moba

NIPH
Norwegian Institute of Public Health

The Norwegian Mother, Father and Child Cohort Study (MoBa)

The 27th Norwegian Conference on Epidemiology

Bergen, 3-4 November 2021

Ragnhild E. Brandlistuen, PhD

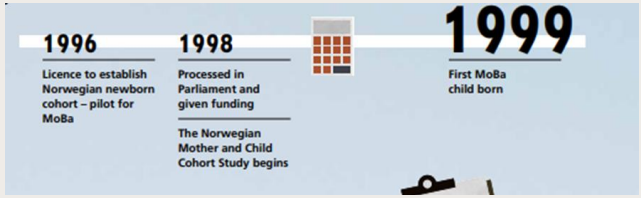
Scientific Director of The Norwegian Mother, Father and Child Cohort Study, NIPH, Oslo, Norway

It started in Bergen

1990: The first Norwegian epidemiology conference

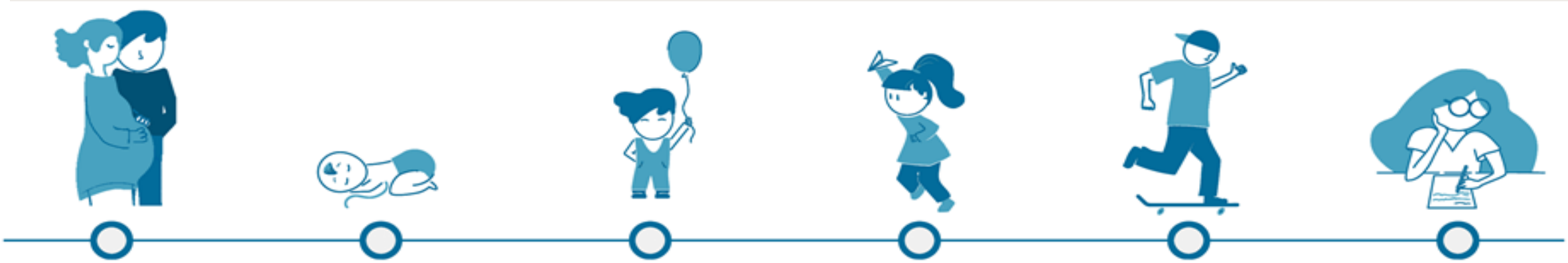
Topic: How to improve our medical registry data?

Panel debate: *Shall we jointly <u>establish a great prospective study</u> of the causes of chronic diseases based on our registries?*



NOFE
Norwegian Epidemiological Association
Norsk forening for epidemiologi

Bakketeig, L. S. (2014). Why did we start the MoBa study?. *Norsk epidemiologi*, *24*(1-2).



