Life course of children with parental multiple sclerosis

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THE THREE ORIGINAL PAPERS ARE

1. Moberg JY, Magyari M, Koch-Henriksen N, Thygesen LC, Laursen B, Soelberg Sørensen P. Educational achievements of children of parents with multiple sclerosis: A nationwide register-based cohort study. J Neurol 2016;263(11), 2229-2237.
2. Moberg JY, Laursen B, Koch-Henriksen N, Thygesen LC, Brødsgaard A, Soelberg Sørensen P, Magyari M. Employment, disability pension and income for children with parental multiple sclerosis. Mult Scler. Epub 2016 Sep 1. DOI: 10.1177/1352458516672016.
3. Moberg JY, Larsen D, Brødsgaard A. Striving for balance between caring and restraint. Young adults' experiences with parental multiple sclerosis. J Clin Nurs 2017;26(9-10):1363-1374.

ABBREVIATIONS

ADL	Activities of daily living
CI	Confidence interval
GLM	General linear model
GPA	Grade point average
MS	Multiple sclerosis
N/A	Not applicable
OR	Odds ratio
SD	Standard deviation
SE	Standard error
χ^2	Chi-square test

INTRODUCTION

Multiple sclerosis (MS) is a chronic illness with a complex interaction between genetic susceptibility and environmental factors. It is an inflammatory demyelinating disease of the central nervous system.[1-4] Historically, Jean-Martin Charcot first described the clinical features of MS as a disease in 1868.[5,6] Description of this neurological disease dates as far back as a 12th-century Icelandic saga, and later case reports and diaries describe symptoms corresponding with MS.[7,8] The majority of people diagnosed with MS experience onset of MS between the ages of 20 and 40.[9,10] The ratio of women to men has increased to >2:1 from the 1970s.[11-13]

About 2.3 million people have MS worldwide.[14] In Denmark, the Danish Multiple Sclerosis Registry has registered more than 25,000 cases since 1948, and more than 13,000 are currently living with this diagnosis in Denmark, yielding a prevalence of 232 per 100,000 persons, one of the highest in the world. On average almost 500 new cases are registered each year.[15]

The symptoms of MS vary from mild to disabling, and the disease may affect motor skills, vision, bladder and bowel control, and cognitive function.[16,17] Cognitive impairment can involve difficulties with short-term memory, learning new skills, and executive functions.[18,19] Between 40%–65% of persons with MS are increasingly impeded by cognitive difficulties, with adverse impacts on their work and social skills.[20] Fatigue is a dominant symptom, which impacts at least 75% of persons with MS persistently or sporadically and which necessitates frequent rest periods in between work, activities of daily living (ADL) and outings.[21-23] When the fatigue is severe or the need for rest is inadequately fulfilled, a person with MS can be exhausted for several days. Hence, both on an everyday basis and when insufficiently heeded, fatigue has a severe impact on working ability and family life.[24,25]

The symptoms of MS thus range from mild to disabling and are dependent on each individual's disease trajectory.[21,26,27] The worse the MS-related disabilities, the worse the effects of MS can be on employment status, ability to initiate or maintain a partnership, and ability to perform ADL as well as on energy for family activities, emotional availability, and parenting.[28-30] Living with MS for decades can have serious socioeconomic, familial, and emotional effects on the person diagnosed with MS.[29-31]

At disease onset, many persons with MS already have children or are planning to have children because MS primarily affects young adults in their childbearing years.[32-34] It is estimated that 10% of children in the world live with a parent with a chronic illness.[35]

Background: Children of parents with multiple sclerosis

There is little knowledge about the influence of parental MS on children, and knowledge about adult children and their life course after growing up with parental MS is especially scarce (Appen-

dices\Table 1). This section provides the general background for the three studies comprising the PhD thesis. The potential influence of parental MS on children is based on symptoms of the chronic illness and the derived effects on family life.

Review studies and one meta-analysis have shown that the effects of parental chronic illness on children are primarily negative.[36-42] These effects may include overwhelming responsibilities, such as time-consuming household tasks, caregiving (including personal hygiene), emotional distress, isolation, and help with ADL.[35,43,44] Many children had limited time to spend on education, leisure, and friends due to the increased caretaking and household tasks.[44-47] Some children developed anxiety, separation anxiety, health worries, or depression.[43,48,49] Most children lacked knowledge about the symptoms and possible future development of the parent's MS, which was very stressful and created uncertainty and disproportionate worries for them. In some families, the parent's chronic illness or the children's caretaking were not openly acknowledged, which made the children's added responsibilities invisible and therefore overlooked.[43,50] Parental depression and emotional distress have been associated with lower coping and psychological difficulties in children.[51,52] One study found that it was the ability of the partner without MS to cope with a partner with MS that most strongly influenced how the children adjusted to parental MS.[51]

Some studies found beneficial effects for the children in addition to the adverse effects. These may include increased empathy and responsibility, strong familial bonds, or pride in administrative and caretaking skills.[44,45,53-57]

Other studies found no significant differences, e.g. in body image,[58] mother-daughter interactions,[59] or in adverse early childhood development in main outcomes between children with a parent with MS and a reference population. There were, however, significant associations between duration of exposure to parental MS and parental mental health comorbidity and developmental vulnerability.[60]

In a review, the 11–18 year-old adolescents with parental MS had a greater risk of psychosocial difficulties than did the younger age group of 5–11 years.[38] Previous studies have mostly focused on young children, with just a few on teenagers, and they often included parents or relatives with various chronic illnesses, including MS. Some of the studies concentrated on the parents' perspective on the well-being of their children by having the parents, and sometimes also the children, filling out questionnaires.[61-64]

Research looking at the long-term life course of children with parental MS is very limited. An overview of previous studies is provided in Table 1 in the appendices. We found only two studies about adult children between 19 and >65 years who were formerly young caregivers to family members with a chronic illness, and a few people in these two studies had a parent with MS; these two studies used interview and questionnaire methods.[45,65]

Because the current knowledge concerning the long-term influence of parental MS on children is scarce, and because no other studies have been conducted using nationwide register-based data, we designed this PhD work to investigate the area using original approaches:

- Age group: Primarily adults
- Long-term: From childhood up to 58 years of age
- Two complementary methods: A nationwide epidemiological register-based method and a phenomenological interview method.

OJECTIVES

The general objective of this PhD thesis is to investigate whether parental MS influences children at different stages in their life course. The general objective is investigated in three studies with specific objectives:

I: To investigate the educational attainments of children with parental MS compared with a reference population in a register-based study.

II: To investigate the employment-related attainments of children with parental MS compared with a reference population in a register-based study.

III: To explore and describe young adults' experiences with parental MS in a phenomenological interview study.

Hypotheses

Study I: Parental MS influences children's grade point average in basic school, highest attained educational level, and probability of attaining a health-related education.

Study II: Parental MS influences children's employment, disability pension, and income.

Aim

Study III: This study is descriptive and aims to explore and describe young adults' experiences of growing up with a parent with MS and how the parental MS continues to influence their daily lives.

METHODOLOGICAL CONSIDERATIONS

To investigate the almost uncharted research area of adult children with parental MS, we used two different study designs as a means of attaining both a broad and a deep perspective. We applied only one method to each study, never both.

Studies I–II investigate the broad perspective, using a quantitative cohort design based on nationwide Danish registers with 37,593 people aged 15 to 58 (Paper I) and 22,104 people aged 30 to 57 (Paper II).

Study III explores the deep perspective, using a qualitative interview design based on an exploratory phenomenological approach with 14 young adults aged 18 to 25 in face-to-face interviews (Paper III).

Quantitative nationwide register-based study method

The register-based studies are quantitative, meaning that we can apply statistical analyses to quantify the attained level of education, employment rate, and income. The general strengths of quantitative studies include the ability to use statistical analyses to get a sense of numeric proportion and to be able to generalize.[66] Among the strengths of register-based studies are their inclusion of vast numbers of people, permitting us to randomly include people into each cohort. Also, since Denmark's registers are nationwide, our studies are based on the whole population of

people with onset of MS between 1950 and 1986, compared with a matched group of people by sex and year of birth from the background population. In addition, register data in Denmark are available for research purposes – although collected independently for administrative purposes because the collection and reporting are mandatory for all public institutions. Another strength is that there is no recall bias or selection bias because the objective endpoints were independent of the people's memory or responsiveness. The limitations of a quantitative study are the difficulties in accessing the detailed reasons or reflections behind people's decisions and in investigating complex concepts or feelings.[66]

Studies I–II featured deductive reasoning, meaning that the approach to investigating the phenomenon was to start with the general and then, after undertaking several steps of analysis, to arrive at the specific.[66,67] In each of these two studies, we first formulated a hypothesis and then applied the observational data from the relevant registers to either confirm or reject the hypotheses.

Qualitative exploratory phenomenological study method

The interview study is qualitative, meaning that we can explore experiences of growing up with a parent with MS in depth through the participants' own detailed narrations. The major strength of a qualitative study is the ability to investigate a complex phenomenon in depth and detail.[66] Another strength is to make connections across different areas of the participants' lives.[68] Yet another strength is the ability for participants to elaborate upon their responses and thereby introduce new topics or gain insights not initially considered.[67] The limitations of a qualitative study are the difficulties in applying it to a large number of people and in using statistical analyses meaningfully.[66]

We used the phenomenological framework and method.[69,70] We had few preconceived ideas as to what the participants would tell us since the age group in question (young adults between 18 to 25 years of age) had not been in exclusive focus before. This also makes the study exploratory and open-ended because we were open to whatever findings would emerge from the data.[67,71,72]

Study III featured inductive reasoning, meaning that we began from the specific observations (in this case, participants' statements) and then moved through several analytical steps to detect more and more condensed themes toward general observations.[73] We thus formulated the research aim at the start and then condensed our data through analysis until we arrived at the general finding – the phenomenological 'essence of the phenomenon' – that had emerged from the interviews as a whole.[70]

Complementary study methods

The two study methods have opposing strengths and limitations, and each method's limitations are counterbalanced by the other method's strengths. The register-based method and the phenomenological interview method are thus complementary. The broad perspective with large populations provides statistical significance and power and is complemented by the deep perspective with in-depth narrations of participants' complex experiences.

METHODS OF THE REGISTER-BASED STUDIES

Study design

Studies I–II are register-based cohort studies including children of all Danish-born people with onset of MS between 1950 to 1986 as well as a reference cohort of children from the background population of parents without MS.

The children of a parent with MS are termed the 'MS offspring' cohort and the children of parents without MS matched by sex and year of birth to each MS offspring child are termed the 'reference cohort'.

Establishing the study database

The study database applied in Studies I–II was established by linking data from many different Danish registers. Denmark has extensive nationwide population-based registers on all residents as well as data on socioeconomic factors, with mandatory reporting for all public institutions and both private and public employers. Some of the Danish registers are partly established for administrative purposes, and they serve as unique data sources for research. The author combined, managed, and analyzed data in the database by developing SAS algorithms specifically for these purposes.

