MoBa Magazine

Research findings from the Norwegian Mother and Child Cohort Study

moba

RESEARCH FOR 15 YEARS

A cohort study is a long-term effort. From the first concept to the start of MoBa it took five years. It took ten more years to reach the goal of 100,000 included pregnancies. Only when the children become adults will we get answers to the questions we posed at the start. We want to follow the children and their parents for years to come.

1993
First planning meeting with Danish researchers

1996
Licence to establish Norwegian newborn cohort – pilot for MoBa

1998
Processed in Parliament and given funding

1999
First MoBa child born

The Norwegian Mother and Child Cohort Study begins

2000
Fathers included in the study

2005
Start of the autism study (ABC) – the first sub-project with additional data collection and clinical examination of participants

2006
First scientific publication from MoBa

2009
Last MoBa child born

2011
Biobank moves to new, larger facilities

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CONTENTS

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THE IMPORTANCE OF MOBA

MoBa is an outstanding study. Since its birth in 1999, the Norwegian Mother and Child Cohort Study – or, as I prefer to call it, the mother, father and child study – has been a world leader. Together with our Danish neighbours, we are regarded as a major force in this field.

MoBa is unique in that it provides a good starting point for finding the causes of disease and death. The study also provides a solid basis for investigating normal development of children – and adults. In addition, we have a good opportunity to look at which interventions work. We can use MoBa in many different ways, for a variety of purposes that will become apparent with time.

It is therefore no coincidence that a number of leading research nations want similar studies. They have tried in the USA without success, now the UK and China hope to succeed.

I think one of the most important scientific results in MoBa so far, is that we have managed to show that folate intake early in pregnancy may protect against severe language delay and autism. If the findings are repeated in new research, which I believe they will be, MoBa results are a major scientific breakthrough that could have implications for public health worldwide.

MoBa is a prospective study. That means we collect data before disease develops so we can be confident that the answers parents give are not affected by how the child develops later. We avoid recall bias, and can make conclusions about the causes of disorders. This is essential for success.

MoBa is far more than just questionnaire data. Researchers also have access to millions of samples of biological material that can be used to study environmental effects, infections and genetic components – and particularly the interaction between them.

Being able to confirm the answers about causes of disease requires many, many years of data collection and analysis. MoBa has been around for 15 years. In research terms, this is a short time. For many of the MoBa-participants, it is a lifetime: From womb to puberty. And MoBa is a progressive family study which makes it possible to follow our first participants and their siblings throughout the course of their life.

In the UK, researchers are soon ready to make the first data collection in their MoBa-inspired study – the Life Study. I hope they succeed, but even though several countries will follow in the years to come, Norway will be in the top division in family research for a long time. We have a head start of 15 to 20 years thanks to a tremendous effort by families from across the country. In addition, we have health registries that make it easier, more reliable and less costly to follow up over time.

Thanks to everyone who has invested time and effort into MoBa.

MOBA HAS BEEN AROUND FOR 15 YEARS. IN RESEARCH TERMS, THIS IS A SHORT TIME. FOR MANY OF THE MOBA-PARTICIPANTS, IT IS A LIFETIME.

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LOOKING BACK – AND FORWARD

A lot has happened in the last 15 years, but our basic aim remains the same. We need more knowledge to enable us to prevent and treat serious diseases. Continued research is needed!

Almost 300 scientific articles have been published in international journals using data from MoBa. We can use this as a measure of great interest from researchers both in Norway and worldwide. Are we any closer to preventing serious diseases? The answer is both yes and no.

We have not solved any of the major mysteries yet. However, a number of theories and myths about links between environmental factors and disease can be discarded. They are incorrect and we do not need to introduce measures. We have removed the uncertainty.

We have also found many signs of potential causal relationships. When these results are published internationally, other research groups can take our findings and work on these issues using other samples and methods.

WE NEED MORE KNOWLEDGE TO PREVENT AND TREAT SERIOUS DISEASES. CONTINUED RESEARCH IS NEEDED!

We have big ambitions for cutting-edge research using data from MoBa in the years to come. We will continue to communicate our results as best we can to participants, decision-makers in government and business, and other researchers.

We will also invite some of the participants to take part in the sub-projects, and we will send out more questionnaires. To solve more mysteries we need our participants to stay active. I hope that you and your children will stay on the journey!

FACTS

Autism spectrum disorder (ASD) is a type of developmental disorder involving difficulties in social interaction, communication and repetitive behaviour. The symptoms of ASD vary from person to person. Some have severe developmental delay and very little speech, while others have good intellectual ability and normal speech.

FOLATE MAY PREVENT AUTISM

Ten years of Norwegian-American collaboration in identifying the risk factors for developing autism have borne fruit. The main finding is that folate supplements before and during pregnancy can reduce the incidence of autism by 39 per cent.

The ABC study (Autism Birth Cohort) is a collaboration between the Norwegian Institute of Public Health, Columbia University in the USA and the Nic Waals Institute at Lovisenberg Hospital in Norway. The main funding – over $ 16 million – comes from the National Institutes of Health (NIH) in the USA. The purpose of the ABC study is to identify children with autism in MoBa, find causes of autism and study what happens to children living with autism.

When the project began in 2003 the researchers were very optimistic. They thought they would find MoBa children with autism and autistic-like conditions by means of the questionnaire that mothers completed when their child was 36 months. It turned out that it was not so easy, and they concluded that screening must be performed at several ages to find children with autism spectrum disorders (ASD). Most that were discovered by the age of three had such large deviations in language development and behaviour that they most likely would have been identified by the health service regardless of this screening.