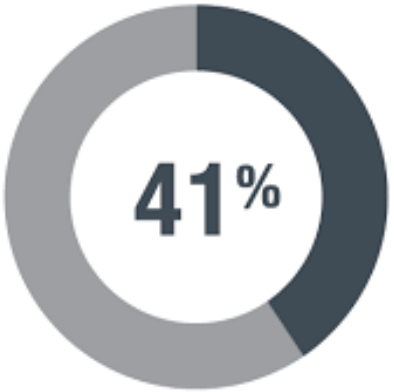
MoBa firstborn

Kay Siver (7) from Rong

Recruitment

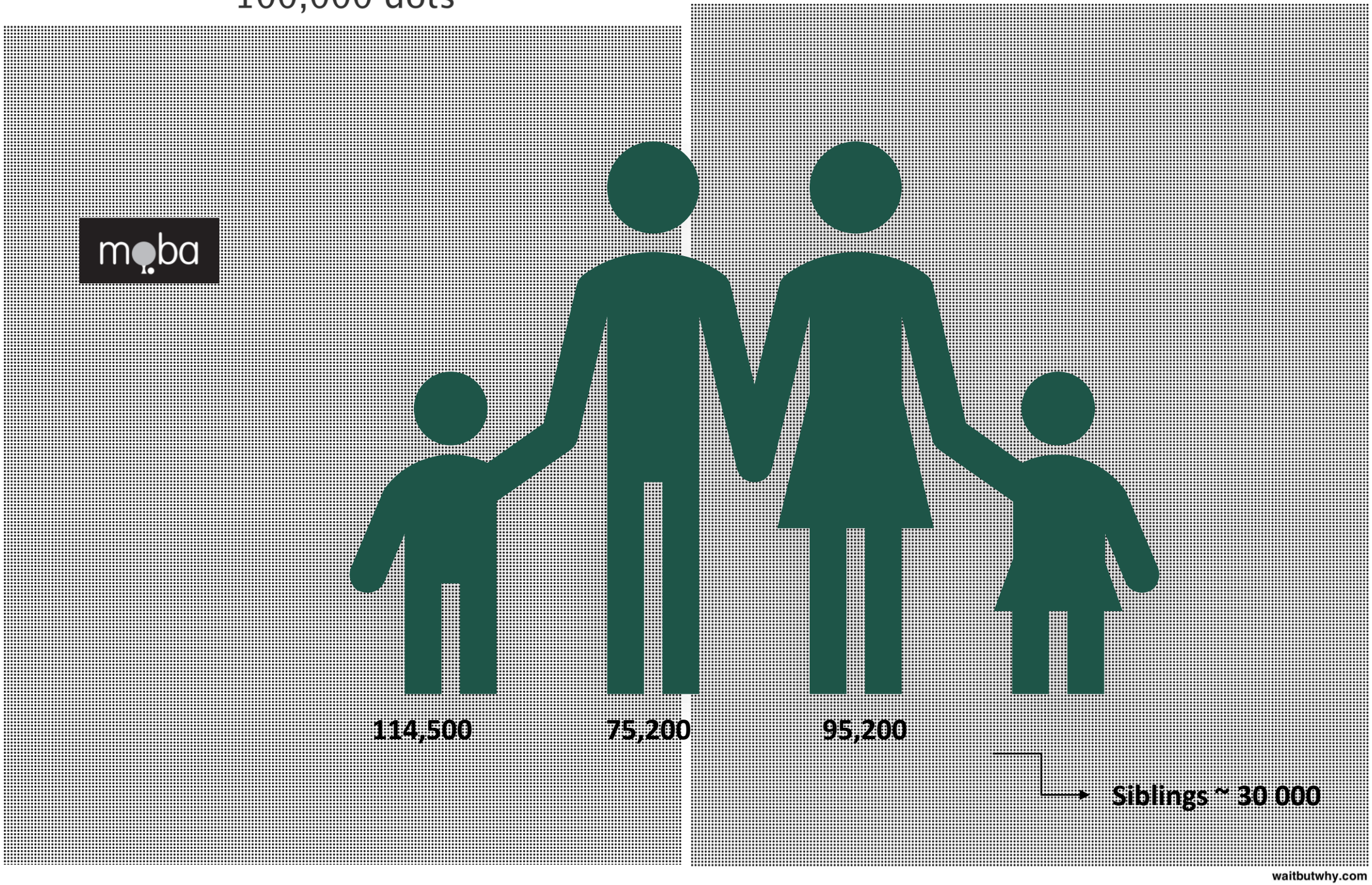
First MoBa child was born in 1999
Last MoBa child was born in 2009

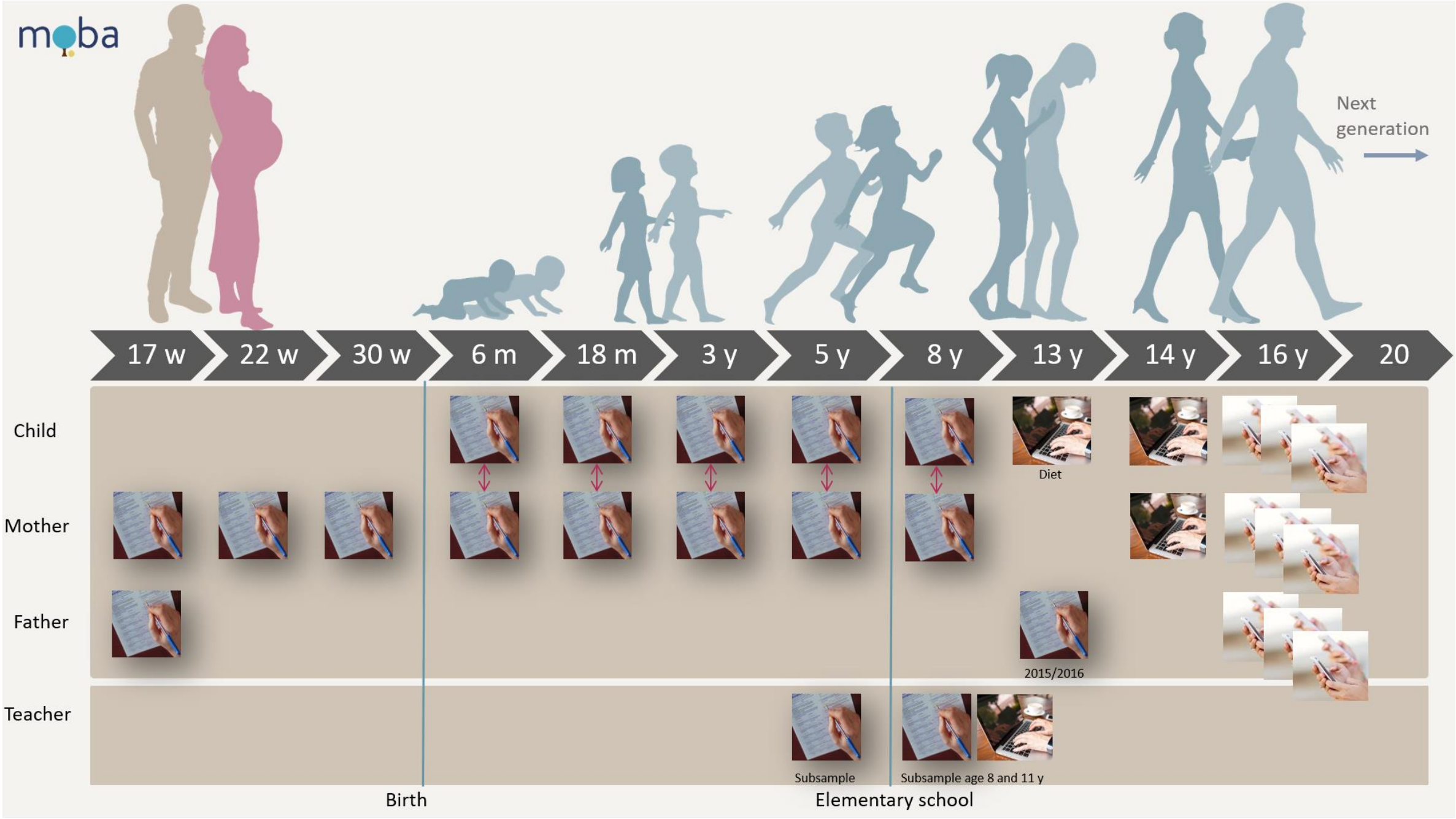
- Hospitals with < 1000 births per year
- Hospitals with > 1000 births per year