Since 1968, all Danish residents have been assigned an exclusive personal identification number through the Danish Civil Registration System (CRS) at birth or immigration.[74] The Danish registers utilize this CRS number to store and report the data at the level of the individual person.

Statistics Denmark is the main provider of register data in Denmark, and its secure and logged servers store all the register data following anonymization and encryption. Access to data involves a comprehensive application procedure and is financed by the researcher. By linking the anonymized CRS number to the relevant nationwide registers, we established our study database with information on several socioeconomic factors at the level of the individual person for the two cohorts and their parents. The variables in the database are presented in Table 2 Variables in Studies I–II in the appendices.

The two cohorts: MS offspring and reference children

From the nationwide Danish Multiple Sclerosis Registry,[15] we retrieved all Danish-born people with clinical onset of MS between 1950 and 1986 and definite MS according to the current diagnostic criteria: Allison & Millar[75] until 1994, Poser[76] until 2004 and McDonald[77,78] from 2005. There were 7,409 residents who had a confirmed MS diagnosis, and 2,879 of the persons with MS (38.9%) were childless by December 31, 2012.

Statistics Denmark identified the children by the 4,530 persons with MS (61.1%) who had children. We randomly included one child from each sibship with one biological parent with MS to avoid clustering. For each MS offspring child, we randomly matched eight children of parents without MS by sex and year of birth. Both cohorts of children as well as their parents needed to have been born in Denmark. We excluded children from both cohorts if they were diagnosed with MS, were twins, or had emigrated from Denmark.

The large number of reference children per individual MS offspring was chosen to calculate more precise parameter estimates.

This in turn provided higher precision and power in obtaining true associations between exposure and outcome. All covariates and measured outcomes were collected similarly for the two cohorts, since the children were compared on the same factors.

Depending on the timeframes of the registers in question and on the analyzed outcomes, we included children from different age ranges and maximum ages at the time of the parent's MS diagnosis, as summarized below.

Population for Study I
Children born between 1955 and 1998 were included following the inclusion, exclusion, and match criteria described above. The final study population consisted of 4,177 MS offspring and 33,416 reference children aged 15–58 years at follow-up in 2013 (Paper I\Figure 1). In 2013, at follow-up, the median age of the included individuals was 44 years, and 88% were between the ages of 30 and 58.

Among the MS offspring, 2,149 (51.5%) were not yet born or were a maximum of 12 years old at their parent's MS diagnosis. The proportion of females in the MS offspring cohort was 47.6% (*n* = 1,987). Among the parents with MS, the female to male ratio was 1.6:1.

Population for Study II
Children born between 1955 and 1982 were included following the inclusion, exclusion, and match criteria described above. The final study population consisted of 2,456 MS offspring and 19,648 reference children aged 30–57 years at follow-up in 2012 (Paper II\Figure 1).

In the MS offspring cohort, 1,711 (69.7%) were not yet born or were a maximum of 12 years old at the time of the parent's MS diagnosis, and 1,190 (48.5%) were women. The female to male ratio of the parents with MS was 1.4:1.

The included children were a maximum of 18 years old at the time of parental MS diagnosis to ensure that the parental MS could potentially exert an influence on the children's employment and income probabilities.

We chose to analyze the children regarding employment and disability pension at the ages of 30, 40, or 50 because these three ages covered three different stages in their working lives. Age 30 was chosen as the minimum age because we wished to allow sufficient time for the children to attain education and employment. Ages 40 and 50 were chosen to investigate the time until loss of working capacity.

According to Statistics Denmark, the background Danish population of men and women generally earn their highest level of income between the ages of 45 to 49.[79] Therefore, we chose this five-year age interval in our income analyses for each individual as well as included and corrected the income for inflation, with 2012 as baseline.

We analyzed the probability of attaining a gross personal annual income above DKK 250,000 (~ EUR 33,650)**.**[80] People earning below this income level in Denmark in 2012 had low-income jobs, part-time jobs, or received social benefits.[80] Attaining DKK 250,000 annually is sufficient for the bare necessities and is equivalent to double the poverty level, which is less than 50% of the median income, according to OECD.[81]

Data sources
The study database links data on the level of the individual person from multiple nationwide Danish registers, which are presented here.

The Danish Multiple Sclerosis Registry was established in 1956 and comprises all prevalent MS cases in 1948 and incident cases with onset after 1947.[15,82] Presently, there are more than 25,000 people with a definite MS diagnosis registered. MS is diagnosed by a staff neurologist in accordance with the current MS criteria detailed above.[83] The Danish Multiple Sclerosis Registry is the oldest nationwide population-based MS registry in the world.[15,83]

The Civil Registration System was established in 1968 and contains all Danish residents; tracks their histories of residency; and maintains identity of spouses, children, parents, deaths, and migration.[84] It provides individual person identification for all residents. This number is life-long and is used by all public authorities, employers, and registers concerning education, employment, and income.

The School Grade Register was established in 2002 and contains grades in the 9th class of basic school. Students complete the 9th class when they are about 15 years old. By Danish law, this is the minimum level of schooling that children must attain, and subsequent education is optional. An officially appointed external examiner reviews the student in written examinations and co-examines the student in verbal examinations. The School Grade Register uses the European Credit Transfer and Accumulation System grading scale: -3, 0, 2, 4, 7, 10, and 12. The first two grades indicate failure. The outcome is calculated as the grade point average (GPA) per pupil. We had access to grades from 2002 to 2013.

The Population's Education Register was established in 1981 and contains individual-level information on all educational achievements from preschool up to PhD level. The Population's Education Register has a high degree of validity and coverage (96.4% in 2008).[85] The outcome is determined as the highest completed educational levels of the cohorts and their parents, both dichotomized in 'basic school level or above basic school level' and in four categories at follow-up in 2013. We define the health-related educations as an attained degree in physiotherapy, occupational therapy, nursing, public health, psychology, or medicine. The health-related educational outcome is dichotomized in 'achieving a health-related education or not' at follow-up. We had access to educational data from 1981 to 2013.

The Employment Classification Module was established in 1980 and contains information as to whether a Danish resident has been in employment for more than 6 months, is unemployed, is undergoing education, is on maternity/paternity/sick leave, is on disability pension, is retired, or has not been working for any other reason for more than 6 months. We had access to employment data from 1980 to 2012.

The Disability Pension is a part of the Employment Classification Module and includes all people who received disability pension for at least 6 months due to e.g. illness or accidents and not due

to the state-required retirement age. We had access to disability pension data from 1980 to 2012.

The Income Statistics Register was established in 1970.[86] Statistics Denmark defines personal gross income as income for 18–59 years of age (excluding students) that is taxed and stems from an individual's main activity for a minimum of half of the year: employment pay (employed or self-employed); benefits (retirement, disability pension, maternity/paternity leave); income from stocks, bonds, saving accounts, and pension accounts; and income from abroad (employment pay, pension, stocks, etc.). Our aim in using the personal income was to test for the difference in income earned by the study individual per year. If we had chosen the alternative of family income, it might have lowered or raised the income of the studied individual if the partner attained more or less, thereby distorting the individual's income, which would defeat our purpose. Following the same argument, we chose gross income instead of disposable income because the Danish welfare state[87] supports, for example, single parents by paying for a portion of childcare or housing costs dependent on the parent's level of income. These benefits might equalize the disposable incomes to some extent and thereby conceal underlying differences. We had access to gross personal annual income data from 1980 to 2012.

Covariates

Parental age at childbirth

We assumed that the parent's age at childbirth might impact the child because of the parent's maturity and social circumstances, which is often associated with parental age. The sex of the MS parent was matched with the reference parent within each matching group. The parents were not matched by age. We divided the parent's age at birth of the included child into four categories: <20; 20–29; 30–39; ≥40.

Parental educational level

We assumed that the parent's educational level might impact the child with regard to educational attainments, employment, risk of disability pension, and income level. We thus divided the parent's education into four categories: basic school; secondary school; vocational educational training, short or medium higher education, BA; and long higher education, PhD.

Statistical analyses

In Studies I–II, descriptive statistics were used to describe the included populations. Logistic regression was applied to estimate unadjusted and adjusted odds ratios (OR) with a 95% confidence interval (CI) for dichotomized outcomes. The adjusted ORs included two covariates pertaining to parental age at childbirth and highest attained level of education. We applied both an independent two-sample *t*-test to compare the means and a general linear model (GLM) to calculate parameter estimates for the continuous data: grades and income. A chi-square test was used when analyzing occurrence of death in the two cohorts and when comparing the number of people attaining an outcome stratified by sex. Statistical significance was defined at p value <0.05.

In Study I, we conducted some additional analyses. The Cochran-Armitage trend test was used to analyze educational levels when specified into four levels. We performed a sensitivity test for children aged 30 to 58 to analyze their probability of attaining a level above basic school. In a logistic regression, we tested for a possible calendar year effect on the highest attained educational level. For descriptive purposes, the children's year of birth was stratified into three categories: 1955–1964, 1965–1979, and 1980–1998.

All statistical analyses in Studies I–II were conducted using SAS software version 9.4.

Ethics

Statistics Denmark encrypts, anonymizes, and stores all register data on its secure and logged servers. A remote online access is granted specifically for each researcher, and each login to the Statistics Denmark servers is logged and time stamped with the researcher's identification number. Even though the researcher has access to information on the level of an individual person, the data encryption and anonymization ensure that it is impossible to identify individuals within the datasets.

We linked the datasets using the encrypted personal identification numbers, but even though we conducted research on individual person-level data, all people were anonymized and thus unidentifiable. The Danish Data Protection Agency approved the studies for research and statistical usage [reference numbers 30-1141 and 2008-54-0482]. Ethical committee approval is not required by Danish law since the studies were entirely register-based and non-interventional.

METHODS OF THE INTERVIEW STUDY

Study design

Study III is a qualitative study with an exploratory inductive design. Because knowledge is scarce concerning the investigated phenomenon, it was important to ensure an exploratory and inductive approach in both reasoning and analysis. To achieve an exploratory inquisitiveness, our approach was based on Husserl's phenomenological philosophy.[69] We used the phenomenological four-step method of analysis by Giorgi.[70] By in-depth interviewing 14 young adults between 18 and 25 years of age, we aimed for detailed and deep reflections concerning their experiences of having a parent with MS.

Phenomenology

Phenomenology is the philosophy concerning the structures of human experience and consciousness.[69,88] Phenomenology is thus the study of *how* people experience or are conscious of a particular object, where the object can be material (such as a house) or immaterial (such as a feeling or a concept).[71] Phenomenologists seek to describe and understand – rather than explain – a phenomenon; they aim to make the implicit explicit by describing a phenomenon so its meaning is clarified.[71,89] The six important aspects of phenomenology are: First-person perspective; subjective; phenomenon in phenomenology; the 'thing' in itself; lifeworld; and bracketing of preconceptions.[69] These aspects are elaborated below.