Autism spectrum disorders (ASD) is a type of developmental disorder involving difficulties in reciprocal social interaction, communication and repetitive behaviour. The symptoms vary from person to person. Some have severe developmental delay and very little speech, while others have good intellectual ability and normal speech.

As the researchers did not find children with autism via the questionnaire at three years, they had to find another way. In 2008, the ABC study was the first in Norway to link data from the Norwegian Patient Registry to MoBa data to find children with ASD. This was a breakthrough. Without this ability to couple data from multiple registries, the ABC study would have been unsuccessful.

Through the first link to the Norwegian Patient Registry, researchers found almost a hundred children with ASD in MoBa. They were invited to participate in the ABC study. After this, annual couplings have been performed and invitations to participate sent out.

MoBa researchers had a hypothesis that a lack of folate before and during pregnancy could lead to autism. British researchers had previously shown that folate deficiency can lead to a variety of developmental disorders called neural tube defects in the child. One of the most serious is spina bifida.

MoBa researchers showed that folate supplementation four weeks before conception and during the first eight weeks of pregnancy could reduce the number of children developing autism and Asperger syndrome with a startling 39 per cent. Researchers have thus strengthened the theory of the importance of folic acid for the repair and reconstruction of the cell's genetic material in the foetus.

The researchers have followed the development of folate intake in pregnant women participating in MoBa and have seen that usage has risen. 43 per cent took folate supplements in 2002, but six years later, 84 per cent of women said they had taken supplements in this important, early stage.

The goal, of course, is that all pregnant women – regardless of nationality – should get folate supplementation, either through fortified foods or a simple vitamin pill.

GPs and health centres are often the first to meet a child with suspected autism. The ABC study has shown that there is considerable variation between Norwegian counties in terms of diagnosis. Four to five times as many children have autism diagnosis in counties with the most diagnoses compared with those counties that have the fewest autism diagnoses. The researchers do not yet know what the reasons are for these differences.

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DOES IT MATTER WHAT MOTHER EATS?

Diet before and during pregnancy can affect the health of both mother and child. What the father eats may also be important.

MoBa has many sub-studies that have examined the relationship between the diet and health of nearly 90,000 mothers and their children. The researchers have studied the importance of diet for:

- Birth weight
- Length and head circumference at birth
- The child's size in relation to length of pregnancy, i.e., whether the child is large or small at birth
- Length of pregnancy
- Premature birth
- Pre-eclampsia
- Maternal weight gain and weight after birth

The results support the official Norwegian recommendations that pregnant women should regularly eat vegetables, fruit, whole grain products, fish and dairy products, and drink water. They also show that it is beneficial to reduce the consumption of sugar, sweetened drinks, ready meals and salty snacks. Those who follow the advice reduce the risk of pregnancy complications such as premature birth, pre-eclampsia and low birth weight.

MoBa research also shows that a diet rich in whole grain products and vegetables protects against premature birth, even when pregnant women also eat some less healthy foods.

The results suggest that it is more important for pregnant women to increase their intake of whole grain products and vegetables than to totally avoid eating hot dogs, hamburgers and crisps.

It is important to examine all possibilities to prevent premature birth because premature birth leads to an increased risk of disease in the child both at birth and in the longer term. 75 per cent of all deaths in childbirth happen among premature infants.

MoBa researchers want to inspire health personnel to discuss the importance of diet in pregnancy. They want to show pregnant women that it is very important to eat a little more whole grain products, fruit and vegetables without having to overhaul their diet.

Other MoBa studies have shown that:

- a mainly whole grain and vegetable diet can prevents pre-eclampsia
- mothers who follow the dietary recommendations are more likely to avoid obesity in the months after birth
- the advice to avoid eating foods that are known to contain environmental contaminants is sound
- there is a positive correlation between the consumption of lean fish and fetal growth
- It is good to consume so-called probiotic dairy products (Biola etc). This appears to give a good intestinal flora which strengthens the body's immune system
- pregnant women who eat organic vegetables have a lower risk of pre-eclampsia. Researchers did not see this association if pregnant women ate organic fruit, cereal, eggs, milk or adhered to a predominantly organic diet. Researchers believe one possible reason for reduced risk when consuming organic vegetables is that organically grown vegetables contain fewer pesticides.

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SEARCHING FOR EARLY SIGNS

Children with ADHD are probably born with the disorder. However, they are not properly identified and treated before school age. Early identification is important because early intervention may be a significant help to these children.

Official estimates are that three to five per cent of Norwegian children under 18 have Attention Deficit Hyperactivity Disorder (ADHD). Children are diagnosed partly because their difficulties have been ongoing for at least six months, and that they cause problems for the child at home or at school.

The diagnostic criteria are not suitable for infants and children of pre-school age so researchers are looking for other signs that can be spotted earlier.

Using data from the MoBa study, researchers now follow over 1,200 children from birth to early school age. Thanks to the questionnaires that parents completed, there is a lot of information about the children from a very early age.

Now the researchers want to monitor the progress of these children through school.

They hope to identify the children who developed ADHD, and find out what distinguished them when they were small. Were there some obvious early features or signs of later difficulties?

In addition to looking for early warning signals, researchers want to learn more about how ADHD develops over time. They will also try to find the causes of the condition, as well as factors that increase the risk.

The ADHD Study began in 2008 and is a collaboration between the Norwegian Institute of Public Health and Oslo University Hospital. So far, the study has been through two rounds and new data are now collected. Initially, 1,200 three-year-olds came to Oslo University Hospital, where the families completed questionnaires, participated in interviews and the children carried out some tests. When the children turned eight, many of the families attended the next round of the study. Researchers are now starting to analyse the material from both rounds and hope to collect even more information as the children get older.