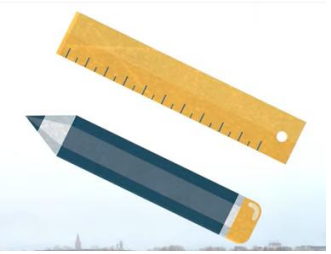
Younger women, smokers, and women with low educational level were less likely to participate in MoBa (Nilsen et al., 2009).

100,000 dots




moba
Next generation
17 w
22 w
30 w
6 m
18 m
3 y
5 y
8 y
13 y
14 y
16 y
20
Child
Mother
Father
Teacher
Diet
2015/2016
Subsample
Subsample age 8 and 11 y
Birth
Elementary school

Wide range of measured environmental factors



The general aim of MoBa:

To find causes of disease

A broader discussion of aims and methods is given in:

- Magnus P et al. Cohort profile: The Norwegian Mother, Father and Child Cohort Study. Int J Epidemiol 2006; 35: 1146-50
- Magnus P et al. Cohort Profile Update: The Norwegian Mother and Child Cohort Study. Int J Epidemiol 2016; 45:382-8.

Adolescence

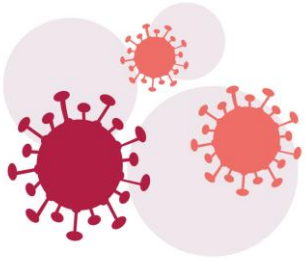
Data collection is ongoing

- Computer based questionnaires by e-mail (13 and 14 yrs)
- Short mobile phone questionnaires (16-17 yrs) (MoBaYoung)
  - New questionnaire every month
  - 5 minutes!
  - Can be combined with online cognitive tests/games (in progress)

Topics in data collections in adolescence

- Physical activity (Q14 and MoBaYng)
- Screen time (Q14 and MoBaYng)
- Social media use (Q14 and MoBaYng)
- Friends (Q14 and MoBaYng)
- Well being (Q14 and MoBaYng)
- Mental health (Q14 and MoBaYng)
- Bullying (Q14 and MoBaYng)
- Parent-child relationship (Q14 and MoBaYng)
- Eating habits/problems (Q14 and MoBaYng)
- Pain (Q14 and MoBaYng)
- Sleep (Q14 and MoBaYng)
- School functioning and behavior (Q14 and MoBaYng)
- School grades (Q14 and MoBaYng)
- Rule breaking (Q14 and MoBaYng)
- Personality (Q14)
- Life events (Q14 and MoBaYng)
- Puberty (Q14)
- Substance use (Q14 and MoBaYng)
- Religion (MoBaYng)
- Sex (MoBaYng)
- Harassment (MoBaYng)
- Suicide thoughts and attempts (MoBaYng)
- Repeated measures of mental health and life satisfaction (MoBaYng)

