatric disorders among siblings of subjects with SM (Kristensen 2000). However, the case-control study by Steinhausen and Adamek (1997) did not find a statistically significant difference between the rates of psychiatric diagnoses among siblings of subjects and siblings of controls. They only collected information from parents, which may have increased risk for reporting bias (Steinhausen and Adamek 1997). This could explain why their results differ from the findings of the current study. Another possible explanation for different results could be that the current study had more data and a longer follow-up period than previous studies.

The strongest association was found with childhood-onset disorders. When different diagnostic categories were investigated separately, categories that were not associated with SM among siblings were disorders that are usually diagnosed in adulthood, such as bipolar disorder, substance abuse disorder and schizophrenia. As the mean age of siblings was 15 years at the end of the follow-up, possible late-adolescence- or adulthood-onset disorders were not recorded. There could be other explanations for the stronger association with childhood-onset disorders. When parents already have a child with a psychiatric or neurodevelopmental disorder, they might be more prone to notice symptoms among other siblings and seek medical advice. Mental health problems of siblings could affect the relationship among siblings or affect how parents treat the siblings. One meta-analysis found that conflict between siblings and siblings being treated differently from each other by their parents are both associated with higher rates of internalizing and externalizing problems between probands (Buist et al. 2013).

In the current thesis, many kinds of disorders among siblings were associated with SM. The meta-analysis by Ma et al. (2015) found that siblings of children with psychiatric diagnoses had elevated levels of at least one type of psychiatric disorder. Even though the strongest evidence was found with similar disorders (internalizing disorders being a risk factor for internalizing disorders and externalizing for externalizing disorders), there was limited evidence for psychiatric disorders among subjects being a risk factor for various kinds of psychiatric and neurodevelopmental disorders among siblings (Ma et al. 2015). Siblings partly share the same genes and environmental factors. A twin-sibling study by Ehringer et al. (2006) found that both genes and non-shared environmental factors played a role in the onset of different psychiatric disorders, when shared environmental factors were only associated with depression and generalized anxiety disorder (GAD). They also found that the effect of shared environmental factors was similar for twin siblings as it was for other siblings (Ehringer et al. 2006).

6.2.3.3 Neurodevelopmental disorders among siblings

In this study, among other individual diagnostic groups, the highest odds were seen for neurodevelopmental disorders, ASD and ADHD among siblings of subjects with SM. This is in line with the epidemiological study by Sharkey and McNicholas (2012) (described in **Table 2)**, which reported ASD among 43% of the families with a child with SM. ASD and ADHD among subjects have been found to be associated with a range of different psychiatric and neurodevelopmental disorders among siblings, including childhood emotional disorders (Jokiranta-Olkoniemi et al. 2016; Jokiranta-Olkoniemi et al. 2019). Family clustering of SM and neurodevelopmental disorders could be genetic. A study by Stein et al. (2011) found SM to be associated with a genetic variant that was also associated with social anxiety and the language impairment component in ASD. This could imply a shared background between SM and ASD, but further studies are warranted (Stein et al. 2011). Neuropsychiatric disorders in the family, especially ASD, could cause stress for the family; therefore, it could be an environmental risk factor for SM (Quintero and McIntyre 2010). Neurodevelopmental diagnoses tend to aggregate in families (Rosa et al. 2016), and in some cases SM could be misdiagnosed as ASD or the other way around. One study investigating childhood diagnoses of adults with ASD found a small (<0.6%) proportion of subjects with a former SM diagnosis in childhood (Rødgaard et al. 2021). Still, it seems unlikely that this would completely explain the current finding.

Although studies on neurodevelopmental disorders among siblings of subjects with SM are scarce, previous studies have associated SM with neurodevelopment symptoms (Kristensen 2000; Kristensen 2002). In one study by Kristensen (2000), 68% of the SM subjects (n=54, mean age 9.0 years) also fulfilled the diagnostic criteria for a developmental disorder. Another study by Kristensen et al. (2002) found that a significantly higher proportion of subjects (n=54, mean age 9.0 years), compared to matched controls (n=108), had non-specific markers of a neurodevelopmental disorder, including lower scores on a motor performance test and minor physical anomalies. This could imply that neurobiological factors also play a role in the development of SM (Kristensen 2002). Further, autism-related symptoms have been seen among subjects with SM (Steffenburg et al. 2018; Muris et al. 2021). It has been suggested that both SM and ASD share a similar temperament trait of behavioral inhibition (Muris and Ollendick 2021a). It should be noted that, as current diagnostic classifications advise caution when diagnosing SM and ASD together (American Psychiatric Association. 2013; World Health Organization 2019), studying the relationship between these two disorders is difficult.

6.2.3.4 Anxiety disorders among siblings

In this study, among separate diagnostic categories, the highest odds were seen for childhood emotional disorders. This category is based on ICD-10 classification and mainly applies to different kinds of anxiety disorders. When different anxiety disorders were investigated separately, there were significantly higher odds for siblings of subjects to have GAD, SP, an unspecific anxiety disorder or SM. Three previous cohort studies also reported high rates of SP or SM among siblings of subjects (Black and Uhde 1995; Remschmidt et al. 2001; Sharkey and McNicholas 2012). However, a case-control study by Steinhausen and Adamek (1997) did not find the rate of SM to be significantly higher among siblings of subjects than among siblings of controls. No previous studies have investigated rates of anxiety disorders other than SM and SP among siblings of subjects with SM. However, a previous meta-analysis found that SM is also highly comorbid with anxiety disorders other than SP (Driessen et al. 2020). A register study that examined sibling risk for anxiety disorders found that having a sibling with any anxiety disorder elevated the risk for several other anxiety disorders (Li et al. 2011). A twin-sibling study on the heritability of anxiety disorders theorized that genetic factors pose a risk for several kinds of anxiety disorders, and that unique environmental factors and life experiences direct which anxiety disorders individuals develop (Hettema et al. 2005).

6.2.4 Long-term outcomes of elective mutism (Study III)

The systematic literature review that was performed as part of this thesis found recovery rates from SM symptoms to be good. This is in line with previous conceptualizing of SM as a disorder of childhood and early adolescence (Viana et al. 2009; Muris and Ollendick 2015). Still, as most of the studies end their follow-up before adulthood, no conclusions can be made on if symptoms persist into adulthood in some form or if the symptoms take another form, for example as another anxiety disorder.

In the current review, most of the subjects received some kind of treatment, and poorer outcomes could have been expected without treatment. Some studies also found that SM symptoms notably improved when the subject changed schools (Arajärvi 1965; Wergeland 1979). This could imply that there are some environmental risk factors that are associated with school. This could also explain recovery during adolescence, a common time to change schools. For example, interaction with the teacher could be a sustaining factor for SM symptoms if the teacher always speaks for the child or makes a fuss every time the child talks (Oerbeck et al.). The systematic literature review by Steinert et al. (2013) on the long-term outcomes of SP found poorer recovery rates (27–40%) than the current

findings on the recovery rate of SM (80%). For SP, after five years, only a 27% recovery rate was seen among clinical subjects, and in a non-clinical sample, 40% recovered in that time (Steinert et al. 2013). It could be that SM symptoms are more likely to be noticed and treated than SP symptoms.