If difficulties are detected early, there are several behavioural measures that can be introduced to give the child a better daily life. Parents and childcare staff can get relevant information to understand ADHD better, so that whenever the child's behaviour is challenging, it is easier to cope with. They can also be trained in good child-rearing practices and learn to establish daily routines to make the day more predictable for the child.

These measures are good alternatives to medication for some children, and can help the child to cope and develop positive patterns of interaction. According to research from the UK, measures that are introduced early can be as effective as medication is for older children.

FACTS

ADHD is a neurodevelopmental disorder characterised by restless and inattentive behaviour. The child may have difficulties concentrating over time, and may find it difficult to follow instructions. Bodily restlessness is often expressed as fiddling, fidgeting and a lot of running and climbing. In addition, children with ADHD are impulsive or very talkative. They often do things without thinking.

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WHEN WORDS GET STUCK

It is common for some children to take longer than others to develop their language skills. Some never catch up and have long-term language difficulties. MoBa researchers are trying to figure out why.

FACTS

The SOL study started in 2007 and is a collaboration between the Norwegian Institute of Public Health, the Ministry of Education, schools and childcare centres. The goal is to provide the best possible knowledge base for understanding the causes and pathways of language difficulties, so that preventive measures can be introduced at an early stage.

It begins with imitation. An infant follows their parents' sounds and movements. After a while, the child begins to imitate, and sounds become words. The child has been given a tool for learning, coping and bonding with other people.

For seven to ten per cent of children, words do not come easily. Some also struggle to understand what others say. When these children grow older, they lack the tools used for homework and playtime. Language difficulties can often lead to other problems.

The Language and Learning Study (SOL study) aims to find out what contributes to good language development, the early signs of language problems and why some children develop language difficulties.

Most children begin to utter their first words at around one year old. Over the next year, many parents realise that children understand much of what they say, and learn new words daily. By the age of two, children can make two-word phrases. By the age of three, most children will have developed quite a lot of speech. This is why researchers want to study children in this period.

The SOL study started in 2007 and is a collaboration between the Norwegian Institute of Public Health, the Ministry of Education, schools and childcare centres.

The goal is to provide the best possible knowledge base for understanding the causes and pathways of language difficulties, so that preventive measures can be introduced at an early stage.

MoBa has given teachers and parents a unique opportunity to do just this. Using questionnaires that the mothers filled out when the child was 6, 18 and 36 months old, researchers have information about children at an important language development period. At five years old, parents and the educational leader in the childcare centre will give more details about the child's language development and various development processes throughout the preschool years. By eight years old, some of them may have been diagnosed with specific language impairments. Some will be invited to participate in a clinical study (Språk-8) in which their scores are compared to children without specific language difficulties in a variety of language tests. This allows researchers to compare children with language disorders with those with normal language development, and to see if there are common characteristics that distinguish them earlier in life. They hope this will provide clues to what causes language difficulties.

Studies abroad have concluded that boys are more prone to develop language difficulties than girls. The SOL study confirms that this is the case in Norway. Both in the group of "persistent" and "transient" language difficulties, boys are in the majority. The researchers also found that children are at higher risk for language impairment if literacy problems already exist in the family. They also found that children with language impairment have more frequent occurrence of other problems, such as motor difficulties, social difficulties and behavioural problems.

In addition, the SOL study has investigated how childcare affects the development of a child's language and learning abilities. Researchers found that children who have good relationships with adults in the childcare centre do better linguistically and psychologically than children with poor relationships. Other aspects of childcare, such as educational practice, material resources, number of staff and group size had little effect.

As the children are part of the MoBa study, the researchers will be able to follow them. These data will be used to find out how language disorders affect children when they get older.