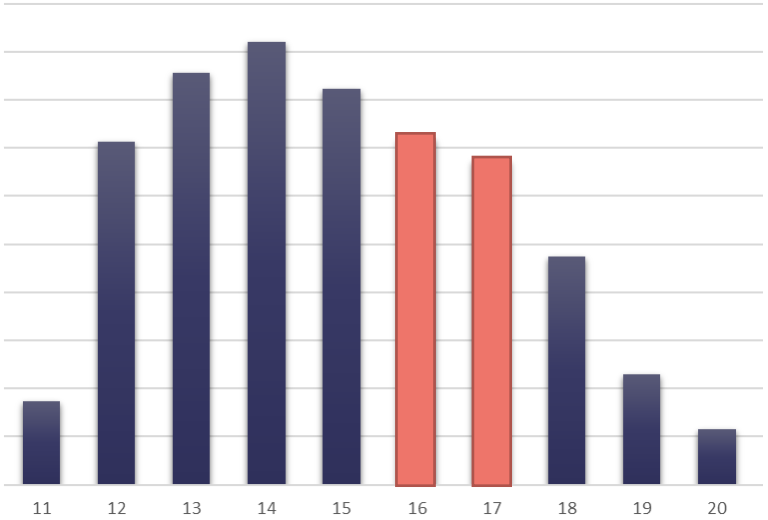
MoBa Corona



- Mother, father, youth (16-17,5 years)
- Every other week since march-april 2020

Invited:

- 149 000 parents – responded: 75% (111 750)
- 17 250 youth – responded: 50% (8 625)



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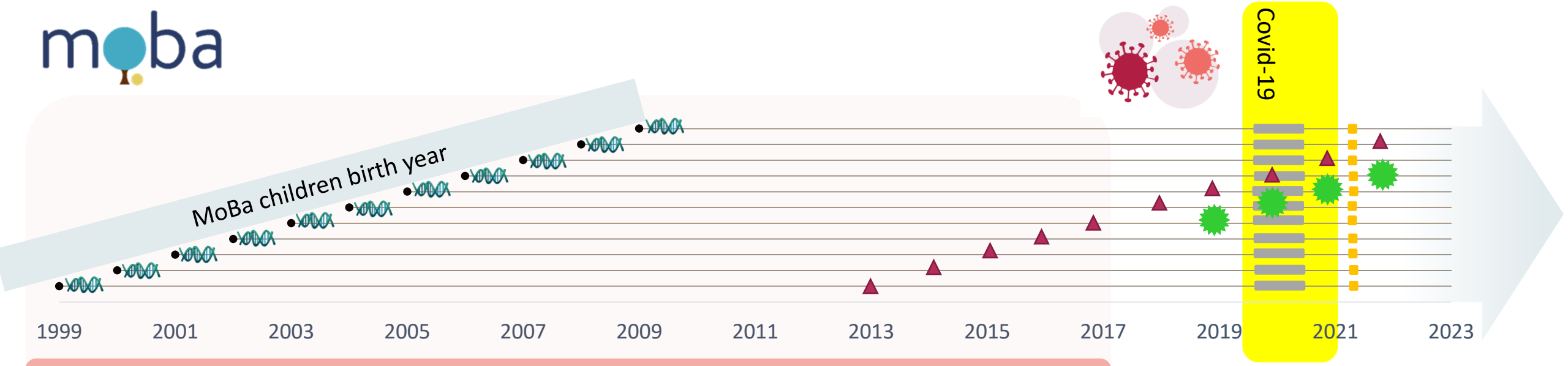
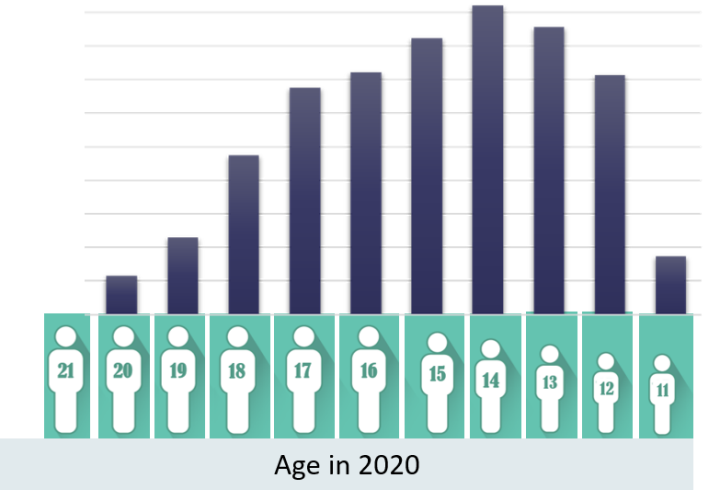


Rich pre pandemic data on adults and adolescents from 10 MoBa data collections from pregnancy until the children were 8 years old

Pre: DNA collected at birth

Pre, peri, post: Diagnostic data from 2006 onwards (from health registries)