Although in the current review, the recovery rate from SM symptoms was found to be almost 80%, previous cohort and case-control studies report that 20% of subjects have persistent SM symptoms (Arajärvi 1965; Wergeland 1979; Lowenstein 1979; Kolvin and Fundudis 1981; Sluckin et al. 1991; Remschmidt et al. 2001; Steinhausen et al. 2006; Lang et al. 2016; Oerbeck et al. 2018; Kamani and Monga 2020). Three studies that followed subjects through puberty also reported subjects with persistent symptoms (Wergeland 1979; Remschmidt et al. 2001; Steinhausen et al. 2006). More studies are needed to investigate how SM manifests in adulthood. The duration of SM symptoms varied in studies, between 2.2 (Dogru et al. 2023) and 8 years (Remschmidt et al. 2001). Some factors, such as anxiety symptoms later in life, could affect if the subject objectively feels recovered from SM or not. A study that assessed adults with self-reported SM during childhood found that those who did not feel recovered from SM symptoms experienced more interpersonal anxiety (a form of social anxiety) during adulthood (Tomohisa et al. 2022).

Apart from persisting SM symptoms, other psychiatric and social problems are common later in life among subjects with SM (Remschmidt et al. 2001; Kamani and Monga 2020; Tomohisa et al. 2022). However, studies about comorbid diagnoses later in life are scarce and have a significant limitation of ending the follow-up before puberty. Still, moderate rates of anxiety disorders were found at follow-up (Wergeland 1979; Steinhausen et al. 2006; Lang et al. 2016; Oerbeck et al. 2018; Kamani and Monga 2020), and the association of SM and other anxiety disorders has been seen in previous studies (Driessen et al. 2020). SM and SP, in particular, have been found to be highly comorbid (Muris and Ollendick 2015; Driessen et al. 2020). In the current review, the prevalence of SP varied from 23% (Oerbeck et al. 2018) to 41% (Kamani and Monga 2020). One explanation for the association between these disorders could be that SM is a manifestation of SP (Yeganeh et al. 2003; Yeganeh et al. 2006) or avoidance behavior due to anxiety in social situations (Young et al. 2012; Vogel and Schwenck 2021). One study speculated that SM might change into SP during adulthood in some cases (Kamani and Monga 2020). However, it should be noted that not all subjects with SM have an additional anxiety disorder (Driessen et al. 2020). There are no guidelines that specify in which cases a clinician should diagnose SM and SP as separate disorders. This most likely explains, in part, why comorbidity rates varied widely in the reviewed studies. Even though SM is conceptualized as an anxiety disorder, its diagnostic criteria does not include anxiety (American Psychiatric Association. 2013; World Health

Organization 2019). Findings about psychiatric symptoms or disorders other than anxiety remained limited in the current literature review.

Some of the reviewed studies also included analyses on prognostic factors, but in most studies, due to the small number of subjects, statistically significant findings were not achieved. There was some evidence that psychiatric disorders, especially SM in the family, could predict a poorer outcome of SM symptoms (Sluckin et al. 1991; Remschmidt et al. 2001; Oerbeck et al. 2018). The reason behind this could be, for example, that there are more risk factors for psychiatric disorder in the home environment that prevent recovery from SM. Also, existing studies imply that later discovery could lead to longer duration of SM symptoms (Oerbeck et al. 2018). More studies are needed to see if SM becomes chronic over time.

6.2.4.1 Quality of follow-up studies (Study III)

The quality of the reviewed studies on the long-term outcomes of SM is something that must be considered, as it affects the quality of the current findings. There were no register- or population-based studies, so the number of subjects was small (n=11–49), even considering that SM is relatively rare disorder. Only seven studies received more than 50% of the scores in the performed quality assessment (Sluckin et al. 1991; Remschmidt et al. 2001; Steinhausen et al. 2006; Lang et al. 2016; Oerbeck et al. 2018; Kamani and Monga 2020; Dogru et al. 2023). Only two case-control studies were found (Kolvin and Fundudis 1981; Steinhausen et al. 2006). There was major variation in how the outcomes were measured and how methods were reported. The included studies used different diagnostic criteria for SM, which makes interpretation of the results difficult. Six studies used DSM-III classification or older diagnostic criteria for SM (Arajärvi 1965; Wergeland 1979; Lowenstein 1979; Kolvin and Fundudis 1981; Sluckin et al. 1991; Remschmidt et al. 2001). Subjects in these studies do not necessarily fulfill the diagnostic criteria for SM according to the DSM-V or the ICD-11. As mentioned previously, only three studies followed subjects until early adulthood (Wergeland 1979; Remschmidt et al. 2001; Steinhausen et al. 2006). Therefore, there is no information on psychiatric disorders during adulthood or about subjects with persistent symptoms lasting through adolescence.

6.3 Strengths and limitations

6.3.1 Study design

Studies I and II were register-based nested case-control studies, which formed a study protocol that has not been used to study SM before. The benefits of this type

of protocol were that it allowed the identification of family members of the subjects and controls so that information could be collected on all diagnoses given in specialized health care in Finland to subjects, controls and their family members. In a nested case-control design, there are several controls, and controls are chosen from the same population as the subjects, which makes them more comparable. Information can be obtained before the first diagnosis, allowing follow-up of the subjects and controls, which is more beneficial than traditional case-control settings. For a nested case-control study, subjects and controls can be collected from registers with little effort, and larger samples can be obtained than in cohort studies. Moreover, compared to cohort studies, a nested case-control design is, in most cases, less expensive (Ernster 1994).

There are also limitations in using a nested case-control design. This design allows the investigation of associations but not causality. There can be differences in how consistently information on cofounders are recorded. Also, cofounders are limited to those that are collected in the registers, and it is not cost-effective to gather additional information later. There could be additional factors that partly explain associations but which are not registered. For example, school-related factors, such as bullying, receiving special support or being absent from school, cannot be studied from the registers.

Although a great majority of SM diagnoses were valid according to the ICD-10 criteria in the validation study, there are limitations to consider. The subsample included subjects only from one hospital district in Finland, and there could be differences in the use of the SM diagnosis between hospitals. Therefore, the study should be replicated in another hospital district in Finland or, in an ideal situation, by collecting a cohort from all Finnish hospitals. Only information from specialized health care was available, and there was no direct assessment of the subjects. Therefore, the evaluation relied on written reports by clinicians.

Study III was a systematic literature review that followed the PRISMA protocol (Page et al. 2021). The research plan was registered beforehand in OSF (Koskela et al. 2022). The validated tool, QuADS, was used to conduct a quality assessment of the included studies (Harrison et al. 2021). There are limitations of the study methods that need to be considered. Many articles were descriptive, and only two studies had controls. Therefore, it was not possible to conduct a meta-analysis. As some articles were inaccurate on reporting how subjects were diagnosed and how long they had been followed up with, some relevant articles might have been excluded. Also, as inclusion criteria was restricted to subjects with verified SM diagnoses, follow-up studies on subjects with only SM symptoms or self-, parent- or teacher-reported symptoms were excluded. This mostly caused exclusion of case series studies, and most likely did not affect the results significantly. Further, the study excluded papers

written in languages other than English, so there could have been studies that fulfilled other inclusion criteria but were not accepted in the review.

6.3.2 Registers and study population

Using nationwide registers makes it possible to have large sample sizes, even with rare diagnoses like SM, and registers are not likely to suffer from loss at follow-up since public health care for children in Finland is free of charge. As practically all (99.5%) children attend routine health check-ups, even families that do not actively seek help from health professionals, or those who mainly use private healthcare, are spotted and referred to specialized health care if needed (Gissler, M 2015). Healthcare professionals document the information in the registers at the time of the visit. Therefore, the chance for recall bias in register data is low. Collecting subjects from registers reduces the chance of selection bias.