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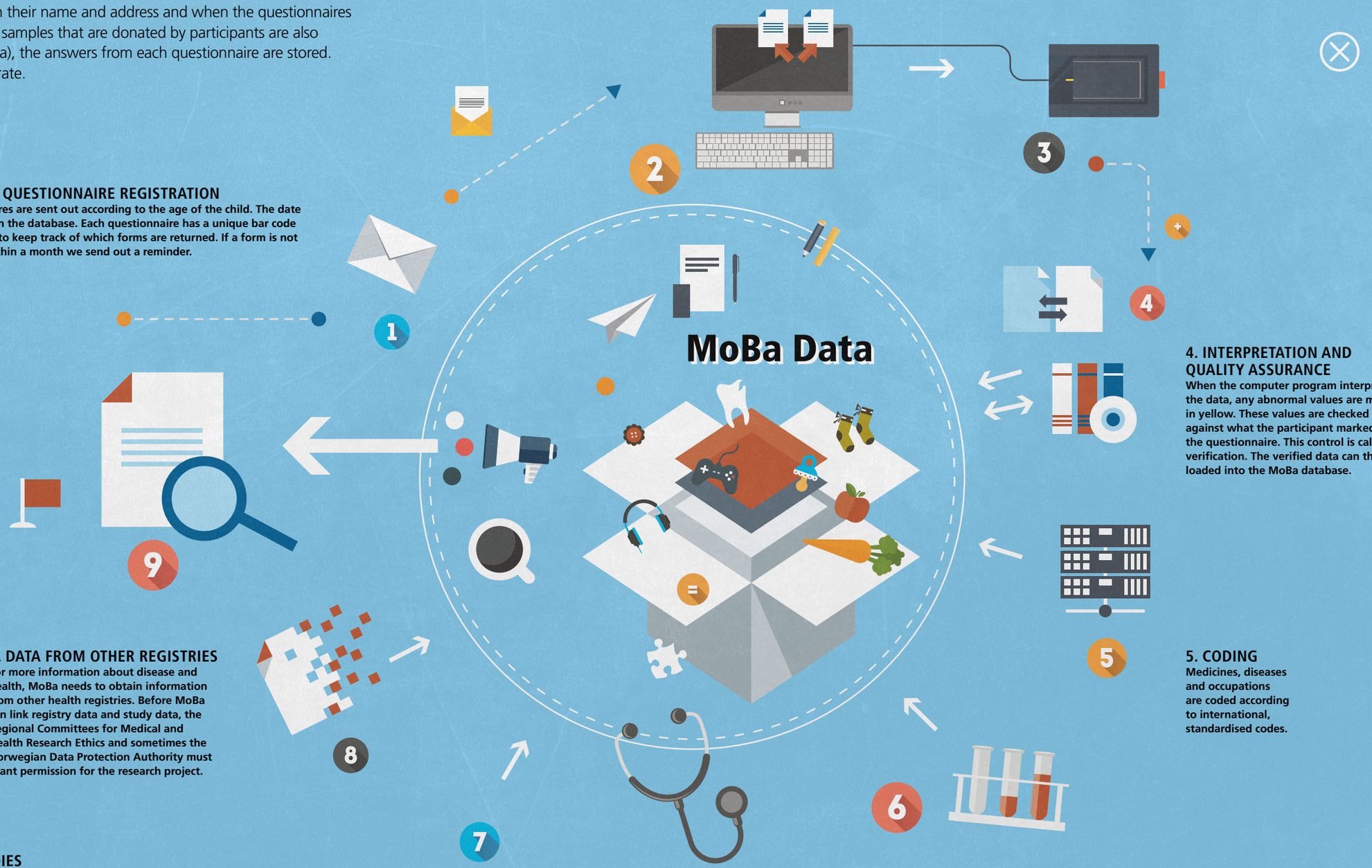
STUDIES IN OTHER COUNTRIES HAVE CONCLUDED THAT BOYS ARE MORE PRONE TO DEVELOP LANGUAGE DIFFICULTIES THAN GIRLS. THE SOL STUDY CONFIRMS THAT THIS IS ALSO THE CASE IN NORWAY.

FROM QUESTIONNAIRE TO RESEARCH

So far, MoBa has received about 800,000 questionnaires. Making an analysis file from the questionnaires for use in research is a time-consuming and complex process. To keep track of the progress of the questionnaires, an administrative database system (MoBaStudy) has been developed. Participants are registered with their name and address and when the questionnaires were sent out and returned. All biological samples that are donated by participants are also registered. In another database (MoBaData), the answers from each questionnaire are stored. These two databases are completely separate.



1. AND 2. QUESTIONNAIRE REGISTRATION

Questionnaires are sent out according to the age of the child. The date is recorded in the database. Each questionnaire has a unique bar code that is used to keep track of which forms are returned. If a form is not returned within a month we send out a reminder.

3. SCANNING

All questionnaires are designed so that they can be scanned by a computer program. On each page of the questionnaire there are five crosses which the scanner uses to recognise the form. If something has been ticked off or written that doesn't make sense, for example, a date that does not exist, the computer program will capture this.

4. INTERPRETATION AND QUALITY ASSURANCE

When the computer program interprets the data, any abnormal values are marked in yellow. These values are checked against what the participant marked in the questionnaire. This control is called verification. The verified data can then be loaded into the MoBa database.

5. CODING

Medicines, diseases and occupations are coded according to international, standardised codes.

6. BIOLOGICAL SAMPLES

During pregnancy and at birth, blood samples were taken from mother, father and the child's umbilical cord. These blood samples are stored in the MoBa biobank (see article page 16). Blood samples are sent for analysis and the laboratory results are returned to MoBa.

7. ADDITIONAL STUDIES

Participants may be asked to participate in additional studies where we need more detailed information about individual conditions or health problems. Additional studies must be specifically approved by the Regional Committee for Medical and Health Research Ethics. In addition, MoBa participants who agree to take part must complete a consent form for that study. The ABC Study is an example of an additional study (see page 6).

8. DATA FROM OTHER REGISTRIES

For more information about disease and health, MoBa needs to obtain information from other health registries. Before MoBa can link registry data and study data, the Regional Committees for Medical and Health Research Ethics and sometimes the Norwegian Data Protection Authority must grant permission for the research project.

9. ANALYSIS FILE

When all the data from the questionnaires, any additional investigation studies, and analysis results from blood samples are quality assured and coded, an anonymised data analysis file is available to researchers. Since each participant is given a random number, their questionnaire data can be followed over the years, but information that could identify participants is never released to researchers.

MANY QUESTIONS BUT FEW ANSWERS

Researchers hope that blood from the mother, father and child can provide new knowledge about childhood epilepsy.

The idea came from Scotland. Professor Richard Chin at the University of Edinburgh wanted to use MoBa data to study the incidence, cause and risk factors, and development of children with epilepsy. In 2013, the EPYC project (Epilepsy in Young Children) became a reality with funding from the Research Council of Norway.

Childhood epilepsy is one of the most common serious neurological disorders in children and we estimate that the incidence is between 0.5 and 1 per cent. This means that between 300 and 600 Norwegian children are born every year who will receive this diagnosis.

Research has shown that the incidence in recent years has fallen in countries with high living standards. Unfortunately, this field of research is small and there is still a lot we do not know about epilepsy in children.