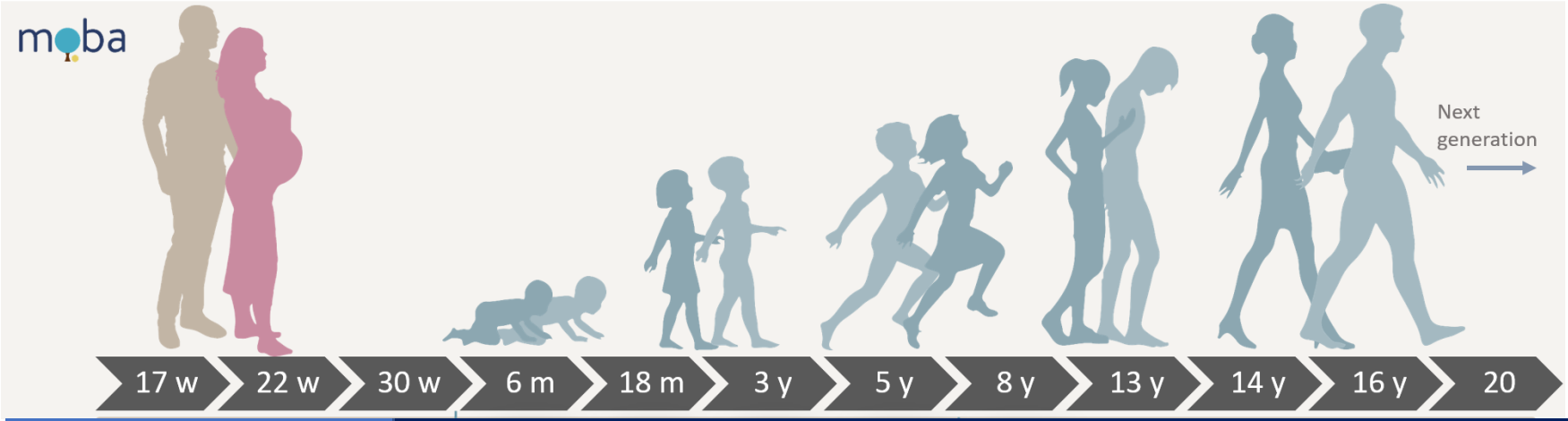


- **Q 14 year** (mothers/adolescents)
- **MoBaYoung** (monthly to adolescents)
- **Corona Qs** (biweekly to adults/adolescents)
- **Post Corona Qs** (adults/adolescents)

Testing and diagnostic interviews

ABC
Autism Birth Cohort Study
Autismestudien

Språk-8



Overview of the national health registries

Table 1. Overview of the mandatory national health registries

Register	Paragraph in Personal Health Data Registries Act	Data Responsible (Data Processor)
Cause of Death Registry	§ 11	Norwegian Institute of Public Health
Cancer Registry of Norway	§ 11	Oslo University Hospital
Medical Birth Registry of Norway	§ 11	Norwegian Institute of Public Health
Norwegian Surveillance System for Communicable Diseases (MSIS)	§ 11	Norwegian Institute of Public Health
Norwegian Immunisation Registry (SYSVAK)	§ 11	Norwegian Institute of Public Health
Registry of the Norwegian Armed Forces Medical Services	§ 11	Armed Forces Medical
Norwegian Patient Registry (NPR)	§ 11	Norwegian Directorate of Health
Norwegian Cardiovascular Disease Registry	§ 11	Norwegian Institute of Public Health
System for reporting of unwanted effects	§ 11	Norwegian Medicines Agency
Norwegian Register of Primary Health Care	§ 11	Norwegian Directorate of Health
Medical Archives Registry	§ 12	National Archives of Norway
Norwegian Information System for the Nursing and Care Sector (IPLOS)	§ 9b	Norwegian Directorate of Health
Norwegian Surveillance System for Antibiotic Use and Healthcare-Associated Infections (NOIS)	§ 9b	Norwegian Institute of Public Health

Linked registries with continuous follow-up

- Birth registry
- Primary care
- Specialist care
- Prescriptions
- School tests scores and grades
- Educational attainment
- Income
- Social security support
- Family structure
- Neighbourhood