There are also limitations in using register-based data. Registers do not include information on relationships inside the family, or information on life events, which both play an important role in a child's mental health. Further, Finnish national registers do not include information on results of standardized assessments or results of neuropsychological examinations. There is no information on treatment methods used. It is not possible to trace how individual diagnoses were given or what kind of assessments and diagnostic methods were used. The same applies to registering cofounders. There is always a possibility of human error—information can be entered incorrectly or be left unregistered altogether. There have also been changes in using the registers over the years of the study period. Maternal SES and marital status are only started being registered from 1991 onwards. Diagnoses were coded with ICD-9 diagnoses from 1987 to 1995 and with ICD-10 diagnoses since 1996. This might have affected how clinicians have made different diagnoses. Also, diagnoses of outpatient visits have only been registered since 1998.

Register-based study populations have several previously mentioned strengths, such as a large number of subjects, the possibility of collecting controls from the same population and the low chance of recall bias. Still, there are limitations in the current study population that need to be considered. Included subjects most likely only represent subjects with moderate or severe SM symptoms. As SM can be unrecognized if the symptoms are mild, it is likely that there are subjects with less severe symptoms who are never referred to specialized healthcare and therefore are not detected. Especially, during 1987–1998, when only inpatient diagnoses were registered, there were most likely several subjects with mild or moderate symptoms that were not detected, and incidence cannot be calculated for that period. Still, as SM is a persistent disorder, most likely, many subjects were diagnosed during the time when outpatient diagnoses were registered, and in Study I it was found that only

18 subjects received an SM diagnosis prior to 1998. In Study II, only subjects with diagnoses given after 1998 were included.

The same limitation applies when considering diagnoses among parents or siblings. Mild depression or anxiety disorders might be treated in primary health care and not referred to specialized health care. Also, some disorders, such as substance abuse disorders, might be completely unrecognized by health care but still affect a child's life greatly. When parental diagnoses given prior to 1998 were excluded, only paternal anxiety lost its significance in unadjusted analyses. However, it should be noted that the diagnoses of the controls and their families are also registered in a similar way, so subjects, controls and their families are comparable to each other.

One major limitation in forming the study population was that, because the current data is derived from larger amounts of data collected for the FIPS Anxiety study, all anxiety disorders were excluded from the controls. Because of this, we were not able to compare levels of comorbidity on anxiety disorders among subjects and controls in Study I. This could also affect how comparable subjects and controls are to each other, especially when comparing rates of anxiety disorders between family members of subjects and controls. This should be considered when extrapolating these findings in the general Finnish population. In Study II, sensitivity analyses were conducted with a subset without any anxiety disorders, and the results remained similar. Also, as incidence of anxiety disorders during the study period is a bit under 6% (Khanal et al. 2022), it seems unlikely that this limitation would explain the results completely.

Diagnoses were collected until 2016, and controls had not received an SM diagnosis prior to that. Still, it is possible that there are a few subjects that received an SM diagnosis after the observation period.

6.3.3 Statistical analyses

There are also some statistical limitations that must be considered. As maternal SES and marital status are only recorded after 1991, there is information missing from part of the subjects. There were some subjects and controls with no information on fathers. In Study I, where maternal SES was investigated as a risk factor, subjects with missing information were placed into a "missing" category. Otherwise, missing data was dealt with by only using data with complete information in the analyses. Maternal SES before 1991 was considered to be "missing at random" as it was missing from all subjects. As with other missing variables, information was missing from under 5–10%, so consequences were most likely small (Dong and Peng 2013). Still, this method could have caused bias to the results.

In Study II, more than one sibling among the subjects and controls were included. Therefore, multilevel modeling would have most likely been the best way to control

the variation among families. As there were not enough dimensions of variations in the data, it was not possible to use this method.

In Study III, the synthesis of the results remained narrative as there were not enough case-control studies. Therefore, no statistical analyses were conducted.

7 Conclusions

This study found association between SM among offspring and advanced paternal age, single motherhood and lower maternal SES. It is important for clinicians to notice the various risk factors in families with a child with SM and take them into account when planning treatment as SES-related factors could impact how symptoms are maintained. These findings are important for future researchers; comparing risk factors to other disorders can help identify patterns that cause comorbidity and clustering of psychiatric disorders.

Both parental and sibling psychiatric and neurodevelopmental disorders were associated with SM among subjects. This is an important finding considering that there was also some evidence that family psychopathology could be associated with longer duration of SM symptoms. Therefore, taking the whole family into account when planning treatment of SM is important. Parental and sibling psychopathology showed clustering of many different kind of psychiatric disorders. This supports previous findings that there are shared origins behind various psychiatric disorders. Relatively stronger association with maternal psychiatric disorders points towards shared or non-shared pre- and perinatal environmental factors that could affect the possibility of a child developing a psychiatric disorder later in life.

The current finding that ASD and ADHD cluster among siblings of SM is novel. This finding is valuable considering the previously reported association between SM and neurodevelopmental factors. It is important for clinicians to remember the possibility of SM among siblings when there are neurodevelopmental disorders elsewhere in the family. It is also important to be cautious in differing between an SM and an ASD diagnosis, as these disorders can share similar features, but should be treated differently. There is also an implication for future research: to investigate the clustering of SM and neurodevelopmental disorders.

Almost one in five subjects seemed to have chronic SM symptoms. Also, there was evidence that especially anxiety disorders occurred often among subjects with SM, even after SM symptoms were cured. Therefore, subjects with SM could benefit from longer follow-up periods after treatment for SM, and treatment should not only be aimed towards non-speaking behaviors but also against anxiety.

7.1 Implications for future research

This thesis has several implications for future research. As SM is a rare disorder, replicating these results by connecting information from different registers or studies from different countries could help to form stronger conclusions. Although the current thesis gives important information on the etiology of SM, several factors need to be studied further.

This study found no association between immigration and SM, which contrasts with previous studies. Further studies are required to determine if, for example, the reason for immigration affects the risk for SM. The immigration rate in Finland is currently higher than during the study period, and repeating the study with newer data would show if the lack of a finding was due to a low immigration rate during that time. Cross-cultural studies should also be conducted to investigate how different cultural backgrounds effect the risk of SM during childhood.

The findings regarding maternal psychopathology imply that there are pre- and perinatal factors that play a role in the onset of SM. This needs further study. Twin studies, for example, could be key in determining what factors during pregnancy and delivery play a role in the development of SM.

Future studies on families and SM and ASD are also warranted. Confirming the clustering of the two disorders in families would help unravel the association between these two disorders.

Follow-up studies with larger samples, standardized assessments and research methods plus follow-ups lasting into adulthood are needed. Register studies investigating subjects retrospectively as well as studies with longer follow-up periods after treatment could provide important information on the course and future of psychosocial problems among subjects with SM.

There are also important implications for future research that are outside the scope of the current thesis. Register studies cannot answer questions on how different life events or family interactions effect a child's mental health. As these factors have been previously associated with SM, it would be important to study families with a child with SM to determine if there is a scientific background for this theory. Most treatment studies focus on CBT, and there is only a handful of RCTs, most of which have a low number of subjects. More RCTs on CBT-based treatments and other types of psychosocial treatments are needed. As the duration of SM is usually several years, and long-term psychosocial treatment can be time consuming for families and healthcare systems, digital interventions could offer affordable easy-access treatment for SM in the future; this needs to be further developed. Conducting intervention studies with the Finnish population would also be beneficial.

Finally, SM is conceptualized as a childhood-onset disorder. Studies focus on children, but there are also cases of SM symptoms starting during adolescence or

persisting until adulthood. Studies on SM during late adolescence or adulthood are scarce, and there are only few studies about the quality of life of subjects later in life. Afterall, it is not the disorder that we are treating, but the individual.