First-person perspective

Edmund Husserl (1859–1938) formulated the groundwork of phenomenology as a corrective to naturalism, in which consciousness is seen as part of nature and is analyzed using methods focused on empirical facts and causality.[69] Naturalism takes the objective third person as its ideal whereas Husserl states that the subjective first person must be the starting point because an individual who experiences anything does so by directing his or her intentionality toward something.[69] Intentionality is thus of

paramount importance in phenomenology since all consciousness is consciousness *of* something.

Subjective

To be subjective is an inherent trait of being human in phenomenology because we cannot escape experiencing something from the first-person perspective. Our experiences are always embedded in the world and related to it. In opposition to naturalism and its ideal of objectivity, we should always take this subjective interrelatedness into account; otherwise our analyses of phenomena will be faulty.[69]

Phenomenon in phenomenology

A phenomenon to be studied in phenomenology is more than an object like a house, a feeling like love, or a concept like learning. When we take the interrelatedness into account, the experiencing subject and the experienced object are inseparable simply because we, as humans, always bring our subjective first-person perspective into any experience. This unification of subject and object is the *phenomenon* that is the basis of a descriptive phenomenological analysis.[69]

The 'thing' in itself

In phenomenology, researchers study the structures of experience or consciousness by investigating the phenomenon as it appears, which is also termed the 'thing' in itself.[69] The aim is thus to describe the 'thing' or phenomenon as it is experienced by a person and thereby to understand the 'thing' better.[71] So a phenomenological study concentrates on how a particular person experiences something. To investigate our phenomenon as directly as possible, we directed our attention to the 'thing' in itself by interviewing young adults with parental MS.

Lifeworld

When researchers aim to investigate a particular phenomenon phenomenologically, they investigate the subjective first-person perspective of the participant's experiences of the phenomenon – also termed the 'lifeworld'.[69] Phenomenologists argue that, as humans, we cannot set ourselves outside and objectively experience a phenomenon from the third-person perspective. Instead, a person encountering any phenomenon will bring everything of which he or she consists into the experience of the phenomenon. A researcher investigating the phenomenon is thus said to investigate the 'lifeworld' of the participant.[70,71]

Bracketing of preconceptions

An important aim in phenomenology is for researchers to remain conscious of their own preconceptions. This is termed 'bracketing' or epoché.[69,90] The researcher seeks to prevent preconceptions or prior thoughts and judgements concerning the phenomenon from interfering with openness to the description. By bracketing or setting aside preconceptions, the researcher places the phenomenon in epoché.[71] We endeavored to describe the young adults' experiences of the phenomenon as accurately as possible without unduly influencing them with our own preconceptions.

We thus reflected phenomenologically upon the young adults' experiences and our subsequent analysis while remaining conscious of our own preconceptions. The preconceptions derived from our backgrounds in nursing (author and supervisor AB) and psychology (supervisor DL), from work with persons with MS and their relatives over several years (author and DL), and from the literature about children with a chronically ill parent.

Data collection

The participants volunteered as a result of online and printed advertisements through the Danish and Faroese MS Society and MS hospital clinics across Denmark. Volunteers were included or excluded through purposeful sampling,[68] meaning that volunteers should be relevant to the research question and study criteria: Participants should be between 18 to 25 years old, have one or two parents with MS, and have lived with the parent with MS at least two years following diagnosis. They should not themselves have a chronic diagnosis. Three people were excluded because of age older than 25 or because the parents were diagnosed with MS less than one year earlier.

Demographic questionnaire

All participants filled out a written questionnaire regarding demographic information about their parents and themselves before the interview (Paper III\Table 1). We conceived the questionnaire in such a way as to gather demographic information on each participant and family.

Sample

We included 14 young adults aged 18–25 years. All participants were white, 13 were from Denmark, and 1 was from the Faroe Islands (a self-governing country belonging to Denmark). There were 12 women and 2 men, and their mean age was 20.6 years (range: 18–25 years) when interviewed. Their mean age at the time of the parent's MS diagnosis was 8.9 years (range: before birth to 16 years). They had lived with the parent with MS following the diagnosis 3–19 years: 4 still lived with the MS parent, and 10 had moved out of their childhood homes. Their parental socioeconomic backgrounds ranged from low income and no formal education to high income and highest educational level of parents with or without MS. All five regions of Denmark were covered. The majority of the parents remained married, and five were divorced. All but one of the participants had one or more siblings.

Interviews

The 14 separate in-depth interviews with the young adults were conducted by the author between May and August 2014. Each participant was interviewed separately and face-to-face in a location of his or her own choosing (the participant's home, the author's home, or a public place). To encourage the participants to share their experiences of growing up with a parent with MS, the author endeavored to establish a trusting atmosphere and to remain open during the interview to whatever the participant wished to discuss.

In accordance with phenomenology, the questions were mostly open-ended to allow the participant express himself or herself freely. For example, the author would ask 'How did you experience…?' or 'What was it like to…?' Follow-up questions were used to encourage the participant to elaborate upon or explain something in greater depth and detail. For example, 'How did that make you feel?' or 'Would you mind giving me an example of this?' Another set of questions was related to check whether the author understood the participant as this was of paramount importance for the subsequent analysis (cf. Rigor) because the intention was to understand, analyze, and portray the participants' experiences as accurately as possible. For instance, 'Did I understand you correctly that…?' or 'Does it mean that…?' If the

participant disagreed with the author's description, then he or she would correct the misunderstanding and elaborate further, until the author understood the participant correctly. Participants thus validated the author's understanding and descriptions.

The interviews lasted an average of 114 minutes (range: 53 minutes to 3 hours and 30 minutes), amounting to 26 hours and 42 minutes in total. They were digitally recorded with the participants' consent. When transcribed, there were 861 single-spaced A4 pages of interview data.

Data management program: NVivo 10

The computer program NVivo version 10 from QSR is specifically constructed for managing qualitative data. We used NVivo to store the interview data from the 14 interviews and to visually rearrange participants' verbatim quotes as well as the increasingly condensed themes that emerged through the phenomenological analysis (Appendices\Figure 1). We managed the interview data in NVivo and analyzed the data using Giorgi's phenomenological analysis method.[70]

Data analysis

Amedeo Giorgi has developed the descriptive phenomenological method[70] in psychology upon which we based our analysis and which has been used in many different fields, including nursing studies.[91] Giorgi's four steps of analysis are illustrated with examples from the participants in Paper III\Table 2.

Step 1: Sense of the whole

This first step of analysis aims for immersion in the participants' perceptions of the phenomenon and to gain a sense of the whole. This is achieved by reading each transcript several times as well as listening to the interviews.

The author transcribed the first three interviews verbatim to understand the process of transcription and to establish a template for transcription applied in this study, e.g. symbols to denote inaudible sounds, laughter, concurrent speech, and pauses. The template was established to ensure that all transcriptions followed the same conventions. The 14 interviews lasted 26.7 hours in total. The transcription process averaged 8.7 hours per 1 hour of interview and amounted to 232 hours in total. Due to the sheer volume of data that needed to be transcribed, a secretary transcribed the next 11 interviews. To ensure that all transcripts were as consistent and verbatim as possible, the author listened to the interviews while editing the secretary's transcripts based on the transcription template. The transcripts thus applied the same conventions regardless of whether the secretary or the author transcribed the recorded interviews.

Step 2: Meaning units

This step aims to determine each 'meaning unit' as it is expressed by participants. A 'meaning unit' is a natural expression by a person that can be seen as a complete entity in itself. We determined 2,068 meaning units across the interviews. An example of a meaning unit in the participant's own words can illustrate this step of analysis: 'Is she too tired to vacuum or cook dinner, or should I do it?'

Step 3: Thematizing

This step aims to condense the meaning units into increasingly general themes emerging from the interview data. The analysis is thus data driven from the bottom up. We rephrased the meaning units that are relevant to the research question into dominant themes. To continue the example from Step 2, we rephrased the meaning unit into the following theme: 'The participant worries about domestic chores and whether the parent is too tired to perform them.'

We synthesized the above theme into the dominant theme 'Worry', then into the subtheme 'Worry and guilt' and then into the essential theme 'Caring'. This process of condensing the meaning units relevant to the phenomenon was applied to all the interviews. Over the course of this process, eight subthemes and two essential themes emerged from the data.

Step 4: Essence of the phenomenon

This final step aims to synthesize the themes across all the interviews into a description of the studied phenomenon. The synthesis is the final result in Giorgi's phenomenological analysis method, in which each step and theme of analysis is data driven from the bottom up.[70] The synthesis is based on a rigorous analysis process during which participants' verbatim quotes are condensed into natural meaning units, themes, subthemes, essential themes, and finally the essence of the phenomenon. The essence of the phenomenon emerged as a result of the phenomenological condensation of themes into increasingly synthesized themes.[70,91]

Rigor

To claim scientific trustworthiness in a qualitative study, researchers must employ a systematic and rigorous process and thereby establish trustworthiness in the results.

Bracketing of our preconceptions

As detailed above, humans always bring their subjective first-person perspective into any experience. Although this is unavoidable, researchers should do their utmost to bracket and remain conscious of their preconceptions and not allow them to interfere with the study of a phenomenon.[90] We were conscious of our own preconceptions from clinical practice and literature, and we regularly discussed them in order to identify and thereby bracket them.

Validation

The author's understanding of the phenomenon was regularly validated during each interview by asking the participant to clarify, for example, 'Does this mean that…?'[73] The participant would then either respond affirmatively or provide an alternative description. This form of questioning seeks to validate the author's understanding of participants' experiences. This ensures the dependability of the subsequent analysis and the credibility of the results.[73]

Triangulation

One way to avoid the subjective bias of a single researcher is to use analyst triangulation, meaning that multiple researchers are involved and are thus able to discuss with and challenge each other's preconceptions, descriptions, analyses, and understandings.[68,73] Three researchers read the raw transcripts and continually discussed the analyses and the emerging results over the course of the interview study. Whenever we encountered diverging views, we discussed the meaning units, themes, and essence of the phenomenon until we reached unanimity.

Ethics

We obtained approval for the study from the Danish Data Protection Agency (no. 30–1141). The Regional Committee on Health Research Ethics stated that because the interview study contained no biomedical material, Danish regulations were not applicable for this study. Each participant was informed in writing and verbally about the study and given time to reconsider his or her participation, in accordance with the Declaration of Helsinki.[92] Participants were given contact information for a psychologist from the Danish MS Society in the event that difficult emotions arose following the interview.

To summarize the methods of Study III, we

- Used Giorgi's phenomenological method,[70] which is suitable and relevant to the research question
- Bracketed our preconceptions by discussing them openly several times
- Used investigator triangulation during the entire analysis process to avoid the bias of a single researcher
- Were systematic in data collection and analysis of data emerging from the interviews
- Based our analysis on regular participant validation to ensure dependability of the analysis and credibility of the results.