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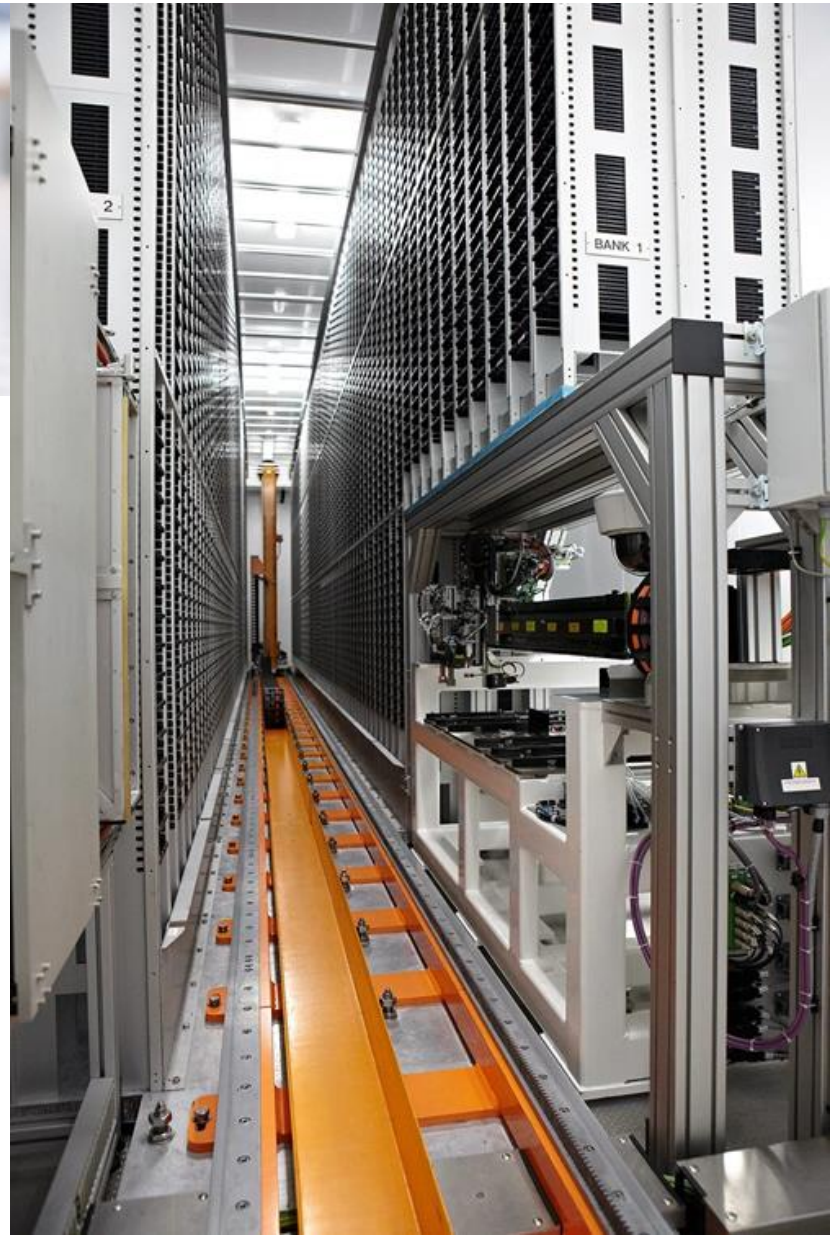
THE NIPH BIOBANK



MoBa Biospecimens available:

- EDTA whole blood and plasma (frozen -80ºC)
- DNA extracted from whole blood (frozen -20ºC)
- Urine (frozen -80ºC)
- RNA: from cord blood (Tempus-tubes; RNase free, -80º C)

All samples stored with barcodes in freezers or automation storage systems

370 000 sample sets

4.5 million aliquots stored

Rønningen, K. S., Paltiel, L., Meltzer, H. M., Nordhagen, R., Lie, K. K., Hovengen, R., ... & Hoppin, J. A. (2006). The biobank of the Norwegian Mother and Child Cohort Study: a resource for the next 100 years. *European journal of epidemiology*, *21*(8), 619-625.