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References

Acuna-Hidalgo R, Veltman JA, Hoischen A (2016) New insights into the generation and role of de novo mutations in health and disease. Genome Biol 17:241. https://doi.org/10.1186/s13059-016-1110-1

Albrigtsen V, Eskeland B, Mæhle M (2016) Ties of silence--Family lived experience of selective mutism in identical twins. Clin Child Psychol Psychiatry 21:308–323. https://doi.org/10.1177/1359104515591225

Alyanak B, Kilinçaslan A, Harmanci HS, Demirkaya SK, Yurtbay T, Vehid HE (2013) Parental adjustment, parenting attitudes and emotional and behavioral problems in children with selective mutism. J Anxiety Disord 27:9–15. https://doi.org/10.1016/j.janxdis.2012.10.001

American Psychiatric Association. (2013) Diagnostic and Statistical Manual of Mental Disorders, Fifth edition, 5th edn. American Psychiatric Association

American Psychiatric Association (1980) Diagnostic and statistical manual., 3rd edition. APA Press, Washington DC

American Psychiatric Association (2000) Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, 4th edn. American Psychiatric Association, Arlington, VA

Arajärvi T (1965) Elective mutism in children. A clinical and follow-up study. Ann Paediatr 11:46–52

Arigliani E, Giordo L, Vigliante M, Romani M (2020) Two Cases of Selective Mutism: To Speak Does Not Mean to Recover. Clin Pediatr (Phila) 59:1137–1140. https://doi.org/10.1177/0009922820941628

Bilszta JLC, Tang M, Meyer D, Milgrom J, Ericksen J, Buist AE (2008) Single Motherhood Versus Poor Partner Relationship: Outcomes for Antenatal Mental Health. Aust N Z J Psychiatry 42:56–65. https://doi.org/10.1080/00048670701732731

Black B, Uhde TW (1995) Psychiatric characteristics of children with selective mutism: A pilot study. J Am Acad Child Adolesc Psychiatry 34:847–856

Boneff-Peng K, Lasutschinkow PC, Colton ZA, Freedman-Doan CR (2023) An Updated Characterization of Childhood Selective Mutism: Exploring Clinical Features, Treatment Utilization, and School Services. Child Psychiatry Hum Dev. https://doi.org/10.1007/s10578-023-01589-8

Bradley RH, Corwyn RF (2002) Socioeconomic Status and Child Development. Annu Rev Psychol 53:371–399. https://doi.org/10.1146/annurev.psych.53.100901.135233

Buist KL, Deković M, Prinzie P (2013) Sibling relationship quality and psychopathology of children and adolescents: A meta-analysis. Clin Psychol Rev 33:97–106. https://doi.org/10.1016/j.cpr.2012.10.007

Capozzi F, Manti F, Di Trani M, Romani M, Vigliante M, Sogos C (2018) Children's and parent's psychological profiles in selective mutism and generalized anxiety disorder: a clinical study. Eur Child Adolesc Psychiatry 27:775–783. https://doi.org/10.1007/s00787-017-1075-y

Caspi A, Houts RM, Belsky DW, Goldman-Mellor SJ, Harrington H, Israel S, Meier MH, Ramrakha S, Shalev I, Poulton R, Moffitt TE (2014) The p Factor: One General Psychopathology Factor in the Structure of Psychiatric Disorders? Clin Psychol Sci 2:119–137. https://doi.org/10.1177/2167702613497473

Chavira DA, Shipon-Blum E, Hitchcock C, Cohan S, Stein MB (2007) Selective mutism and social anxiety disorder: All in the family? J Am Acad Child Adolesc Psychiatry 46:1464–1472. https://doi.org/10.1097/chi.0b013e318149366a

Chavira DA, Stein MB, Bailey K, Stein MT (2004) Child anxiety in primary care: Prevalent but untreated. Depress Anxiety 20:155–164. https://doi.org/10.1002/da.20039

Chudal R, Joelsson P, Gyllenberg D, Lehti V, Leivonen S, Hinkka-Yli-Salomäki S, Gissler M, Sourander A (2015) Parental Age and the Risk of Attention-Deficit/Hyperactivity Disorder: A Nationwide, Population-Based Cohort Study. J Am Acad Child Adolesc Psychiatry 54:487-494.e1. https://doi.org/10.1016/j.jaac.2015.03.013

Chudal R, Leivonen S, Rintala H, Hinkka-Yli-Salomäki S, Sourander A (2017) Parental age and the risk of obsessive compulsive disorder and Tourette syndrome / chronic tic disorder in a nationwide population-based sample. J Affect Disord 223:101–105. https://doi.org/10.1016/j.jad.2017.07.033

Çöpür M, Görker I, Demir T (2012) Selective serotonin reuptake inhibitors for treatment of selective mutism. Balk Med J 29:99–102

Crosier T, Butterworth P, Rodgers B (2007) Mental health problems among single and partnered mothers: The role of financial hardship and social support. Soc Psychiatry Psychiatr Epidemiol 42:6–13. https://doi.org/10.1007/s00127-006-0125-4

Cunningham CE, McHolm A, Boyle MH, Patel S (2004) Behavioral and emotional adjustment, family functioning, academic performance, and social relationships in children with selective mutism. J Child Psychol Psychiatry 45:1363–1372. https://doi.org/10.1111/j.1469-7610.2004.00843.x

Dogru H, Ucuz I, Uzun Cicek A, Comertoglu Arslan S (2023) Clinical characteristics according to sex and symptom severity in children with selective mutism: a four-center study. Nord J Psychiatry 77:158–164. https://doi.org/10.1080/08039488.2022.2146748

Dong Y, Peng C-YJ (2013) Principled missing data methods for researchers. SpringerPlus 2:222. https://doi.org/10.1186/2193-1801-2-222

Driessen J, Blom JD, Muris P, Blashfield RK, Molendijk ML (2020) Anxiety in Children with Selective Mutism: A Meta-analysis. Child Psychiatry Hum Dev 51:330–341. https://doi.org/10.1007/s10578-019-00933-1

Edison SC, Evans MA, McHolm AE, Cunningham CE, Nowakowski ME, Boyle M, Schmidt LA (2011) An investigation of control among parents of selectively mute, anxious, and non-anxious children. Child Psychiatry Hum Dev 42:270–290. https://doi.org/10.1007/s10578-010-0214-1

Ehringer MA, Rhee SH, Young S, Corley R, Hewitt JK (2006) Genetic and Environmental Contributions to Common Psychopathologies of Childhood and Adolescence: A Study of Twins and Their Siblings. J Abnorm Child Psychol 34:1–17. https://doi.org/10.1007/s10802-005-9000-0

Elizur Y, Perednik R (2003) Prevalence and Description of Selective Mutism in Immigrant and Native Families: A Controlled Study. J Am Acad Child Adolesc Psychiatry 42:1451–1459. https://doi.org/10.1097/00004583-200312000-00012

Elson A, Pearson C, Jones CD, Schumacher E (1965) FOLLOW-UP STUDY OF CHILDHOOD ELECTIVE MUTISM. Arch Gen Psychiatry 13:182–187

Ernster VL (1994) Nested Case-Control Studies. Prev Med 23:587–590. https://doi.org/10.1006/pmed.1994.1093

Gabis L, Raz R, Kesner-Baruch Y (2010) Paternal Age in Autism Spectrum Disorders and ADHD. Pediatr Neurol 43:300–302. https://doi.org/10.1016/j.pediatrneurol.2010.05.022

Gissler, M (2015) Perinatal statistics: parturients, deliveries and newborns 2014.