RESULTS

Paper I Educational achievements of children of parents with multiple sclerosis: a nationwide register-based cohort study

In the first register-based study, we compared the MS offspring cohort with the matched reference cohort regarding three educational outcomes. The included children were maximum 12 years old at the time of parental MS diagnosis regarding grades and educational level and maximum 18 years old regarding health-related education to allow the parental MS sufficient time to exert any possible influence on the educational outcomes of the children. Also, the youngest children included in the first two analyses were 15 years old. The baseline characteristics of the included children for each analysis are detailed in Figure 1 and Table 1 in Paper I.

Regarding the parental covariates, the median age of the MS parents was 27 years (range: 15–54) and 26 (range: 13–60) for the reference parents. The MS parents and the reference parents had similar educational levels in a Cochran-Armitage trend test (p=0.54).

Grade achieved in basic school

The MS offspring achieved a statistically significant higher grade point average (GPA) in the 9th class of basic school than the reference children (Table 3). In an unadjusted general linear model (GLM), the MS offspring achieved 6.55 GPA (95% CI 6.29–6.80) and reference cohort 5.98 GPA (95% CI 5.89–6.06).

This difference was observed for both sexes: MS offspring women versus reference women had a grading difference of 0.52 (95% CI 0.16–0.88; p=0.005), and the men had a difference of 0.61 (95% CI 0.25–0.97; p=0.0008). We adjusted the GLM for the two covariates of parental age at childbirth and the parental educational level, and the mean GPA continued to be significantly higher in the MS offspring cohort than in the reference cohort (estimate 0.46; standard error (SE) 0.12; 95% CI 0.22–0.69; p=0.0002). The sex of the MS parent had no significant influence on the MS offspring's GPA (χ^2=0.75; df=1; p=0.39).

Table 3 Grade achieved in basic school, probability of educational level above basic school, and probability of health-related education comparing children of an MS parent with reference children of parents without MS (cited from Paper I\Table 4)

Grade achieved in basic school[a]

	N	Mean	SD	95% CI	*p* value
Reference cohort	2372	5.98	2.12	5.89–6.06	
MS offspring	300	6.55	2.26	6.29–6.80	
Difference		0.57	2.14	0.31–0.83	0.0001

	Unadjusted GLM				Adjusted GLM[b]			
	Estimate[c]	SE	95% CI	*p* value	Estimate[c]	SE	95% CI	*p* value[b]
Reference cohort	0.00				0.00			
MS offspring	0.57	0.13	0.31–0.83	0.0001	0.46	0.12	0.22–0.69	0.0002

Age at attainment of highest educational level aged 15–58 in 2013

Reference cohort, median (range)	22 (13–56)
MS offspring, median (range)	22 (13–55)

Probability of education above basic school for cohorts aged 15–58 years in 2013

	Unadjusted OR[d]	95% CI	*p* value	Adjusted OR[d]	95% CI	*p* value[b]
Reference cohort	1.00			1.00		
MS offspring	1.03	0.93–1.15	0.58	1.04	0.98–1.10	0.20

Health-related education attained for cohorts aged 21–58 years in 2013

	Unadjusted OR[d]	95% CI	*p* value	Adjusted OR[d]	95% CI	*p* value[b]
Reference cohort	1.00			1.00		
MS offspring	1.21	1.00–1.45	0.05	1.10	1.00–1.21	0.06

CI confidence interval, *GLM* general linear model, *MS* multiple sclerosis, OR odds ratio, *SD* standard deviation, *SE* standard error.
[a] Unadjusted independent two-sample *t*-test
[b] Adjusted for parental age at childbirth and parental educational level
[c] Estimate denotes the difference between the cohorts' mean grade point average in 9th class in basic school
[d] Logistic regression.

Probability of education above basic school level

The MS offspring attained similar educational levels as the reference children (Table 3). This was true in an unadjusted logistic regression where 77.4% among the MS offspring and 76.8% of the reference children (OR 1.03; 95% CI 0.93–1.15; p=0.58) attained an education above basic school. The difference remained non-significant when adjusted for the two parental covariates (OR 1.04; 95% CI 0.98–1.10; p=0.20).

We also analyzed the dichotomized outcome in a sensitivity test including children from the two cohorts between 30 and 58 years in 2013 which confirmed the main finding of no significant difference in the probability of attaining an educational level above basic school (OR 1.00; 95% CI 0.94–1.06; p=0.99). When dividing the educational levels into four categories, a trend test also showed no difference (p=0.42). The same non-significant difference was found when we tested for a possible calendar year effect where we adjusted for the cohort's year of birth and the two parental covariates (OR 1.01; 95% CI 0.95–1.07; p=0.73).

When analyzing the cohorts in the GPA subgroup of 300 MS offspring and 2,372 reference people, there was no significant difference between them either (OR 0.98; 95% CI 0.87–1.11; p=0.78). The sex of the MS parent had no significant influence on the MS offspring's educational level (χ^2=0.08; df=1; p=0.78).

Probability of health-related education

The MS offspring tended toward attaining health-related educations 4.8% (135/2,695) compared with 4.0% (897/21,623)

reference people (OR 1.21; 95% CI 1.00–1.45; *p*=0.05) (Table 3). This trend continued when we adjusted for the two parental covariates of parental age at childbirth and parental educational level (OR 1.10; 95% CI 1.00–1.21; *p*=0.06). The difference originated solely from the 8.7% (119/1,248) MS offspring women compared with the 7.0% (759/10,130) reference women who attained health-related educations (χ^2=5.50; df=1; *p*=0.02). No significant difference was found when comparing the 1.1% (16/1,447) MS offspring men and the 1.2% (138/11,493) reference men who attained health-related educations (χ^2=0.10; df=1; *p*=0.76).

The sex of the MS parent had no significant influence on the MS offspring's probability of health-related educations (χ^2=0.14; df=1; *p*=0.71).

Paper II Employment, disability pension and income for children with parental multiple sclerosis

In the second register-based study, we compared the MS offspring with the matched reference cohort regarding the outcomes of employment or disability pension at ages 30, 40, or 50 and regarding income at a five-year interval of ages 45 to 49. The baseline characteristics of the included children for each analysis are detailed in Figure 1 and Table 1 in Paper II.

Regarding the parental covariates, the median age of the MS parents was 28 years (range: 15–54) and 26 (range: 14–60) for the reference parents. The MS parents and the reference parents had similar educational levels in a Cochran-Armitage trend test (*p*=0.15).

Regarding the children's highest educational level in a trend test, the levels were similar (*p*=0.44) (Paper II\Table 2).

Employment status

At age 30, 85.0% MS offspring were employed versus 87.2% reference children (Table 4). This was statistically significant both in the unadjusted logistic regression and when adjusted for parental covariates (OR 0.89; 95% CI 0.84–0.95; *p*=0.0003). There was no sex difference. At ages 40 and 50, the employment status was similar for the two cohorts.

Table 4 Results for employment and disability pension comparing children of an MS parent with matched reference children of parents without MS at age 30, 40 and 50 (cited from Paper II\Table 3)

	Unadjusted OR	95% CI	*p* value	Adjusted OR[a]	95% CI	*p* value[a]
Employment						
Age 30	0.83	0.74–0.94	0.003	0.89	0.84–0.95	0.0003
Age 40	1.05	0.90–1.23	0.55	0.99	0.92–1.08	0.87
Age 50	0.88	0.70–1.11	0.27	0.90	0.80–1.02	0.11
Disability pension						
Age 30	1.64	1.27–2.12	0.0001	1.31	1.15–1.50	<0.0001
Age 40	1.34	1.06–1.69	0.01	1.20	1.06–1.35	0.005
Age 50	1.15	0.85–1.56	0.37	1.13	0.97–1.33	0.13

CI confidence interval, *MS* multiple sclerosis, *OR* odds ratio.
[a] Logistic regression adjusted for parental age at childbirth and parental educational level.

Regarding the MS offspring, the offspring's age (younger than 13 years or between 13–18 years) at the time of the parent's MS diagnosis had no influence on employment status (OR 1.07; 95% CI 0.95–1.21; *p*=0.26) nor the MS parent's sex (OR 1.01; 95% CI 0.90–1.14; *p*=0.84) (Paper II\Supplementary Table 1).

Disability pension

Significantly more MS offspring received disability pension at age 30 (OR 1.31; 95% CI 1.15–1.50; *p*<0.0001) and at age 40 (OR 1.20; 95% CI 1.06–1.35; *p*=0.005) compared with the reference cohort (Table 4). At age 50, there was no difference between the two cohorts (OR 1.13; 95% CI 0.97–1.33, *p*=0.13).

At age 30, both men and women MS offspring received disability pension more often than reference children. At age 40, the difference originated from the MS offspring women as they received disability pension more often than reference women (OR 1.28; 95% CI 1.08–1.51; *p*=0.006). Regarding men, there was no significant difference between the MS offspring men and the reference men (OR 1.12; 95% CI 0.95–1.33; *p*=0.20).

The offspring's age at parent's MS diagnosis had no influence on the MS offspring's disability pension (OR 1.08; 95% CI 0.83–1.40; *p*=0.57). Neither did the sex of the MS parent (OR 1.06; 95% CI 0.83–1.36; *p*=0.64).

Annual personal income

The number of MS offspring with an income above DKK 250,000 (~ EUR 33,650) annually in gross personal income was lower (Table 5). The difference was statistically significant since 51.9% MS offspring compared with 55.6% reference cohort attained above DKK 250,000 (OR 0.91; 95% CI 0.84–0.99; p=0.04). There was no sex difference.

Table 5 Results for personal gross annual income corrected for inflation comparing children of an MS parent with matched reference children of parents without MS in the age interval 45–49 years (cited from Paper II\Table 4)

Income in DKK annually

	Mean[a]	SE	95% CI	*p* value
Reference cohort	300434	2814.2	294917 – 305951	
MS offspring	289127	6970.1	275439 – 302815	
Difference	-11307	8325.6	-27627– +5015	0.17

Probability of attaining above 250000 DKK ~ 33650 EUR annually in personal gross income[b]

	Unadjusted OR	95% CI	*p* value	Adjusted OR[c]	95% CI	*p* value[c]
Reference cohort	1.00			1.00		
MS offspring	0.86	0.73– 1.01	0.07	0.91	0.84– 0.99	0.04

Income difference

	Unadjusted general linear model				Adjusted[c] general linear model			
	Estimate[d]	SE	95% CI	*p* value	Estimate[d]	SE	95% CI	*p* value[c]
Reference cohort	0.00				0.00			
MS offspring	-11307	8325.6	-27627– +5015	0.17	-11164	8657.6	-28137– +5808	0.20

CI confidence interval, *DKK* Danish krone, *EUR* euro, *MS* multiple sclerosis, *OR* odds ratio, *SE* standard error.
[a] Independent two-sample *t*-test.
[b] Logistic regression.
[c] Adjusted for parental age at childbirth and parental educational level.
[d] Estimate denotes the difference between the cohorts' mean gross personal annual income in DKK.