Some cases of childhood epilepsy have known causes, such as intracranial bleeding, infections and other brain damage before, during or after birth. Of the other cases, 30 per cent had identifiable causes, usually genetic mutations. However, the remaining 70 per cent had an unknown cause. The researchers believe that many of these also have a genetic cause, but not enough is known about which genes are involved.

EPYC aims to contribute new knowledge about the causes and risk factors in childhood epilepsy that currently has an unknown cause.

MoBa researchers can use blood from the mother, father and child to study genetic factors. This provides unique opportunities to study heredity and identify genes that may be involved in disease development.

There are no other population studies of the scale of MoBa that have the blood from the mother, father and children so MoBa can really make a difference. By studying the blood of parents and children, researchers could uncover new knowledge with potential to help with prevention, and perhaps new treatment methods for childhood epilepsy.

In the future, MoBa researchers plan to study the epigenetic factors that may be involved in the development of epilepsy. No researchers have done this before. Researchers now know that it is not only changes in the genes of the child – inherited gene mutations and spontaneous mutations – that can lead to developmental disorders.

Genes can also be switched on and off during critical periods of fetal development by external factors. These epigenetic changes may damage the fetus and lay the foundation for disease later in life.

The researchers will study risk factors such as maternal diet, lack of folate intake, smoking during pregnancy, high blood pressure and stress in the mother, parental age and complications during pregnancy and childbirth, as well as the child's birth weight.

840 MoBa children have been diagnosed with epilepsy and 600 are in the EPYC study.

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MILLIONS IN THE BANK

The biobank contains biological material donated by participants in health studies organised by the Norwegian Institute of Public Health. These samples will provide invaluable knowledge about health and diseases.

The biobank was established in 1999 when the Norwegian Mother and Child Cohort Study (MoBa) began. Responsibility for the biobank was given to the Norwegian Institute of Public Health when the institute was established in 2002.

The biobank has an area of around 2,000 square metres for storage of biological samples in various units. We have many chest freezers in the storage areas, but the majority of samples are kept in two large automated freezers that are maintained at minus 20 and minus 80 degrees. Both freezers can store several millions of samples and use robots to deposit and extract the samples. The biobank contains samples from many different research projects, but MoBa is by far the largest, with over 270,000 participants (mother, father and children) who have donated biological material.

Although the biobank is primarily a storage facility, with enough space to store millions of samples, we also provide other services:

Collection of biological material
- The biobank sends equipment to a participant, doctor's office or hospital so that samples can be taken and returned to the biobank
- All samples received by the biobank are registered in a database and information management system
- Samples are processed, e.g. plasma and DNA are isolated from blood samples
- The different samples are divided into smaller parts, known as aliquots, and frozen

Distribution of biological material
- Samples are thawed and the required amount is sent to researchers whose applications to use the biological material have been approved

For most studies, the biobank contains many aliquots per participant. In total, there are several million aliquots. From MoBa alone we have four million aliquots of DNA.

Researchers can apply to receive biological samples from the biobank for use in research projects. All applications are considered by steering groups at the institute who will grant access to data according to set guidelines.

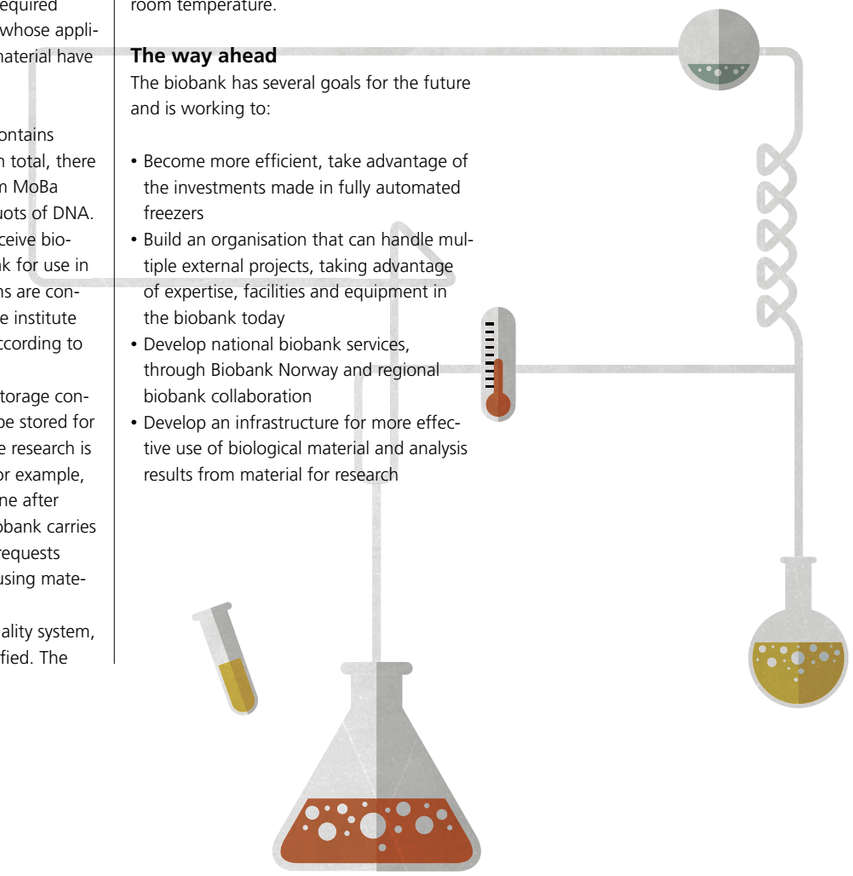
In theory, with the correct storage conditions, biological material can be stored for a hundred years. However, more research is needed to know more about, for example, the condition of plasma and urine after several years of storage. The biobank carries out regular quality control and requests feedback from the researchers using material from the biobank.