Golombok S, Zadeh S, Freeman T, Lysons J, Foley S (2021) Single mothers by choice: Parenting and child adjustment in middle childhood. J Fam Psychol 35:192–202. https://doi.org/10.1037/fam0000797

Guhn M, Emerson SD, Mahdaviani D, Gadermann AM (2020) Associations of Birth Factors and Socio-Economic Status with Indicators of Early Emotional Development and Mental Health in Childhood: A Population-Based Linkage Study. Child Psychiatry Hum Dev 51:80–93. https://doi.org/10.1007/s10578-019-00912-6

Gyllenberg D, Gissler M, Malm H, Artama M, Hinkka-Yli-Salomäki S, Brown AS, Sourander A (2014) Specialized Service Use for Psychiatric and Neurodevelopmental Disorders by Age 14 in Finland. Psychiatr Serv 65:367–373. https://doi.org/10.1176/appi.ps.201200544

Gyllenberg D, Sourander A, Surcel H-M, Hinkka-Yli-Salomäki S, McKeague IW, Brown AS (2016) Hypothyroxinemia During Gestation and Offspring Schizophrenia in a National Birth Cohort. Biol Psychiatry 79:962–970. https://doi.org/10.1016/j.biopsych.2015.06.014

Hakulinen-Viitanen T, Hietanen-Peltola M, Hastrup A, Wallin M, Pelkonen M (2012) Laaja terveystarkastus: Ohjeistus äitiys- ja lastenneuvolatoimintaan sekä kouluterveydenhuoltoon. Terveyden ja hyvinvoinnin laitos, Tampere, Finland

Hare EH, Moran PAP (1979) Raised Parental Age in Psychiatric Patients: Evidence for the Constitutional Hypothesis. Br J Psychiatry 134:169–177. https://doi.org/10.1192/bjp.134.2.169

Harrison R, Jones B, Gardner P, Lawton R (2021) Quality assessment with diverse studies (QuADS): an appraisal tool for methodological and reporting quality in systematic reviews of mixed- or multi-method studies. BMC Health Serv Res 21:144. https://doi.org/10.1186/s12913-021-06122-y

Helenius D, Jørgensen PM, Steinhausen H-C (2013) A three generations nation-wide population study of family load estimates in bipolar disorder with different age at onset. J Affect Disord 150:146–151. https://doi.org/10.1016/j.jad.2012.12.013

Helenius D, Munk-Jørgensen P, Steinhausen H-C (2014) Family load estimates and risk factors of anxiety disorders in a nationwide three generation study. Psychiatry Res 216:351–356. https://doi.org/10.1016/j.psychres.2014.02.026

Helenius D, Munk-Jørgensen P, Steinhausen H-C (2012) Family load estimates of schizophrenia and associated risk factors in a nation-wide population study of former child and adolescent patients up to forty years of age. Schizophr Res 139:183–188. https://doi.org/10.1016/j.schres.2012.05.014

Henkin Y, Bar-Haim Y (2015) An auditory-neuroscience perspective on the development of selective mutism. Dev Cogn Neurosci 12:86–93. https://doi.org/10.1016/j.dcn.2015.01.002

Hettema JM, Prescott CA, Myers JM, Neale MC, Kendler KS (2005) The Structure of Genetic and Environmental Risk Factors for Anxiety Disorders in Men and Women. Arch Gen Psychiatry 62:182. https://doi.org/10.1001/archpsyc.62.2.182

Hipolito G, Pagnamenta E, Stacey H, Wright E, Joffe V, Murayama K, Creswell C (2023) A systematic review and meta-analysis of nonpharmacological interventions for children and adolescents with selective mutism. JCPP Adv. https://doi.org/10.1002/jcv2.12166

https://www.utu.fi/en/university/faculty-of-medicine/research-centre-for-child-psychiatry/research Accessed: 18.1.2024 Description of FIPS-studies

Hua A, Major N (2016) Selective mutism. Curr Opin Pediatr 28:114–120. https://doi.org/10.1097/MOP.0000000000000300

Jami ES, Hammerschlag AR, Bartels M, Middeldorp CM (2021) Parental characteristics and offspring mental health and related outcomes: a systematic review of genetically informative literature. Transl Psychiatry 11:197. https://doi.org/10.1038/s41398-021-01300-2

Joelsson P, Chudal R, Gyllenberg D, Kesti A-K, Hinkka-Yli-Salomäki S, Virtanen J-P, Huttunen J, Ristkari T, Parkkola K, Gissler M, Sourander A (2016) Demographic Characteristics and Psychiatric Comorbidity of Children and Adolescents Diagnosed with ADHD in Specialized Healthcare. Child Psychiatry Hum Dev 47:574–582. https://doi.org/10.1007/s10578-015-0591-6

Joelsson P, Chudal R, Uotila J, Suominen A, Sucksdorff D, Gyllenberg D, Sourander A (2017) Parental psychopathology and offspring attention-deficit/hyperactivity disorder in a nationwide sample. J Psychiatr Res 94:124–130. https://doi.org/10.1016/j.jpsychires.2017.07.004

Jokiranta-Olkoniemi E, Cheslack-Postava K, Joelsson P, Suominen A, Brown AS, Sourander A (2019) Attention-deficit/hyperactivity disorder and risk for psychiatric and neurodevelopmental disorders in siblings. Psychol Med 49:84–91. https://doi.org/10.1017/S0033291718000521

Jokiranta-Olkoniemi E, Cheslack-Postava K, Sucksdorff D, Suominen A, Gyllenberg D, Chudal R, Leivonen S, Gissler M, Brown AS, Sourander A (2016) Risk of Psychiatric and

Neurodevelopmental Disorders Among Siblings of Probands With Autism Spectrum Disorders. JAMA Psychiatry 73:622. https://doi.org/10.1001/jamapsychiatry.2016.0495

Kaltsas A, Moustakli E, Zikopoulos A, Georgiou I, Dimitriadis F, Symeonidis EN, Markou E, Michaelidis TM, Tien DMB, Giannakis I, Ioannidou EM, Papatsoris A, Tsounapi P, Takenaka A, Sofikitis N, Zachariou A (2023) Impact of Advanced Paternal Age on Fertility and Risks of Genetic Disorders in Offspring. Genes 14:486. https://doi.org/10.3390/genes14020486

Kamani Z, Monga S (2020) Understanding the outcome of children who selectively do not speak: A retrospective approach. J Can Acad Child Adolesc Psychiatry 29:58–65

Karakaya I, Şişmanlar ŞG, Öç ÖY, Memik NÇ, Coşkun A, Ağaoğlu B, Yavuz CI (2008) Selective mutism: A school-based cross-sectional study from Turkey. Eur Child Adolesc Psychiatry 17:114–117. https://doi.org/10.1007/s00787-007-0644-x

Kearney CA, Rede M (2021) The Heterogeneity of Selective Mutism: A Primer for a More Refined Approach. Front Psychol 12:700745. https://doi.org/10.3389/fpsyg.2021.700745

Khanal P, Ståhlberg T, Luntamo T, Gyllenberg D, Kronström K, Suominen A, Sourander A (2022) Time trends in treated incidence, sociodemographic risk factors and comorbidities: a Finnish nationwide study on anxiety disorders. BMC Psychiatry 22:144. https://doi.org/10.1186/s12888-022-03743-3