However, when we analyzed the average annual income there was no statistically significant difference between the two cohorts in an adjusted GLM (estimated difference -11,164 DKK; a reduction of 3.8% for the MS offspring; 95% CI -28,137– +5,808; *p*=0.20).

Regarding the MS offspring, the offspring's age at parent's MS diagnosis had no influence on the MS offspring's likelihood of an income above DKK 250,000 (OR 0.96; 95% CI 0.81–1.15; *p*=0.67). Neither did the sex of the MS parent (OR 0.95; 95% CI 0.80–1.13; *p*=0.54).

Paper III Striving for balance between caring and restraint. Young adults' experiences with parental multiple sclerosis

In the interview study, we explored and described how young adults between 18 and 25 years experienced growing up with a parent with MS and the continued influence of parental MS in their daily lives. The baseline characteristics of the included 14 participants are detailed in Table 1 in Paper III.

Essence of the phenomenon

We found the essence of the phenomenon of having a parent with MS to be 'Striving for balance between caring and restraint'. The essence emerged from two essential themes 'Caring' and 'Restraint' which are equally important aspects of growing up with parental MS. When caring and restraint were synthesized into the essence of the phenomenon, we found that the young adults had experiences of striving to achieve a balance between caring for their parent with MS and showing restraint in their close relationships with the parents with and without MS, friends, and partners. The essential themes each comprised four subthemes based on the participants' experiences with a parent with MS (Figure 2).

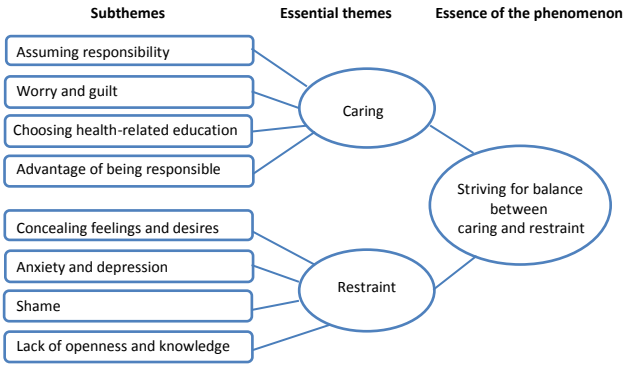

Figure 2 Overview of subthemes, essential themes and essence of the phenomenon (cited from Paper III\Figure 1).

The themes are detailed below with examples of participants' verbatims cited from Paper III to illuminate each theme.

Essential theme: Caring

The 'Caring' theme pertains to the participants' actions and emotions in relation to caring. This theme comprises four subthemes: Assuming responsibility; worry and guilt; choosing health-related educations; advantage of being responsible. To be caring and to take care of was a means for the participants to manage their affective responses to their parents' sadness, physical and cognitive disabilities or fatigue.

> *I've often just taken over if I could see it was too much for her. If it was too exhausting to make dinner, I've taken over and made dinner (cited from Paper III).*

Assuming responsibility

All the participants had helped with household chores, and some had also helped with farm-related chores, gardening, pets, administrative tasks or dealing with authorities. Most participants did not regard the help they provided as burdensome. A few participants had a very heavy workload at home but they gradually assumed a higher responsibility for them and thus the chores were slowly incorporated. It was only in the participant's young adulthood and growing maturity that the chores became visible upon reflection.

> *It wasn't a real choice whether or not to help. I felt it as an inner drive to help. I had to help her in some way instead of just being passive (cited from Paper III).*

Worry and guilt

The participants often experienced a general sense of worry related to the parent with MS, e.g. has she or he fallen, is exhausted or has taken the medicine?

> *I thought about it all the time. Oh, no, is she lying dead at home, has she fallen and hurt herself, has she become paralyzed? (cited from Paper III)*

These worries were very time-consuming and energy-depleting. Related to the participants' high sense of responsibility, most of them occasionally experienced guilt about not helping their parents more. Some of them were reluctant to move out of the childhood home or to another city far away because they experienced guilt about leaving the parent with MS.

Choosing health-related educations

Half of the participants were enrolled in a health-related education in nursing, physiotherapy, psychology, medicine or public health, and they mostly attributed their educational choice to parental MS.

> *I think the greatest impact [from growing up with parental MS] has been in relation to education. I've been with him many times to the hospital and experienced it from the user's perspective and I thought it would be interesting to study physiotherapy. I've seen the health care system from many angles and I think it's influenced my choice of education (cited from Paper III).*

Advantage of being responsible

Some of the participants found advantages to acquiring the characteristic of being responsible as it aided them in organizing their educational and private lives. Their classmates and friends could rely on the responsible participant to know e.g. when homework was due, stay sober at parties so they could drive or be responsible for paying the collective rent for the room mates. One of the participants was given the full responsibility of a little gift shop when she worked there in her spare time or vacations. Another participant was given responsibility of several staff members because she handled both the administrative operations and the human resources well.

> *I've always been very structured as far as I can remember. I like to be on top of my appointments and tasks and write them in my planner. I like to know what I'm doing next year and what's coming up. But my mom is the same way and with a chronically ill family member you have to plan a lot and be structured. Things revolve around my dad because he needs to live with a structured routine (cited from Paper III).*

Essential theme: Restraint

The 'Restraint' theme pertains to the participants' difficulties in expressing their feelings to protect their parents from knowing about the children's sadness, lack of knowledge, or troubles. This theme comprises four subthemes: Concealing feelings and de-

sires; anxiety and depression; shame; lack of openness and knowledge. The participants also showed restraint to avoid burdening their parent with MS, and most of the participants continued this pattern of restraint toward their parent without MS, friends, and partners.

> *One of the reasons I didn't want to burden my parents with my own problems was that it [the mother's MS] also took its toll on my dad. He worked full time and had to see to it that we got to school and he also had to bring us for visits at the hospital when she was admitted. He was pretty tired in those periods and so was she. In fact, he's often had to help her with bathing, dressing and household chores and then you don't want to add to his work load with your own questions or concerns (cited from Paper III).*

Concealing feelings and desires

The participants concealed their feelings of sadness or anger or by keeping desires or problems inside themselves to protect their parents from being hurt or burdened.

> *I had to adapt in many situations. I learned that I couldn't get what I wanted in some instances. I felt I had to be optimistic and exhibit a positive and happy attitude so my parents didn't need to worry about me too (cited from Paper III).*

According to many participants, they had been so accustomed to being caring toward their parent with MS that this could sometimes turn negative because they often found it difficult to express their wishes and insist on following them. They often wished they were better at asserting themselves because they mostly felt it was easier to give in to the wishes of friends and partners.

> *Instead of saying what I think, I just let them [friends and partners] decide because then they won't be upset if I make a different decision. I think I've been so used to be caring for my mom that it's just become part of me: I always take others' feelings into account (cited from Paper III).*

Anxiety and depression

Two of the participants had suffered from anxiety, and two had suffered from both anxiety and depression during their basic school years; all four had made full recoveries after consultations with a psychologist.

> *I closed myself off if there was something I was sad about. Then I wouldn't tell her because I was afraid of upsetting her. She was worse off, and I shouldn't burden her with even more for her to keep track of. She didn't need to know I was sad (cited from Paper III).*

Shame

Some of the participants had experienced shame caused by visible physical disabilities e.g. if the parent had a slow and unsteady gait or used a wheelchair. Shame was also experienced if the parent had cognitive disabilities which made the parent overstep social norms of what and how you say something to other people.

> *It's embarrassing, and it's difficult. I think it's hard to swallow. It's one thing to say, 'OK, it's the disease,' and to understand that, but it feels so surreal when you're in the moment because it's such a complete breach of the usual manners (cited from Paper III).*

Lack of openness and knowledge

All the participants wished there had been more information about MS geared toward their age group, more inclusion of them at hospital visits with treating neurologists, nurses and other health care professionals and more knowledge in the society at large about MS and its symptoms. Most of them also wished for more openness within their own family about MS and its influence on the parent with MS and the rest of the family. In fact, some of the parents with MS had only told the children of the disease initially but then discouraged them from talking about it and this was a major stressor for the children.

> *The most difficult aspect of my dad getting sclerosis was that he was in denial about it. And this continued for many years so it was impossible to be a part of it. Especially as a young child where you don't know anything about the disease then you create all sorts of fantasies about how he's doing and what'll happen. And because he was in denial about it and didn't talk about it, we couldn't ask questions and get our fantasies confirmed or rejected. It was the absolute worst (cited from Paper III).*

DISCUSSION

The general objective of this PhD thesis was to investigate whether parental MS has an influence on children at different stages of the children's life course. We investigated this in Studies I–III, each with specific objectives, using either a register-based method or an interview method.

In Papers I–III, we have discussed the findings specific to each paper. In this chapter of the thesis, the findings from all three papers will be discussed in relation to one another and to the literature in order to gain insights not available from a single study.

Beneficial and neutral influence from parental MS

We found beneficial and neutral influence from parental MS on some of the outcomes. These will be elaborated upon below.

Higher grade point average in basic school

Parental MS is beneficially associated with GPA in basic school since the MS offspring achieved statistically significant higher grades. There may be several explanations for the higher GPA. One is that the children were encouraged by the parent with MS to perform well in school and helped by family members with homework.[45] The other is that the children realized they had to attain a good education to escape the heavy caregiving burden at home.[65] An additional explanation could be that because the children were highly responsible and caring and did not wish to burden or disappoint them, they performed as the parents expected, as shown in the interview study.

Only one study has been conducted previously that investigated grades among children with parental chronic illness, reporting statistically significant lower grades compared with control children.[35] There were several methodological differences between this Dutch study and our own, which might explain the divergent results regarding grades. These differences are elaborated below.

First, the Dutch study applied questionnaires instead of nationwide register-based data. There are several limitations to questionnaires in general, e.g. response rate and recall bias. Our register-based studies do not suffer those two limitations because our data are reported on a mandatory basis from one institution to another. Furthermore, our study's validity is high because we used nationwide data from the entire population.

Second, the children included in the Dutch study had parents with various chronic illnesses, and only a few of the parents had MS, whereas we focused on parental MS. The different symptoms of other chronic parental illnesses might influence the offspring differently than do the symptoms of MS.

Third, their children were 10–20 years old, so their children spanned 11 years whereas our children were all around 15 years old. This makes their age range wide and heterogeneous and thus more difficult to compare. In contrast, the age range in our study is narrow and more homogenous and therefore has a higher statistical power.

Fourth, the Dutch children's self-reported grades covered different educational levels and educations. In contrast, we calculated the MS offspring's grade point average exclusively on the basis of their final exams in the 9th class of basic school. The same limitations and strengths apply as for the previous point regarding age.

Fifth, the Dutch researchers compared 161 adolescents of chronically ill parents with 112 adolescents of 'healthy' parents, whereas we compared 300 MS offspring with 2,372 reference children. This provides our study with a high power because we compared each MS offspring child with eight reference children matched by sex and year of birth.