The biobank has its own quality system, and was recently ISO 9001 certified. The biobank follows internal procedures to ensure that quality and safety are maintained. We have rigorous training programs, a nonconformity handling system, and a continuous improvement focus. We follow best biobanking practice, for example how long the different samples can be stored at room temperature.

The way ahead

The biobank has several goals for the future and is working to:

- Become more efficient, take advantage of the investments made in fully automated freezers
- Build an organisation that can handle multiple external projects, taking advantage of expertise, facilities and equipment in the biobank today
- Develop national biobank services, through Biobank Norway and regional biobank collaboration
- Develop an infrastructure for more effective use of biological material and analysis results from material for research



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TALES FROM A MILK TOOTH

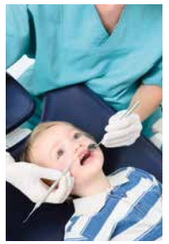
Milk teeth are a kind of black box recorders that give researchers important information about health and disease. The MoBa Tooth Bank in Bergen (MoBa Tann) now contains milk teeth from more than 24,000 children in the MoBa study.

The tooth bank contains milk teeth from children taking part in the MoBa study. They are encouraged to submit one or more shed milk teeth. MoBa sends out information about this shortly before the child reaches seven years of age.

Milk teeth are usually shed early in life and are a kind of data recorder that give researchers important information about health and causes of diseases. Teeth store information about environmental factors that the child has been exposed to since they were in the womb.

Teeth can tell what the mother ate during pregnancy and about uptake of contaminants, such as lead and cadmium. These substances can affect the child in the womb and in early childhood. Along with MoBa information from questionnaires and blood tests, results from tooth analysis can tell researchers about the impact that hazardous substances have on children's health.

Teeth are formed in layers, and we can see the difference between the part of the tooth that is formed before birth and the part that is formed afterwards. Dental tissue is the only stable tissue formed in the fetus and in infancy that is available for analysis on a large scale at a later date. In the future, information gained from the teeth could help to prevent disease or other conditions.



FACTS

Teeth are formed in layers, and we can see the difference between the part of the tooth that is formed before birth and the part that is formed afterwards. Dental tissue is the only stable tissue of the body, formed in the fetus and in infancy, that is available for analysis on a large scale at a later date.

Milk teeth have an almost unlimited shelf life and can therefore be useful to researchers for many years to come. On arrival, the teeth are registered and anonymised and stored in secure storage boxes at the University of Bergen.

Researchers are now working to find the best methods to extract and analyse samples from teeth. New analytical methods can increase the value of dental material even further.

It is also a goal to establish standards for how analyses should be performed so that researchers can compare findings in teeth from different countries. MoBa Tann researchers are working with researchers in Canada, USA, UK and Germany.

MoBa Tann is a collaborative project between the University of Bergen and the Norwegian Institute of Public Health.

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24 000

CHILDREN IN THE MOBA STUDY HAVE SENT US ONE OR MORE MILK TEETH.

10 %

OF CEREBRAL PALSY CASES ARE DUE TO BIRTH INJURY.

UNIQUE NORWEGIAN-DANISH EFFORT FOR CEREBRAL PALSY

Antenatal and maternity care is improving in Norway. Even so, the percentage of children born with cerebral palsy is not falling. Norwegian and Danish researchers have teamed up to find out why.

Previously, it was believed that most cases of cerebral palsy (CP) occurred during birth. Now, researchers reckon that only ten per cent of cases are due to birth injury, and that we should be looking at what happens to the fetus early in development.

Although CP is the most common cause of physical disability in Norway, the condition is rare. Only two out of every 1,000 children is diagnosed with CP.

There is relatively little research into CP. Therefore, researchers in Norway decided to combine their efforts with colleagues from the Danish National Birth Cohort (DNBC) to study the children with CP in the Norwegian and Danish cohorts. A working group from Bergen and Copenhagen has merged relevant data from both studies to create a common Norwegian-Danish MOBAND cohort, something which has never been attempted before.

CP researchers are the first to use the harmonised data in their work. Over 200,000 children are included in the study, and the researchers identified 437 children with CP in MOBAND, of which 246 are from MoBa and 191 are from DNBC. A large database means that the results will be more robust. It is also interesting for researchers to make comparisons between the countries.

Starting in autumn 2014, the researchers will study the responses to the questionnaires, analyse biological samples and look for factors that distinguish children with CP from children without CP. They will study risk factors such as parental weight, diet during pregnancy, smoking and coffee intake, infections during pregnancy and premature birth.

In particular, the researchers want to look at any effect of the mother taking folate supplements during pregnancy. The Norwegian ABC Study has shown that folate supplementation can reduce the risk of autism considerably, and researchers want to know if the same applies for CP (read more about ABC Study on page 6).

FACTS

Cerebral palsy (CP) is a common term for several conditions, all of which cause a permanent impairment in motor function. There are several degrees of the disease, and while some people with the condition are fully active, others have severe symptoms that require more care. The CP-MOBAND study aims to describe the incidence, progress and consequences of CP in children, as well as mortality. It should also identify possible risk factors for CP.

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CAUSES OF RESPIRATORY PROBLEMS

Over 20 per cent of Norwegian children have had asthma-like symptoms at some time. MoBa researchers want to find out whether the causes of respiratory problems already begin in the womb.