MoBa Teeth Biobank

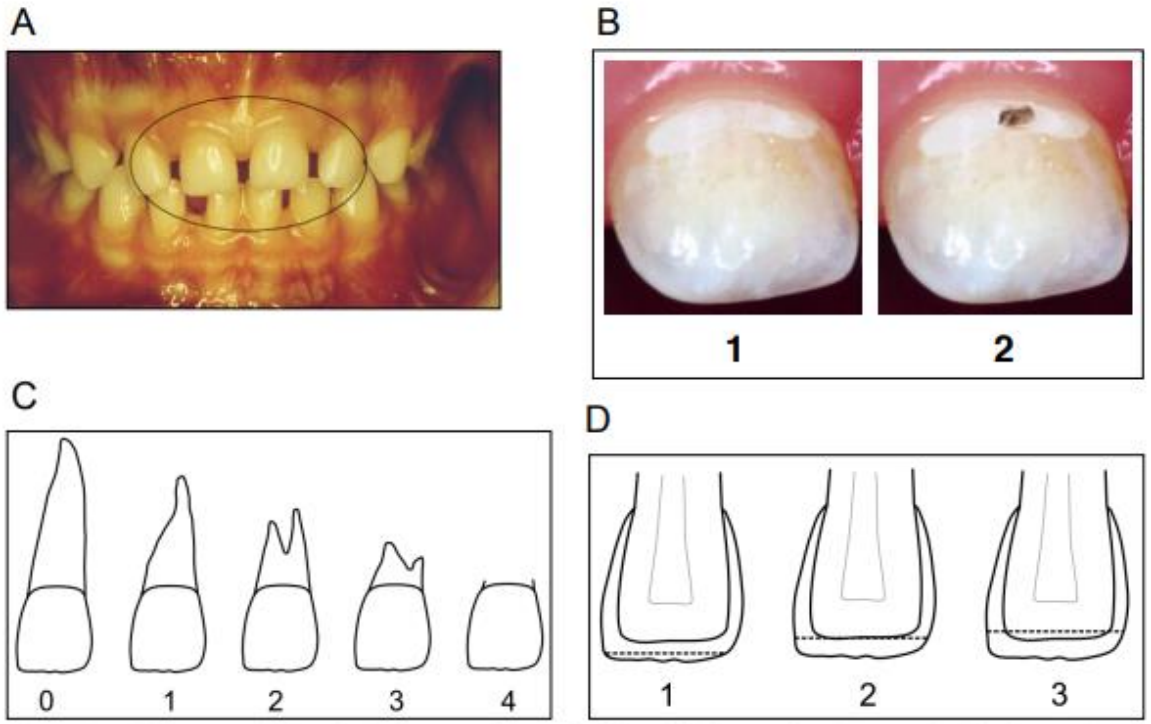


Figure 4. Variables recorded into the database. a: Primary dentition with the actual tooth types encircled. b: Examples of degree of caries (1 = enamel caries; 2 = caries with cavitation to dentine*). c: Degree of root resorption (0-4). d: Degree of attrition/abrasion of incisal edge of the tooth crown (1 = only in enamel, 2 = to the enamel-dentin junction, 3 = further into the dentine). *Courtesy of Prof. Ivar Espelid and Tandläkartidningen (Espelid I, Tveit AB, Mejåre I, Nyvad B. Karies – ny viten eller gamle sannheter? Tandläkartidningen 1997; 89: 19-28.)

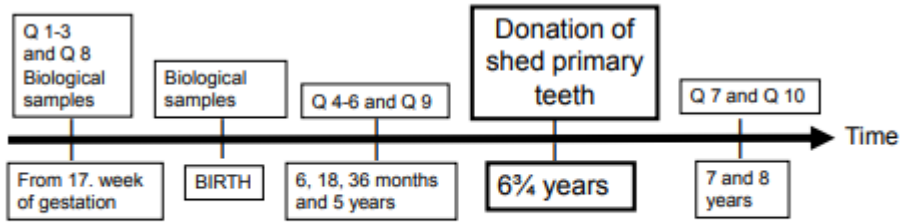
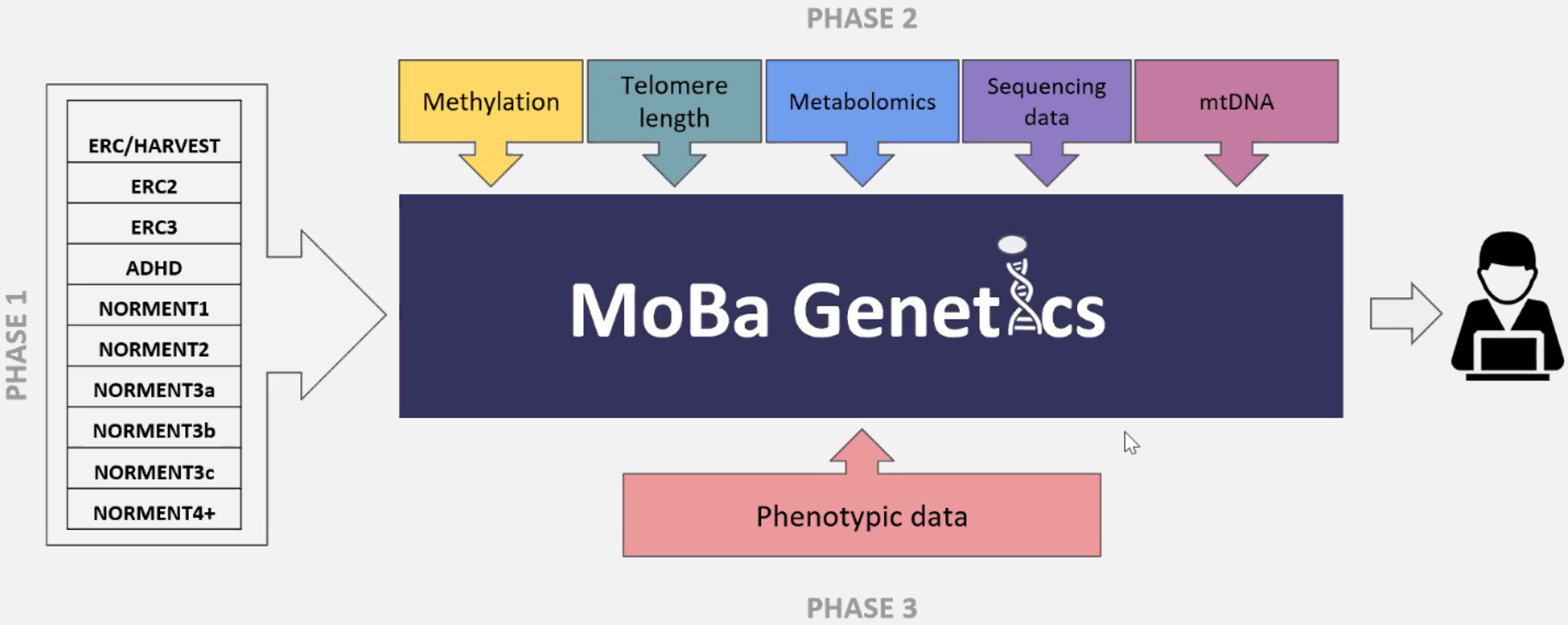