Caring, both privately and professionally

The interview participants were all caring, both in the sense of an emotion or characteristic 'to care about' and in the sense of an action 'to take care of'.[93] The beneficial characteristic of 'being caring' made the participants sensitive to the needs and well-being of others around them, such as friends, family, partners, classmates, colleagues, and even strangers. Participants were often aware of whether others around them were sad and used this skill both privately and at work to help family members, friends, or colleagues.

The caring characteristic was also found to have an influence professionally since MS offspring women tended toward attaining health-related educations in Study I, and half of our interview participants were enrolled in health-related educations in Study III. Our findings confirm two previous interview studies with former young caregivers of family members of various chronic illnesses, including a few with MS, in which almost half of the participants had chosen to work in a caring profession.[45,65] Our interview participants expressed a general curiosity toward biology, epide-
miology, and the complex etiology of illness. Some participants wished to conduct research in MS or to care professionally for persons with MS. Those who had chosen health-related educations attributed this to parental MS.

Advantage of being responsible

Some of the interviewed participants saw advantages in assuming responsibility since others often relied upon them. Most participants were structured and liked to plan and keep track of tasks. This provided them with a good overview of their obligations and yielded opportunities in their working life, e.g. higher work responsibility than their chronological age warranted, supervision of several staff members, and administrative obligations. Some studies have found similar advantages of being responsible,[45,54] but other studies have found the responsibilities related to caretaking of a chronically ill parent exhausting and stressful.[43,44,54,94]

Similar levels of the highest attained education

The parents with MS compared with the reference parents as well as the MS offspring compared with the reference children all had similar levels of highest attained education, as shown in Study I. This outcome has not previously been investigated, and our findings that both the MS parents and the MS offspring attain similar educational levels to reference cohorts are thus original.

Even when we limit an analysis to the MS offspring who had a recorded GPA and compared them with the reference cohort with a recorded GPA, the two cohorts attained similar educational levels (Paper I). A possible explanation could be that many of the children with a higher GPA were still too young to have attained their highest level of education at follow-up in 2013 because their median year of birth was 1990. Their young age might thus partly explain why we found similar levels of education. Or perhaps the MS offspring's higher GPA will not continue and be reflected in statistically significant higher educational levels.

Similar mean income

According to our results in Study II, the MS offspring attain similar mean income to the reference children when income is analyzed as a continuous variable. This outcome has not been investigated before, and the comparison of the income is thus original. Generally, income is associated with employment status, which will be discussed in the next section.

Contradictory results regarding education and employment?

Some of the results regarding education and employment seem to contradict each other since the MS offspring achieve better grades in basic school but are less employed at age 30 and more often receive disability pension at ages 30 and 40. In line with the lower rate of employment, the MS offspring have a lower probability of attaining an income above DKK 250,000 annually, although their mean income was similar. Thus, regarding education, MS offspring attain similar educational levels and better grades than do reference children, but regarding employment MS offspring have worse attainments at ages 30 and 40. There is no one single explanation for the adverse association between parental MS and MS offspring's employment status. Instead, four explanations are elaborated upon below and should be regarded as contributory pieces of the puzzle.

Caregiver role

One possible explanation for the apparent contradiction in the results based on register data is provided by the interview study: The young adults were caring and took care of their parent with MS while also showing restraint by concealing feelings and desires that they regarded as burdensome to the parents. Many of the young adults continued this pattern of being caring and showing restraint toward the parent without MS, friends, and partners. This pattern of caring and restraint might explain the background for the higher grades in basic school because the children chose to stay more at home with the parent with MS to take care of him

or her and then utilized this extra time at home to study diligently, which can be seen as another form of assuming responsibility and as an advantage of being responsible. The MS offspring in the register-based studies were, however, primarily adults, so their parents with MS were older, and their MS symptoms had likely worsened, thereby requiring more physical, cognitive, and emotional assistance.[95]

In Paper III, we found that some of the young adults had already had experiences of doing household chores and helping with ADL during their childhood with parental MS, because some of the parents had considerable disabilities already when the child was at an early age or had rapidly worsening disabilities during the offspring's childhood. If the children were already performing household chores, gardening, looking after siblings, and providing cognitive and emotional support and general help to the parent with MS during childhood, this caregiver role might become even more time-consuming as the parent grows older, and the symptoms of chronic illness worsen in severity.[96]

Striving for balance between caregiving and one's own needs

The essence of the phenomenon of having a parent with MS was to strive for balance between caring for the parent with MS and showing restraint, as the interview participants often concealed their own wishes and desires if they deemed these to be distressing or opposed to those of other people. This finding was confirmed in another study focusing on adolescents with parental MS.[94]

The participants loved their parents, and when a parent has a chronic illness and needs help (for example, physical or emotional assistance, performing household chores, and administrative tasks), the participants developed a high sense of responsibility and capacity for helping, i.e. caring.[93] When we care about another person, we also involve ourselves in their life and this provides meaning and makes us feel connected to them.[93] This caring attitude has also been found in previous studies (Appendices\Table 1).

As young children or adolescents, many participants had great difficulty not helping their parents either directly with a chore or indirectly by concealing feelings or desires that they deemed burdensome. With growing maturity came the ability to reflect and make a conscious decision, but it remained difficult for participants to decide not to help or support the parent even with small, mundane tasks. These internal conflicts between helping and not helping could lead to feelings of guilt, which has also been found in other studies.[43,44,54] It is important to understand that the multitude of needs of the parent with MS are often impossible or very difficult for children not to heed. This conflict between caring for a parent and taking care of one's own needs likely grows as the parent's needs increase and as the adult children acquire the additional obligations of adult life.

The interview finding of being caring and showing restraint might thus partly explain the register finding of lower employment rate at age 30 and that more MS offspring receive disability pension at ages 30 and 40. The parent with MS is about 27 years older than the MS offspring, so when the MS offspring are 30 or 40 years old, the parent with MS possibly requires a substantial amount of care and support from the children. The increasing parental needs for caring in later years might add a heavier burden on adult children. Because they were already accustomed to assuming responsibility during childhood, they might continue their caregiving as adults. The MS offspring might simultaneously have their own children, partner, and other obligations that could lead to the adverse association of parental MS regarding employment and disability pension.

Worsening of MS disability during parents' later years

The oldest MS offspring in the register-based studies (the majority were born between 1955–1983) have parents with MS who were unable to receive or who received disease modifying treatments (DMT) for their MS very late because the first DMT was available in Denmark in 1996 (interferon-β).[97] Worsening of MS disability occurs earlier in untreated MS patients.[98] Based on these circumstances, the parents' MS disabilities were likely increasingly severe and thereby intensified their need for help as they grew older.[99] These circumstances contribute to explaining the adverse association between parental MS and MS offspring's employment and disability pension.

Emotional distress

Another contributory explanation for the seemingly contradictory results is emotional distress. In the interview study, two participants had suffered from anxiety during their basic school years, and two had suffered from both anxiety and depression. These findings of anxiety and depression confirm previous studies.[43,48,52,94] In another study, some of the adult participants expressed the need for years of counseling and various psychological and emotional needs caused by their caregiving as children.[65]

Our interview participants often worried about their parent with MS, which could be both fruitless and time-consuming. Participants expressed worry about hypothetical adverse situations, e.g. worrying during the summer whether the parent might fall half a year later in winter due to snow and ice. Constant worries of this kind would occupy some participants' thoughts and energy, disrupting their focus and diminishing their time and energy for other activities. This has also been reported in other studies.[54,65,94]

All the aforementioned explanations contribute to a better understanding of the complexity of our register-based studies. Results from our interview study and the literature might supplement the explanation of how parental MS can be beneficial in terms of GPA while having adverse effects on employment-related attainments.

Methodological considerations — revisited

Limitations

Although parental employment status and income might impact children, we were unable to adjust for these two covariates. Until the onset of MS, people who are later diagnosed with MS attain the same levels of education (Paper I\Table 3) and employment status as does the background population.[29] Any differences thus occur after onset of MS. In addition, the Danish registers regarding employment and income were established in 1981. Because the median year of birth of the MS parents was 1942, we were unable to access this information for many of the parents.

We were unable to adjust the statistical analyses for clinical characteristics of the parents' MS (e.g. MS course, disease severity, or relapse) as this information was unavailable for specific years. Previous studies have divergent findings regarding the association between parental disability, worsening of MS, coping and depres-

sion, and children's adjustment. One study has found association with all four;[100] another study has only found association with parental coping and depression but not with MS disability or worsening;[52] and yet another study has found no association with parental severity of disability, depression, or coping.[51]

In the interview study, 12 women and 2 men participated and the result might have been different had more men volunteered. Participants might have been particularly likely to volunteer if they were well-adjusted or, in contrast, if they wished to disclose challenging experiences.

Strengths

We investigated the general research question using two very different methods: a quantitative register-based method and a qualitative interview method. The large number of randomly included people provided our register-based data with high validity and statistical power. The 14 interviews provided deep reflections and sensitive accounts concerning the complex phenomenon of having a parent with MS. The essence of the phenomenon emerged as a new insight that young adults with parental MS strive to find a balance between caring and restraint. This insight contributed to understanding the apparently contradictory results in the two register-based studies with regard to beneficial influence from parental MS on grades and adverse influence on employment. We thus find that the methods support and complement each other in our investigation into the PhD thesis' general research objective of ascertaining whether parental MS influences children at different stages over the children's life course.

A contribution to the strength of the study is that, in Denmark, people have free access to education from basic school to university. Students receive an allowance and the possibility of very favorable loans from the state through The Danish students' Grants and Loans Scheme (SU).[87] SU and free access to education are offered to students to alleviate dependence on parents' income so that students can attain an education regardless of their parental socioeconomic circumstances. The only restriction is that the most sought after and expensive educations have a minimum GPA level for admittance.

Another strength is that, according to OECD, Denmark is among the most equal societies in the world in terms of the gap between high and low earners.[80,101] The Danish welfare system is dependent on high taxes from private income and consumption, which is redistributed into free education; health services; infrastructure; and support for single parents, the unemployed, and the disabled — e.g. financial help, disability aids, household help, and child care support.[102,103] The Danish welfare system plays a huge part in our reasoning that, if there are differences between the children of parents with MS compared to children of parents without MS in Denmark, then there will likely be even greater differences in other countries where health services and education are more dependent on parental socioeconomic circumstances.

An additional strength is the many population-based nationwide registers covering nearly all areas of life in Denmark, which are linked by the unique personal identification number that all Danes are assigned at birth or immigration.[74,104,105] Other studies applying a cohort design are often limited to a population belonging to a particular hospital or a geographical area whereas the Danish registers are nationwide as well as population-based.