Childhood asthma seems to have increased over the last 20–30 years. The reasons for this are still not clearly established and researchers want to know if genetic and environmental risk factors are involved.

MoBa has an active research group that is looking at the interaction of various risk factors in pregnancy and the development of respiratory problems in children.

The research group is using questionnaire data and biological material from MoBa, plus data from the national health registries. In addition, researchers are collecting new data from children aged 10–11 years.

MoBa researchers have uncovered new knowledge about the relationship between smoking during pregnancy, maternal body mass index, intake of vitamins, including vitamin D and folate in pregnancy, and the development of respiratory problems in children.

Folate intake by pregnant women in Norway has doubled since 1991, when British researchers found that folate supplements could halve the risk of neural tube defects such as spina bifida in the infant. Recently, MoBa researchers have shown that folate intake can also significantly reduce the risk of developing

language impairment and autism (see page 6).

Folate supplements are particularly important before conception and during early pregnancy. In its natural form, folate is found in green vegetables, beans, peas, whole grain products and citrus fruits. Since 1998, the Norwegian health authorities have recommended taking supplements before conception and in the first three months of pregnancy.

Researchers found that there was a slightly increased risk of the child developing asthma-like symptoms if the mother took folate supplements during early pregnancy. The results are based on responses from 32,000 mothers who completed the 18-month questionnaire in MoBa.

Since we still know too little about whether there is a causal relationship between maternal intake of folate and asthma, the researchers are not recommending changes in the advice about folate supplementation for pregnant women.

One possible mechanism may be that the relationship between maternal smoking, intake of folate and other vitamins including vitamin D, and the development of respiratory problems in the child may be epigenetic. This means that genes can be switched on and off in the womb by environmental influences.

The researchers will study whether there are epigenetic changes in umbilical cord blood, called DNA methylation, in children who are exposed to risk factors in the womb compared with children who are not exposed. They will then study whether this could affect the development of respiratory problems in children.

The research group has received a substantial grant from the Research Council of Norway's Human biobanks program for the Causal Pathways for Asthma (CASPAR) project to continue the research. Part of the work is also funded by the National Institute of Environmental Health Sciences (NIEHS) in the USA.

1/5

NORWEGIAN CHILDREN HAVE EXPERIENCED ASTHMA-LIKE SYMPTOMS.

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ENVIRONMENTAL CONTAMINANTS – A GROWING PROBLEM

Every day, we are exposed to a large number of natural and man-made chemicals. In several MoBa studies, researchers have investigated how these unwanted substances in the environment affect health. In addition, 3,000 MoBa participants will be invited to become regular eco-monitors in a new environmental biobank project.

FACTS

Heavy metals are found in low concentrations in food, air, drinking water and consumer products. They can be detected in blood, breast milk, urine and hair samples.

Environmental contaminants, found in the food we eat, the air we breathe, and the products we apply to our skin, can affect our health. Exposure to noise and UV radiation also affects us. Everyone is exposed, but infants and children are particularly vulnerable to potentially negative effects of environmental contaminants.

We are beginning to understand how individual factors in the environment can affect children's health, but we know too little about how they interact in the so-called "cocktail effect". With better knowledge it becomes possible to develop preventive measures to create a healthy and safe environment for the next generations.

Creating a human environmental biobank is part of the Norwegian Institute of Public Health's strategy for the coming years. Using MoBa data, we will study some of the most vulnerable groups, including pregnant women, fetuses, and young children.

We will therefore invite 3,000 MoBa participants to become regular contributors to the environmental biobank.

The environmental biobank will be suited to study time trends in public exposure to environmental contaminants, and evaluate the effects of measures made to decrease exposure. We will also be able to check older samples for contaminants that have not yet been identified. Furthermore, the project will enable studies of how diet may affect how the body handles toxins. For example, people with low iron levels are apparently more likely to absorb heavy metals such as cadmium and lead. Part of the research project will examine whether dietary factors protect against the harmful effects of toxins.

In a separate project ongoing in 2014/2015, the Norwegian Institute of Public Health has invited 300 MoBa participants living in the Oslo area to participate in the HELIX Child and Environment project, which is part of an EU-funded HELIX research project (The Human Early-Life Exposome).

The HELIX project will also be studying the "cocktail effect". We will study the environment around children, including air quality, noise, access to nature and parks, food and drink, and their physical activity.

Further, we will measure various environmental factors in the blood and urine and examine how genetic material can be affected by exposure. The relationship between environmental impact and various health indicators such as obesity, lung function and the child's neurological development will also be studied.

As we have already gathered a lot of information about the MoBa children, researchers can learn a lot from this study.

300

MOBA PARTICIPANTS FROM THE OSLO AREA ARE INVITED TO TAKE PART IN THE HELIX CHILD AND ENVIRONMENT PROJECT.