Khoury JE, Jamieson B, Milligan K (2018) Risk for Childhood Internalizing and Externalizing Behavior Problems in the Context of Prenatal Alcohol Exposure: A Meta-Analysis and Comprehensive Examination of Moderators. Alcohol Clin Exp Res 42:1358–1377. https://doi.org/10.1111/acer.13805

Knud G (1979) Role Structure and Subculture in Families of Elective Mutists. Fam Process 18:55–68. https://doi.org/10.1111/j.1545-5300.1979.00055.x

Kolvin I, Fundudis T (1981) Elective mute children: Psychological development and background factors. J Child Psychol Psychiatry 22:219–232. https://doi.org/10.1111/j.1469-7610.1981.tb00548.x

Kong A, Frigge ML, Masson G, Besenbacher S, Sulem P, Magnusson G, Gudjonsson SA, Sigurdsson A, Jonasdottir A, Jonasdottir A, Wong WSW, Sigurdsson G, Walters GB, Steinberg S, Helgason H, Thorleifsson G, Gudbjartsson DF, Helgason A, Magnusson OTh, Thorsteinsdottir U, Stefansson K (2012) Rate of de novo mutations and the importance of father's age to disease risk. Nature 488:471–475. https://doi.org/10.1038/nature11396

Kopp S, Gillberg C (1997) Selective Mutistn: A Population-based Study: A Research Note. J Child Psychol Psychiatry 38:257–262. https://doi.org/10.1111/j.1469-7610.1997.tb01859.x

Koskela M, Ståhlberg T, Yunus W, Sourander A (2022) Long term psychiatric outcomes of selective mutism: a systematic review. https://doi.org/10.17605/OSF.IO/X3EVY

Kristensen H (2000) Selective mutism and comorbidity with developmental disorder/delay, anxiety disorder, and elimination disorder. J Am Acad Child Adolesc Psychiatry 39:249–256. https://doi.org/10.1097/00004583-200002000-00026

Kristensen H (2002) Non-specific markers of neurodevelopmental disorder/delay in selective mutism: A case-control study. Eur Child Adolesc Psychiatry 11:71–78. https://doi.org/10.1007/s007870200013

Kristensen H, Torgersen S (2001) MCMI-II personality traits and symptom traits in parents of children with selective mutism: a case-control study. J Abnorm Psychol 110:648–652. https://doi.org/10.1037//0021-843x.110.4.648

Kumpulainen K, Räsänen E, Raaska H, Somppi V (1998) Selective mutism among second-graders in elementary school. Eur Child Adolesc Psychiatry 7:24–29. https://doi.org/10.1007/s007870050041

Kussmaul A (1877) Die Störungen der sprache: versuch einer pathologie der sprache. Verlag von F.C.W. Vogel, Leipzig

Lampi K, Sourander A, Gissler M, Niemelä S, Rehnström K, Pulkkinen E, Peltonen L, Von Wendt L (2010) Brief report: validity of Finnish registry-based diagnoses of autism with the ADI-R:

Validity of registry-based diagnoses of autism. Acta Paediatr 99:1425–1428. https://doi.org/10.1111/j.1651-2227.2010.01835.x

Lang C, Nir Z, Gothelf A, Domachevsky S, Ginton L, Kushnir J, Gothelf D (2016) The outcome of children with selective mutism following cognitive behavioral intervention: a follow-up study. Eur J Pediatr 175:481–487. https://doi.org/10.1007/s00431-015-2651-0

Leivonen S, Scharf JM, Mathews CA, Chudal R, Gyllenberg D, Sucksdorff D, Suominen A, Voutilainen A, Brown AS, Sourander A (2017) Parental Psychopathology and Tourette Syndrome/Chronic Tic Disorder in Offspring: A Nationwide Case-Control Study. J Am Acad Child Adolesc Psychiatry 56:297-303.e4. https://doi.org/10.1016/j.jaac.2017.01.009

Leivonen S, Voutilainen A, Hinkka-Yli-Salomäki S, Timonen-Soivio L, Chudal R, Gissler M, Huttunen J, Sourander A (2014) A nationwide register study of the characteristics, incidence and validity of diagnosed Tourette syndrome and other tic disorders. Acta Paediatr 103:984–990. https://doi.org/10.1111/apa.12708

Li X, Sundquist J, Sundquist K (2011) Sibling risk of anxiety disorders based on hospitalizations in Sweden. Psychiatry Clin Neurosci 65:233–238. https://doi.org/10.1111/j.1440-1819.2011.02199.x

Lowenstein LF (1979) The result of twenty-one elective mute cases. Acta Paedopsychiatr Int J Child Adolesc Psychiatry 45:17–23

Ma N, Roberts R, Winefield H, Furber G (2015) The Prevalence of Psychopathology in Siblings of Children with Mental Health Problems: A 20-Year Systematic Review. Child Psychiatry Hum Dev 46:130–149. https://doi.org/10.1007/s10578-014-0459-1

Manassis K (2015) Pharmacotherapy in Selective Mutism: A review study of pharmacological treatment for Selective Mutism. Eur Child Adolesc Psychiatry 24:S43. https://doi.org/10.1007/s00787-015-0714-4

Manassis K, Fung D, Tannock R, Sloman L, Fiksenbaum L, McInnes A (2003) Characterizing selective mutism: Is it more than social anxiety? Depress Anxiety 18:153–161. https://doi.org/10.1002/da.10125

McGrath JJ, Petersen L, Agerbo E, Mors O, Mortensen PB, Pedersen CB (2014) A Comprehensive Assessment of Parental Age and Psychiatric Disorders. JAMA Psychiatry 71:301. https://doi.org/10.1001/jamapsychiatry.2013.4081

McInnes A, Fung D, Manassis K, Fiksenbaum L, Tannock R (2004) Narrative skills in children with selective mutism: An exploratory study. Am J Speech Lang Pathol 13:304–315. https://doi.org/10.1044/1058-0360(2004/031)

Melfsen S, Jans T, Romanos M, Walitza S (2022) Family Relationships in Selective Mutism-A Comparison Group Study of Children and Adolescents. Child Basel Switz 9. https://doi.org/10.3390/children9111634

Muris P, Büttgens L, Koolen M, Manniën C, Scholtes N, van Dooren-Theunissen W (2023) Symptoms of Selective Mutism in Middle Childhood: Psychopathological and Temperament Correlates in Non-clinical and Clinically Referred 6- to 12-year-old Children. Child Psychiatry Hum Dev. https://doi.org/10.1007/s10578-023-01512-1

Muris P, Monait N, Weijsters L, Ollendick TH (2021) Symptoms of Selective Mutism in Non-clinical 3- to 6-Year-Old Children: Relations With Social Anxiety, Autistic Features, and Behavioral Inhibition. Front Psychol 12:669907. https://doi.org/10.3389/fpsyg.2021.669907

Muris P, Ollendick TH (2015) Children Who are Anxious in Silence: A Review on Selective Mutism, the New Anxiety Disorder in DSM-5. Clin Child Fam Psychol Rev 18:151–169. https://doi.org/10.1007/s10567-015-0181-y

Muris P, Ollendick TH (2021a) Selective Mutism and Its Relations to Social Anxiety Disorder and Autism Spectrum Disorder. Clin Child Fam Psychol Rev 24:294–325. https://doi.org/10.1007/s10567-020-00342-0

Muris P, Ollendick TH (2021b) Current Challenges in the Diagnosis and Management of Selective Mutism in Children. Psychol Res Behav Manag 14:159–167. https://doi.org/10.2147/PRBM.S274538