In the interview study, we systematically and rigorously collected and analyzed data. Participants regularly validated concepts during the interviews, which further strengthened the study alongside the detailed interview data.[73] We bracketed our preconceptions by explicitly acknowledging them. To prevent the perspective of a single analyst from taking precedence,[68] we triangulated our analyses through regular discussions. Participants originated from all five regions of Denmark and from varied sociodemographic backgrounds.

CONCLUSIONS

The main conclusions of the PhD thesis are based on the three papers:

I. Educational achievements of MS offspring in a register-based cohort study
   - Higher grade point average in basic school
   - Similar level of highest education attained
   - Trend toward more MS offspring women attaining health-related educations.

II. Employment, disability pension, and income of MS offspring in a register-based cohort study
   - At age 30, MS offspring less often had employment
   - At ages 30 and 40, MS offspring more often received disability pension
   - At the five-year interval of ages 45–49, MS offspring
     - Had a lower probability of attaining a personal gross income above DKK 250,000
     - Attained a mean income similar to that of the reference cohort.

III. Experiences of having a parent with MS in a phenomenological interview study
   - Essence of the phenomenon: Striving for balance between caring and restraint
     - Caring
       - Assuming responsibility
       - Worry and guilt
       - Choosing health-related educations
       - Advantage of being responsible
     - Restraint
       - Concealing feelings and desires
       - Anxiety and depression
       - Shame
       - Lack of openness and knowledge.

Based on the results from our three studies, we find that parental MS affected children both beneficially and adversely. They were beneficially influenced in terms of grades in basic school, being caring, and being responsible. They were adversely influenced in terms of employment, income level, and emotional restraint in close relationships.

The use of the Danish nationwide registers is a powerful method for investigating long-term influence of parental MS. We could include the whole population of persons with MS over the course of 37 years (onset of MS between 1950–1986) and their children and compare them with parents and children of the background population. The in-depth interview study with young adults provided detailed accounts of growing up with parental MS. By applying two divergent methods, we gained insights across the

three underlying studies that we could not have obtained through one of the methods alone. This methodological approach thus strengthened the PhD work.

My PhD thesis shows that parental MS can affect children for decades because it has long-term influence on children's life course, both socioeconomically and emotionally.

FUTURE PERSPECTIVES

Children are influenced far into their adulthood by parental MS in important aspects of life such as grades, employment, income level, and emotional relationships. The effect of parental MS is multifactorial with long-term impacts and is thus difficult to isolate and investigate.

Previous studies have primarily focused on young children and adolescents. We need more studies into this young age group to investigate whether there are risk factors that we can prevent or mitigate.

Future research could benefit from more studies into the long-term influence from parental MS on children because millions of children worldwide grow up with a parent with MS, and current knowledge about their adult life course is scarce.

The youngest children of an MS parent in our study achieved significantly higher grades in basic school than did children of parents without MS, but as their median year of birth was 1990, many of these children had not yet attained their highest educational level at follow-up in 2013. We therefore propose that a similar study be undertaken in several years to test whether the children's higher grades are reflected in a higher educational level.

The MS offspring cohort achieved similar levels of highest education compared with the reference cohort (Study I), but their employment status was lower at age 30, and they more often attained disability pension at ages 30 and 40 (Study II). This difference in employment status requires investigation and could benefit from

a) An interview study to elucidate various explanations and then, on the basis of the findings from the interview study,
b) A nationwide questionnaire study with MS offspring as the persons of interest compared with reference persons from the background population.

We also need exploratory interview studies focusing on adults to provide insight into the long-term effects of parental MS on partnership, children, education, employment, physical and psychological health, and obligations.

Implications for clinical practice

Health care professionals can support the person with MS, children, partner, and other family members by:

- Encouraging openness and providing knowledge about the chronic illness within the family
- Referring to relevant help, e.g. the MS Society, support groups, and psychological help
- Inviting family members to participate in health care visits to gain knowledge and to ask questions
- Raise parental awareness of the beneficial and adverse effects of parental MS on children.

APPENDICES

Figure 1 NVivo 10 screenshot

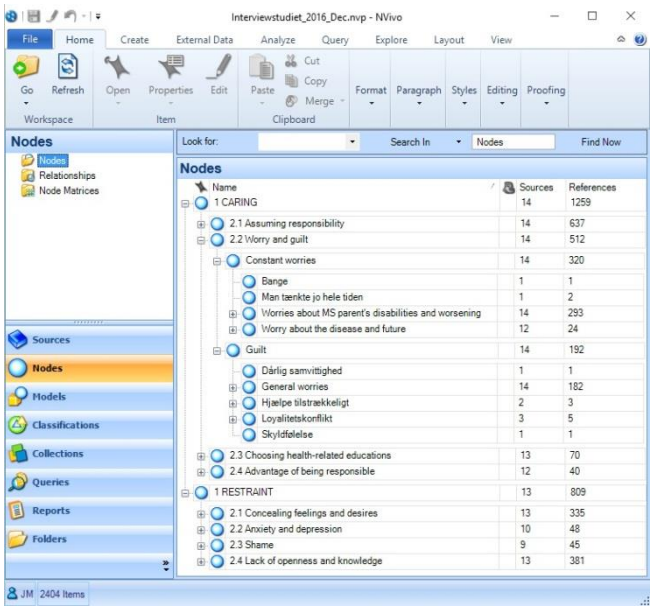

Table 1 Overview of previous studies

Quantitative studies

Sample (age range of children)	Key findings	Country	Ref Year
60 children of MS parents/ 221 children of parents without MS (7–16 years)	Children of an MS parent scored higher in: body concern, dysphoria, hostility, constraint in interpersonal relations and dependency longings. Boys of an MS parent were "reacting with somewhat greater body concern, dysphoria, and aggressive hostility than girls, girls intensifying patterns of compliant overcontrol" (Arnaud 1959, p. 20).[106]	USA	Arnaud [106] 1959
124 children of MS parents/ 60 controls (7–11 years)	Body image scores were similar between groups. Girls with MS mothers tended to show greater body image distortion than girls with MS fathers or boys with MS mothers.	USA	Olgas[58] 1974
33 families with a parent with MS/ 33 control families without MS (12–18 years)	MS families scored higher on the conflict and lower on family cohesion and intellectual-cultural orientation subscales.	Canada	Peters [107] 1985
31 girls of mothers with MS/ 34 girls of mothers without MS (8–12 years)	No differences: Similar interactions and receptive, directive and dissuasive behaviors used by the mothers with and without MS and their daughters during a work task and a play task.	USA	Crist[59] 1993

Control/comparison child of parents without MS; *MS* multiple sclerosis.

Table 1 – *continued*

Quantitative studies

Sample (age range of children)	Key findings	Country	Ref Year
174 children of MS parents/ background population 'norms' (7–17 years)	26% of the children of an MS parent were 'at risk' for a mental health problem compared with the background population of 12%–20%.	USA	Brandt [108] 1998
48 children of MS parents/no comparison group (4–16)	Children of an MS parent experienced more peer problems, more distress and difficulties in managing their lives.	Australia	De Judicibus [61] 2004
56 children of MS parents/ 156 controls (10–18 years)	Children of an MS parent reported more intense emotions in all aspects examined than controls. They had a greater degree of obligation, responsibility and concern for their parents, they worried about parent's inability to perform household tasks, and they hid their personal problems to avoid burdening their parents.	Israel	Yahav[46] 2005
56 children of MS parents/ 64 controls (4–17 years)	Children of an MS parent, especially children of mothers with MS, had more emotional and behavioral problems. Maternal depression and family dysfunction were associated with children's problems. Family dysfunction predicted children's general and externalizing problems. The MS mother's impairment severity predicted children's internalizing problems.	Greece	Diareme [62] 2006
48 children of MS parents/ 145 controls (10–25 years)	Children of an MS parent showed lower adjustment, life satisfaction, positive affect, higher somatization, and they had more caregiving responsibilities. Better adjustment for children of an MS parent was related to higher levels of social support, lower stress appraisals, greater reliance on approach coping strategies (problem solving, seeking support and acceptance) and less reliance on avoidant coping (wishful thinking and denial).	Australia	Pakenham[47] 2006
192 children of an MS parent, 144 parents with MS, 109 partners without MS/no comparison group (4–17)	Children with depressed parents were associated with high risk of mental health problems, especially internalizing disorders. Recommendation: The mental health of both the children and the parents should be addressed.	Switzerland Greece Germany	Steck [109] 2007
56 children of MS parents/ 156 controls (10–18 years)	Children of an MS parent reported a higher degree of depression, anxiety and separation anxiety than controls. Recommendation: Therapeutic intervention for all family members.	Israel	Yahav [48] 2007
56 children of an MS parent, 56 parents with MS, 56 partners without MS/ no comparison group (4–17 years)	Children with 'partial infomation' about parental MS scored higher in social difficulties, social problems, internalizing behaviors and total problems than children with 'total disclosure' or 'no information' about the parent's MS.	Greece	Paliokosta[64] 2009
Time 1, baseline: 127 children of an MS parent, 85 parents with MS in 85 families *Time 2, 12 months:* 90 children of an MS parent, 70 parents with MS/no comparison group (10–20 years)	Parental depression affects family functioning, and this was associated with lower youth adjustment and physical and mental health.	Australia	Pakenkenham[110] 2012
Time 1, baseline: 130 children of an MS parent, 85 parents with MS, 55 partners without MS in 88 families *Time 2, 12 months later:* 91 children of an MS parent, 71 parents with MS, 48 partners without MS/ no comparison group (10–20 years)	Children who had higher levels of instrumental care and social-emotional care at time 1 were associated with poorer adjustment at time 2. There were beneficial effects of higher personal-emotional care on adjustment. *Time 2:* Higher caregiving responsibilities were associated with lower life satisfaction, higher somatization and total difficulties for the children.	Australia	Pakenkenham[53] 2012
126 children of MS parents/ 126 controls (8–20 years)	Children of an MS parent did not differ significantly from controls in somatization, health, prosocial behavior, behavioral-social difficulties, caregiving, attachment and family functioning. Children of an MS parent reported lower peer relationship problems than controls.	Australia	Pakenkenham[111] 2013