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OTHER ENVIRONMENTAL PROJECTS

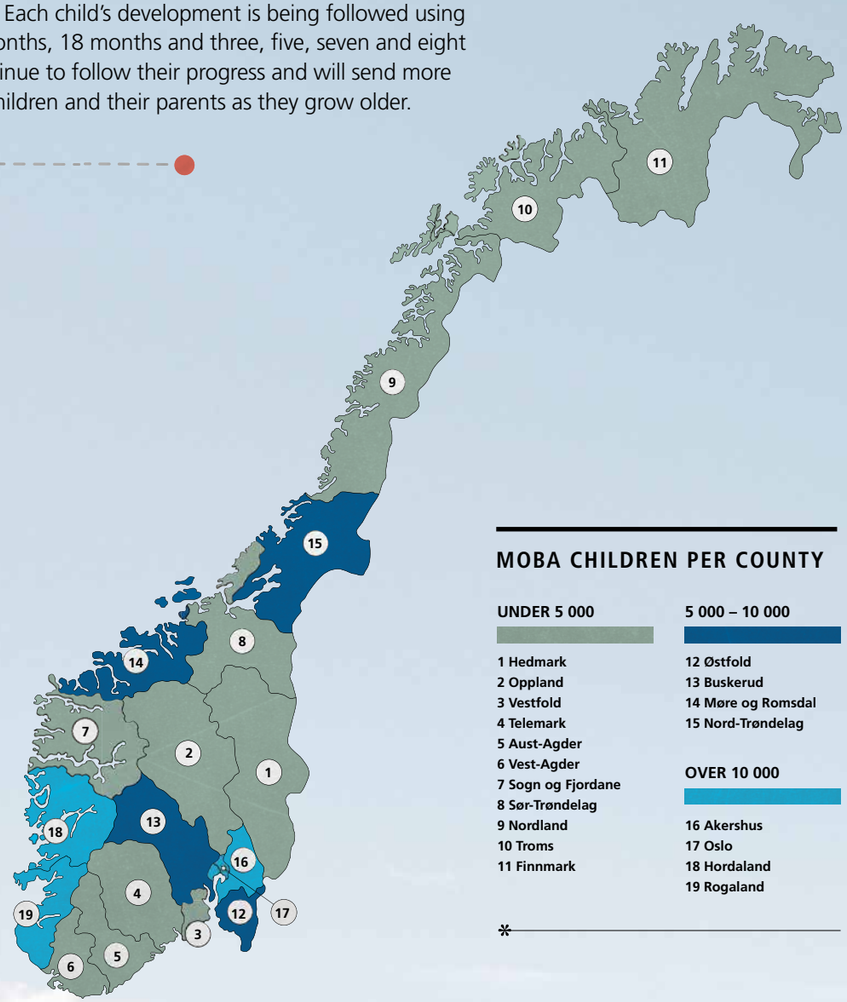
Researchers from the Norwegian Institute of Public Health and other research groups have already begun studies on the relationship between environmental factors and health. Here are a few examples:

- A study looking at the significance of environmental factors, such as drinking water quality, diet (fibre, sugar, vitamin D, fatty acids and probiotics) and air pollution on premature birth in mothers with chronic inflammatory bowel disease.
- For approximately 50 years, per- and polyfluorinated alkylated substances (PFAS) have been used in lubricants, coatings, food packaging, and fire extinguishing foam. Researchers will measure the levels of these pollutants in the blood of mothers and the umbilical cord in children at birth. The researchers also want to measure the levels of PFAS in pregnant women and the extent to which PFAS are absorbed and remain in the body. The project is part of a larger European project.
- Low levels of PFAS are found in food. Recent findings from the US suggest that PFAS may increase the risk of developing pre-eclampsia. 1,250 blood samples from MoBa mothers will be checked to investigate this.
- A study is looking at the relationship between mercury exposure in the maternal diet and possible delayed language development in the child at three, five and seven years of age.
- Researchers want to study how exposure to substances formed during cooking and frying causes changes in the genetic material (mutations) in the gametes. Does this have implications for children's health?

MOBA FACTS AND FIGURES

Pregnant women were invited to take part in the Norwegian Mother and Child Cohort Study when they attended their ultrasound scan at weeks 17–20 of pregnancy. If they agreed to participate, the child's father was also invited. During pregnancy, mothers completed three questionnaires and the fathers completed one. Each child's development is being followed using questionnaires at six months, 18 months and three, five, seven and eight years. We want to continue to follow their progress and will send more questionnaires to the children and their parents as they grow older.

30
DOCTORAL DEGREES



MOBA CHILDREN PER COUNTY

UNDER 5 000

1 Hedmark
2 Oppland
3 Vestfold
4 Telemark
5 Aust-Agder
6 Vest-Agder
7 Sogn og Fjordane
8 Sør-Trøndelag
9 Nordland
10 Troms
11 Finnmark

5 000 – 10 000

12 Østfold
13 Buskerud
14 Møre og Romsdal
15 Nord-Trøndelag

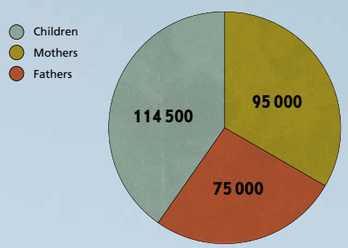
OVER 10 000

16 Akershus
17 Oslo
18 Hordaland
19 Rogaland

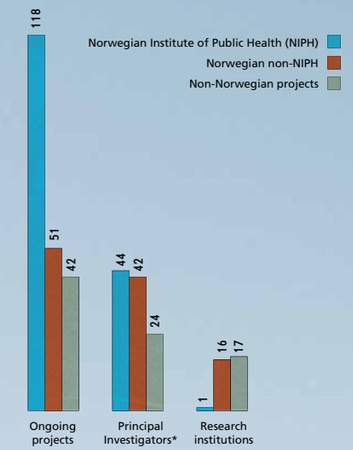
40 %
OF ALL INVITED WOMEN AGREED TO PARTICIPATE

77 %
OF FATHERS TOOK PART IF THE MOTHER DID

PARTICIPANTS



275
PUBLISHED SCIENTIFIC ARTICLES



ONGOING RESEARCH PROJECTS

* Some researchers are employed at several institutes. These are counted once for each institute they work at.