Nowakowski ME, Tasker SL, Cunningham CE, McHolm AE, Edison S, Pierre JS, Boyle MH, Schmidt LA (2011) Joint attention in parent-child dyads involving children with selective mutism: a comparison between anxious and typically developing children. Child Psychiatry Hum Dev 42:78–92

Oerbeck B, Manassis K, Kristensen H Selective mutism. In: JM Rey's IACAPAP e-Textbook of Child and Adolescent Mental Health. International Association for Child and Adolescent Psychiatry and Allied Professions, Geneva

Oerbeck B, Overgaard KR, Stein MB, Pripp AH, Kristensen H (2018) Treatment of selective mutism: a 5-year follow-up study. Eur Child Adolesc Psychiatry 27:997–1009. https://doi.org/10.1007/s00787-018-1110-7

Omdal H, Galloway D (2008) Could selective mutism be re-conceptualised as a specific phobia of expressive speech? An exploratory post-hoc study. Child Adolesc Ment Health 13:74–81. https://doi.org/10.1111/j.1475-3588.2007.00454.x

Østergaard KR (2018) Treatment of selective mutism based on cognitive behavioural therapy, psychopharmacology and combination therapy–a systematic review. Nord J Psychiatry 72:240–250. https://doi.org/10.1080/08039488.2018.1439530

Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, Shamseer L, Tetzlaff JM, Akl EA, Brennan SE, Chou R, Glanville J, Grimshaw JM, Hróbjartsson A, Lalu MM, Li T, Loder EW, Mayo-Wilson E, McDonald S, McGuinness LA, Stewart LA, Thomas J, Tricco AC, Welch VA, Whiting P, Moher D (2021) The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ n71. https://doi.org/10.1136/bmj.n71

Pereira CR, Ensink JBM, de Jonge MV, Wippo E, Lindauer RJL, Utens EMWJ (2019) Speech problems and speech delay: Possible underdiagnosis of selective mutism. Turk J Pediatr 61:817–819. https://doi.org/10.24953/turkjped.2019.05.028

Perrin MC, Brown AS, Malaspina D (2006) Aberrant Epigenetic Regulation Could Explain the Relationship of Paternal Age to Schizophrenia. Schizophr Bull 33:1270–1273. https://doi.org/10.1093/schbul/sbm093

Pettersson E, Larsson H, Lichtenstein P (2016) Common psychiatric disorders share the same genetic origin: a multivariate sibling study of the Swedish population. Mol Psychiatry 21:717–721. https://doi.org/10.1038/mp.2015.116

Pollard J, Reardon T, Williams C, Creswell C, Ford T, Gray A, Roberts N, Stallard P, Ukoumunne OC, Violato M (2023) The multifaceted consequences and economic costs of child anxiety problems: A systematic review and meta-analysis. JCPP Adv 3:e12149. https://doi.org/10.1002/jcv2.12149

Poole KL, Cunningham CE, McHolm AE, Schmidt LA (2021) Distinguishing selective mutism and social anxiety in children: a multi-method study. Eur Child Adolesc Psychiatry 30:1059–1069. https://doi.org/10.1007/s00787-020-01588-3

Quintero N, McIntyre LL (2010) Sibling Adjustment and Maternal Well-Being: An Examination of Families With and Without a Child With an Autism Spectrum Disorder. Focus Autism Dev Disabil 25:37–46. https://doi.org/10.1177/1088357609350367

Rantakallio P (1979) Social background of mothers who smoke during pregnancy and influence of these factors on the offspring. Soc Sci Med Part Med Psychol Med Sociol 13:423–429. https://doi.org/10.1016/0271-7123(79)90077-4

Reed GF (1963) ELECTIVE MUTISM in CHILDREN: A RE-APPRAISAL. J Cfflld Psychol 4:99–107

Reiss F (2013) Socioeconomic inequalities and mental health problems in children and adolescents: A systematic review. Soc Sci Med 90:24–31. https://doi.org/10.1016/j.socscimed.2013.04.026

Remschmidt H, Poller M, Herpertz-Dahlmann B, Hennighausen K, Gutenbrunner C (2001) A follow-up study of 45 patients with elective mutism. Eur Arch Psychiatry Clin Neurosci 251:284–296. https://doi.org/10.1007/PL00007547

Rødgaard E-M, Jensen K, Miskowiak KW, Mottron L (2021) Childhood diagnoses in individuals identified as autistics in adulthood. Mol Autism 12. https://doi.org/10.1186/s13229-021-00478-y

Rodrigues Pereira C, Ensink JBM, Güldner MG, Lindauer RJL, De Jonge MV, Utens EMWJ (2021) Diagnosing selective mutism: a critical review of measures for clinical practice and research. Eur Child Adolesc Psychiatry. https://doi.org/10.1007/s00787-021-01907-2

Rosa M, Puig O, Lázaro L, Calvo R (2016) Socioeconomic status and intelligence quotient as predictors of psychiatric disorders in children and adolescents with high-functioning autism spectrum disorder and in their siblings. Autism 20:963–972. https://doi.org/10.1177/1362361315617881

Rozenek EB, Orlof W, Nowicka ZM, Wilczyńska K, Waszkiewicz N (2020) Selective mutism - an overview of the condition and etiology: Is the absence of speech just the tip of the iceberg? Psychiatr Pol 54:333–349. https://doi.org/10.12740/PP/ONLINEFIRST/108503

Segal NL (2003) "Two" Quiet: Monozygotic Female Twins with Selective Mutism. Clin Child Psychol Psychiatry 8:473–488. https://doi.org/10.1177/13591045030084005

Sharkey L, McNicholas F (2012) Selective Mutism: A prevalence study of primary school children in the Republic of Ireland. Ir J Psychol Med 29:36–40. https://doi.org/10.1017/S0790966700017596

Sharp WG, Sherman C, Gross AM (2007) Selective mutism and anxiety: A review of the current conceptualization of the disorder. J Anxiety Disord 21:568–579. https://doi.org/10.1016/j.janxdis.2006.07.002

Slobodin O (2023) Beyond the language barrier: A systematic review of selective mutism in culturally and linguistically diverse children. Transcult Psychiatry 60:313–331. https://doi.org/10.1177/13634615221146435

Sluckin A, Foreman N, Herbert M (1991) Behavioural treatment programs and selectivity of speaking at follow-up in a sample of 25 selective mutes. Aust Psychol 26:132–137. https://doi.org/10.1080/00050069108258851

Ståhlberg T, Khanal P, Chudal R, Luntamo T, Kronström K, Sourander A (2020) Prenatal and perinatal risk factors for anxiety disorders among children and adolescents: A systematic review. J Affect Disord 277:85–93. https://doi.org/10.1016/j.jad.2020.08.004

Ståhlberg T, Upadhyaya S, Polo-Kantola P, Khanal P, Luntamo T, Hinkka-Yli-Salomäki S, Sourander A (2022) Associations Between Delivery Modes, Birth Outcomes and Offspring Anxiety Disorders in a Population-Based Birth Cohort of Children and Adolescents. Front Psychiatry 13:917299. https://doi.org/10.3389/fpsyt.2022.917299

Starke A (2018) Effects of anxiety, language skills, and cultural adaptation on the development of selective mutism. J Commun Disord 74:45–60. https://doi.org/10.1016/j.jcomdis.2018.05.001

Steains SY, Malouff JM, Schutte NS (2021) Efficacy of psychological interventions for selective mutism in children: A meta-analysis of randomized controlled trials. Child Care Health Dev 47:771–781. https://doi.org/10.1111/cch.12895