Table 1 – *continued*

Quantitative studies

Sample (age range of children)	Key findings	Country	Ref year
Time 1, baseline: 104 children of MS parents *Time 2, 6 months later:* 62 children of MS parents/ no comparison group (12–19 years)	Children's perceptions of parental MS rather than disease severity were associated with their psychosocial well-being 6 months later. Stronger beliefs that MS has negative consequences and is chronic and unpredictable were associated with worse psychosocial adjustment.	UK	Bogosian[112] 2013
783 children and their parent with MS/2988 children and their parents without MS (5 years)	MS in mothers, not fathers, was associated with lower rates of developmental vulnerability, especially regarding social development. Presence of mental and physical comorbidity and greater disability in mothers with MS were associated with higher risk of developmental vulnerability in children.	Canada	Razaz[100] 2015
153 children of MS parents/ 876 children of parents without MS (5 years)	Children of an MS parent scored similar to the comparison children on early childhood developmental outcomes. However, children of parents with mental health morbidity and longer duration of exposure to parental MS tended toward a higher risk of early childhood developmental vulnerability than comparison children.	Canada	Razaz[60] 2015
Time 1, baseline: 75 children of an MS parent, 56 parents with MS, 40 partners without MS *Time 2, 6 months later:* 62 children of an MS parent, 48 parents with MS, 33 partners without MS/ no comparison group (12–19 years)	Higher depression and expressed emotion scores of parents with MS were correlated with their children's psychological difficulties. There was no correlation with the severity, duration or type of MS on adolescents' adjustment neither at baseline nor follow-up.	UK	Bogosian[52] 2016
1028 children of MS parents/ 4010 children of parents without MS (4–18 years)	Children of mothers with MS had higher rates of mood and anxiety disorders than children of mothers without MS. There was no association between fathers with MS and mental health morbidity and their children's mood or anxiety disorders.	Canada	Razaz[113] 2016
360 children and their MS parent/ 1207 children and their parent without MS (4–17 years)	Parental MS was associated with a higher risk of peripartum depression (especially among fathers with MS vs fathers without MS) and increased the risk of psychiatric disorders in children. Children of MS parents had a higher rate of psychiatric disorders than the comparison children.	Canada	Razaz[114] 2016

Mixed method study

Sample (age range of children)	Key findings	Country	Ref year
20 children of an MS parent at a 6–day camp, questionnaires at pre- and post-intervention and at 3–month follow-up; 14 parents with MS/no comparison group (9–14 years)	After the camp-intervention, children reported significant decreases in distress, stress, caregiving compulsion and restriction in activity; and children reported increased social support and knowledge about MS. Parents reported an increase in the children's knowledge about MS at follow-up.	Australia	Coles[115] 2007

Qualitative studies

Sample (age range of children)	Key findings	Country	Ref year
32 children of MS parents/no comparison group (6–17 years)	Positive factors were a good quality of life. Negative factors were little knowledge about MS, feelings of fear, anger and sadness.	Canada	Kikuchi[56] 1987
22 children of MS parents/ no comparison group (not stated)	Positive factors were higher personal competence, hopefulness and spirituality. Negative factors originated more from society's norms and parent's unemployment than MS.	Canada	Blackford[57] 1999
21 children of MS parents/no comparison group (7–14 years)	Children lacked knowledge about MS disease, possible worsening or factors contributing to worsening but could accurately describe the physical and emotional state of their MS parent.	USA	Cross[116] 1999

Table 1 – *continued*

Qualitative studies

Sample (age range of children)	Key findings	Country	Ref Year
87 children of an MS parent, parent with MS and partners without MS in 52 families/no comparison group (3–26 years)	Daughters cope better than sons. Only the daughter's coping was affected by age and parent's disease variables. Coping in parents without MS was correlated with the children's coping and even more with the same-sex children and parents without MS. Daughters and mothers without MS coped better with the MS father's disability than sons and fathers without MS.	Switzerland	Steck [117] 2001
41 children of MS parents/ compared with previously determined coping ability of child (6–18 years)	Half (22 of 41) of the children were estimated to need psychotherapy. This was related to the children's inability to cope with the parent's MS. Depression, single parenthood or emotional inadequacy of the parent with MS adversely affected the children but this could be mediated by the children's parent without MS if their relationship was of a high quality.	Switzerland	Steck [118] 2005
72 children of an MS parent, 44 parents with MS, 36 partners without MS/no comparison group (3–26 years)	Neither parental severity of disability, depression nor coping predicted the coping of the children or the partner without MS.	Switzerland	Ehrensperger[51] 2008
8 children of MS parents/ no comparison group (7–14 years)	Positive factors were pride in caretaking skills. Negative factors were too many responsibilities that limited the children's participation in education and leisure, conflicting emotions, worries, anxiety and isolation. Helpful factors were engaging in age-appropriate activities, time for friends and leisure, sharing household tasks and caretaking, confiding in adults and friends and sharing emotions.	Australia	Turpin [54] 2008
15 children of MS parents/ no comparison group (13–18)	Positive factors were feeling more empathetic and grown-up. Negative factors were family tension, less time with friends and worries about the future.	UK	Bogosian[44] 2011
5 children of an MS parent – 35 siblings, spouses, parents or friends/no comparison group (not stated)	The 40 interviewees either rejected, embraced, enforced or absorbed the identity of carer. Self-identification as a carer relate to expectations about whether one should assume a caring role.	UK	Hughes [119] 2013
11 children of a single parent with MS/no comparison group ('young adults')	The children felt silent, invisible and unacknowledged as caregivers with limited professional support. Recommendation: Health care professionals should provide information, support and guidance for young carers.	Iceland	Bjorgvinsdottir[43] 2014
9 children of an MS parent, 9 parents with MS, 5 partners without MS/no comparison group (12–23 years)	Children, parents with MS and partners all stressed the continual need for information about MS from diagnosis and onwards adjusted to the child's maturity level. Openness in the family about MS and encouragement to ask questions and talk about it was beneficial.	Sweden	Nilsagård[120] 2015
9 children of an MS parent, 9 parents with MS, 5 partners without MS/no comparison group (12–23 years)	The children worried about the health of the parent with MS, and children and partners had difficulties understanding and coping with the MS parent's fatigue, dysfunctional cognition and depression. Recommendation: To recognize the family members' need for information and coping to aid family functioning and adjustment.	Sweden	Boström[50] 2016
15 children of MS parents/ no comparison group (12–18 years)	The children's main concern was to preserve control in an uncertain everyday life. They tried to resolve this concern by balancing the needs of their family with their own needs using four strategies: reflecting, adjusting, taking responsibility and seeking respite.	Norway	Mauseth [94] 2016

Table 2 Variables in Studies I–II

Parents

Variable	Description
Diagnosis	Year of MS diagnosis
FLDRbirth	Parental age at childbirth
FLDRed2	Parental educational levels from basic school to university, dichotomized at basic school or above
FLDRed4	Parental educational levels from basic school to university stratified into four categories: Basic school; secondary school; VET, short or medium higher education, BA; long higher education, PhD
FLDRpnr	Anonymized unique identification number for each parent
FLDRsex	Male or female parent
FLDRtype	MS parent or reference parent
FLDRYoB	Year of birth of the parents

Table 2 – *continued*

Children

Variable	Description
PNR	Anonymized unique identification number for each child
Type	MS offspring or reference child **MS offspring:** Children of one biological parent with MS, randomly selected from each sibship, excluding twins, people emigrated and children with MS **Reference cohort:** Children of biological parents without MS, randomly selected from each sibship, excluding twins, people emigrated and children with MS
Sex	Male or female child
YoB	Year of birth of the children
Death	Dead or alive
GPA	Grade point average in basic school, continuous
ED2	Educational levels from basic school to university, dichotomized at basic school or above
ED4	Educational levels from basic school to university stratified into four categories: Basic school; secondary school; VET, short or medium higher education, BA; long higher education, PhD
Sund	Health-related education: Yes/no
Job30	Employment at age 30: Yes/no
Job40	Employment at age 40: Yes/no
Job50	Employment at age 50: Yes/no
Pen30	Disability pension at age 30: Yes/no
Pen40	Disability pension at age 40: Yes/no
Pen50	Disability pension at age 50: Yes/no
Income	Personal gross annual income during the five-year interval at ages 45–49 corrected for inflation, continuous
IN2	Personal gross annual income during the five-year interval at ages 45–49 corrected for inflation, dichotomized at DKK 250,000 ~ EUR 33,650 or above

SUMMARY

Background

The majority of persons with multiple sclerosis (MS) experience onset of MS between the ages of 20 and 40. Since two-thirds of the persons with MS are young women of childbearing age, parenthood is an essential issue during this period of life. The potential influence of parental MS on children arises from the varied symptoms of the chronic illness, which affect physical and cognitive abilities. MS disabilities and fatigue can restrict daily life and result in less energy for activities or job loss and thus worse conditions for the family.

Objectives and methods

This PhD thesis was designed to investigate whether parental MS influences children in different areas throughout the children's life course (i.e. education, employment, disability pension, and income) as well as to explore the experiences of having a parent with MS.

We investigated the research question using two distinct methods:

- A quantitative method based on nationwide population-based Danish registers comparing a group of children with one biological parent with MS (termed 'MS offspring') with a matched group of children of parents without MS (termed 'reference cohort') up to 58 years of age (Papers I–II).
- A qualitative method based on phenomenological face-to-face interviews with young adults with parental MS (Paper III).

The nationwide register-based epidemiological method complemented by a phenomenological interview method, the long time-span and the age groups of 'children' up to age 58 are original within this area of research.

Results

In Paper I, we investigated the educational achievements of 4,177 MS offspring compared with 33,416 reference children. MS offspring achieved a higher grade point average in the final class of basic school, at age 15, although they achieved similar educational levels as did the reference children at ages 15 to 58. There was a trend toward more MS offspring women attaining health-related educations than did reference women at ages 21 to 58.

In Paper II, we investigated employment and income of 2,456 MS offspring compared with 19,648 reference children. At age 30, the MS offspring were less often employed, and at ages 30 and 40 MS offspring more often received disability pension than did reference children. The mean income at the age interval of 45 to 49 years was similar. Analyzing whether the MS offspring earned more than DKK 250,000 annually (~ EUR 33,650), which is approximately double the level defined as poverty in Denmark in 2012, they earned above this level in annual gross personal income less frequently than did reference children. This income level was only sufficient for the bare necessities.

In Paper III, we explored the experiences of children growing up with a parent with MS by interviewing 14 young adults between 18 and 25 years. The results in the interview study showed two essential themes: 'Caring' and 'Restraint'. Each essential theme emerged from four subthemes. Caring: Assuming responsibility; worry and guilt; choosing health-related educations; advantage of being responsible. Restraint: Concealing feelings and desires; anxiety and depression; shame; lack of openness and knowledge. All the young adults had experiences of the essential themes of caring and restraint. Half of the participants in the interview study were enrolled in a health-related education.

Conclusion

Growing up with a parent with MS can have both beneficial and adverse influences on children late into adulthood. On the one hand, the educational achievements of MS offspring are either better or similar to those of reference children because they attained better grades and similar educational levels. Also, some of the young adults interviewed found advantages to having learned to be responsible. On the other hand, we found an adverse association regarding employment, disability pension, and income. Also, the young adults interviewed had experiences of caring for and of practicing restraint toward the parent with MS, the other parent, and siblings, with most participants continuing this pattern toward friends and partners.

The results of caring and restraint might partly explain some of the associations found in the register-based studies. The children might continue taking care of their parents and striving to find a balance between helping others and fulfilling their own desires. This caregiver challenge might also partly explain the beneficial association between parental MS on education and the adverse association on employment.

Thus, having a parent with MS might be associated with long-term socioeconomic influence on education, employment, disability pension, income, and social relations in children's life course: Parental MS influences children far into adulthood.

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