Steffenburg H, Steffenburg S, Gillberg C, Billstedt E (2018) Children with autism spectrum disorders and selective mutism. Neuropsychiatr Dis Treat 14:1163–1169. https://doi.org/10.2147/NDT.S154966

Stein MB, Yang B-Z, Chavira DA, Hitchcock CA, Sung SC, Shipon-Blum E, Gelernter J (2011) A Common Genetic Variant in the Neurexin Superfamily Member CNTNAP2 Is Associated with Increased Risk for Selective Mutism and Social Anxiety-Related Traits. Biol Psychiatry 69:825–831. https://doi.org/10.1016/j.biopsych.2010.11.008

Steinert C, Hofmann M, Leichsenring F, Kruse J (2013) What do we know today about the prospective long-term course of social anxiety disorder? A systematic literature review. J Anxiety Disord 27:692–702. https://doi.org/10.1016/j.janxdis.2013.08.002

Steinhausen H-C, Adamek R (1997) The family history of children with elective mutism: A research report. Eur Child Adolesc Psychiatry 6:107–111. https://doi.org/10.1007/s007870050015

Steinhausen H-C, Bisgaard C, Munk-Jørgensen P, Helenius D (2013) FAMILY AGGREGATION AND RISK FACTORS OF OBSESSIVE-COMPULSIVE DISORDERS IN A NATIONWIDE THREE-GENERATION STUDY: Family Aggregation of OCD. Depress Anxiety 30:1177–1184. https://doi.org/10.1002/da.22163

Steinhausen H-C, Foldager L, Perto G, Munk-Jørgensen P (2009) Family aggregation of mental disorders in the nationwide Danish three generation study. Eur Arch Psychiatry Clin Neurosci 259:270–277. https://doi.org/10.1007/s00406-008-0865-0

Steinhausen H-C, Jakobsen H, Meyer A, Jørgensen PM, Lieb R (2016) Family Aggregation and Risk Factors in Phobic Disorders over Three-Generations in a Nation-Wide Study. PLOS ONE 11:e0146591. https://doi.org/10.1371/journal.pone.0146591

Steinhausen H-C, Jakobsen H, Munk-Jørgensen P (2017) Family aggregation and risk factors in substance use disorders over three generations in a nation-wide study. PLOS ONE 12:e0177700. https://doi.org/10.1371/journal.pone.0177700

Steinhausen H-C, Juzi C (1996) Elective mutism: An analysis of 100 cases. J Am Acad Child Adolesc Psychiatry 35:606–614. https://doi.org/10.1097/00004583-199605000-00015

Steinhausen H-C, Wachter M, Laimböck K, Metzke CW (2006) A long-term outcome study of selective mutism in childhood. J Child Psychol Psychiatry 47:751–756. https://doi.org/10.1111/j.1469-7610.2005.01560.x

Stone BP, Kratochwill TR, Sladezcek I, Serlin RC (2002) Treatment of selective mutism: A best-evidence synthesis. Sch Psychol Q 17:168–190. https://doi.org/10.1521/scpq.17.2.168.20857

Sund R (2012) Quality of the Finnish Hospital Discharge Register: A systematic review. Scand J Public Health 40:505–515. https://doi.org/10.1177/1403494812456637

Thomson RM, Igelström E, Purba AK, Shimonovich M, Thomson H, McCartney G, Reeves A, Leyland A, Pearce A, Katikireddi SV (2022) How do income changes impact on mental health and wellbeing for working-age adults? A systematic review and meta-analysis. Lancet Public Health 7:e515–e528. https://doi.org/10.1016/S2468-2667(22)00058-5

Tiilikainen M (2007) Etniset vähemmistöt Suomessa. LÄÄKETIETEELLINEN AIKAKAUSKIRJA DUODECIM 123:437–439

Tomohisa Y, Yumi I, Inoue M (2022) Long-term outcome of selective mutism: factors influencing the feeling of being cured. Eur Child Adolesc Psychiatry. https://doi.org/10.1007/s00787-022-02055-x

Toppelberg CO, Tabors P, Coggins A, Lum K, Burger C (2005) Differential Diagnosis of Selective Mutism in Bilingual Children. J Am Acad Child Adolesc Psychiatry 44:592–595. https://doi.org/10.1097/01.chi.0000157549.87078.f8

Tramer M (1934) Elektiver Mutismus bei Kindern = Selective mutism of children. Z Für Kinderpsychiatr 1:30–35

Upadhyaya S, Brown A, Cheslack-Postava K, Gissler M, Gyllenberg D, Heinonen E, Laitinen J, McKeague I, Hinkka-Yli-Salomäki S, Sourander A, Tornio A, Malm H (2023) Maternal SSRI use during pregnancy and offspring depression or anxiety disorders: A review of the literature and description of a study protocol for a register-based cohort study. Reprod Toxicol 118:108365. https://doi.org/10.1016/j.reprotox.2023.108365

Vaalavuo M, Niemi R, Suvisaari J (2022) Growing up unequal? Socioeconomic disparities in mental disorders throughout childhood in Finland. SSM - Popul Health 20:101277. https://doi.org/10.1016/j.ssmph.2022.101277

Viana AG, Beidel DC, Rabian B (2009) Selective mutism: A review and integration of the last 15 years. Clin Psychol Rev 29:57–67. https://doi.org/10.1016/j.cpr.2008.09.009

Vogel F, Gensthaler A, Schwenck C (2022) Frozen with Fear? Attentional Mechanisms in Children with Selective Mutism. Cogn Ther Res 46:629–645. https://doi.org/10.1007/s10608-021-10289-3

Vogel F, Schwenck C (2021) Psychophysiological mechanisms underlying the failure to speak: a comparison between children with selective mutism and social anxiety disorder on autonomic arousal. Child Adolesc Psychiatry Ment Health 15. https://doi.org/10.1186/s13034-021-00430-1

Wergeland H (1979) Elective mutism. Acta Psychiatr Scand 59:218–228

White JC (2023) Exploring the educational views and needs of children with selective mutism. ProQuest Information & Learning

Wong P (2010) Selective mutism: a review of etiology, comorbidities, and treatment. Psychiatry Edgmont Pa Townsh 7:23–31

Wood KA, Goriely A (2022) The impact of paternal age on new mutations and disease in the next generation. Fertil Steril 118:1001–1012. https://doi.org/10.1016/j.fertnstert.2022.10.017

World Health Organization (2019) International Statistical Classification of Diseases and Related Health Problems (11th ed.). In: https://icd.who.int/. https://icd.who.int/

World Health Organization (1993a) The ICD-10 classification of mental and behavioural disorders: diagnostic criteria for research. World Health Organization, Geneva

World Health Organization. (1977) International statistical classification of diseases and related health problems (9th ed.). Geneva

World Health Organization (ed) (1993b) The ICD-10 classification of mental and behavioural disorders. World Health Organization, Genève, Switzerland

Yeganeh R, Beidel DC, Turner SM (2006) Selective mutism: More than social anxiety? Depress Anxiety 23:117–123. https://doi.org/10.1002/da.20139

Yeganeh R, Beidel DC, Turner SM, Pina AA, Silverman WK (2003) Clinical distinctions between selective mutism and social phobia: An investigation of childhood psychopathology. J Am Acad Child Adolesc Psychiatry 42:1069–1075. https://doi.org/10.1097/01.CHI.0000070262.24125.23

Young BJ, Bunnell BE, Beidel DC (2012) Evaluation of Children With Selective Mutism and Social Phobia: A Comparison of Psychological and Psychophysiological Arousal. Behav Modif 36:525–544. https://doi.org/10.1177/0145445512443980

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