Figure 1. Time line for the questionnaires (Q 1-10), the collection of biological samples within MoBa, and the collection of shed primary teeth to the MoBaTooth Biobank.

Close to 35 000 shed primary teeth from MoBa children

Department of Clinical Dentistry, University of Bergen

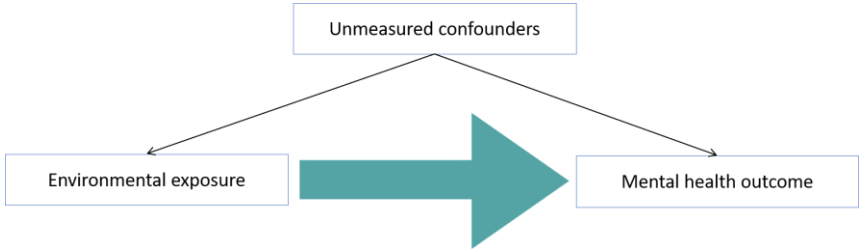
As of June 2021, all 250.000 samples have been genotyped



THE VALUE OF MOBA WILL CONTINUE TO RISE

Examples of study designs

Causal risk factors



Using negative controls (e.g. fathers)
Using sibling control design
Using Mendelian randomization (within-family)

Trajectories

Across development
Premorbid developmental trajectories
Clinical progression trajectories
Before and during the Covid-19 pandemic in adults and youths

Intergenerational transmission of risk

Children-of-twin/sibling design (family pedigrees)
Trio GCTA (genome-wide SNPs)
Polygenic risk scores

Research activity in MoBa 2021

- 171 active research projects
- 13 projects with data collections
- 894 scientific papers (august 2021)
- 57 PhDs (2021)

Human Reproduction, Vol.36, No.4, pp. 1074–1082, 2021
Advance Access Publication on February 17, 2021 doi:10.1093/humrep/deab007

human reproduction ORIGINAL ARTICLE Reproductiv

Growth in children

Maria C. Magnus[1,2,3,*], Allen J. Wi
Håkon K. Gjessing[1,6], Signe Opdal
Liv Bente Romundstad[1], and Siri I

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Submitted on October 20, 2020; resubmitted on December 27, 20

STUDY QUESTION: Is the growth pattern of children conceived by ART differ
SUMMARY ANSWER: Both ART and underlying parental subfertility may con children conceived with and without the use of ART.
WHAT IS KNOWN ALREADY: Children conceived by ART weigh less and a ferences in growth according to mode of conception persist during childhood, unclear.
STUDY DESIGN, SIZE, DURATION: We conducted a prospective study pop pating in the Norwegian Mother, Father and Child Cohort Study (MoBa) and 544
PARTICIPANTS/MATERIALS, SETTING, METHODS: Conception by AR pared maternally reported length/height and weight among children in MoBa fro tion using mixed-effects linear regression. Differences in self-reported height conscription were assessed with linear regression.
MAIN RESULTS AND THE ROLE OF CHANCE: At birth, children conceived by ART were shorter (boys −0.3 cm; 95% CI, −0.5 to −0.1), girls −0.4 cm; 95% CI, −0.5 to −0.3) and lighter (boys −113 grams; 95% CI, −201 to −25, girls −107 grams; 95% CI, −197 to −17). After birth, children conceived by ART grew more rapidly, achieving both greater height and weight at age 3. Children conceived by

RESEARCH

OPEN ACCESS

Role of maternal age and pregnancy history in risk of miscarriage: prospective register based study

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Additional material is published online only. To view please visit the journal online.
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http://dx.doi.org/10.1136/bmj.l869
Accepted: 11 February 2019

ABSTRACT
OBJECTIVES
To estimate the burden of miscarriage in the Norwegian population and to evaluate the associations with maternal age and pregnancy history.
DESIGN
Prospective register based study.
SETTING
Medical Birth Register of Norway, the Norwegian Patient Register, and the induced abortion register.
PARTICIPANTS
All Norwegian women that were pregnant between 2009-13.
MAIN OUTCOME MEASURE
Risk of miscarriage according to the woman's age and pregnancy history estimated by logistic regression.
RESULTS
There were 421 201 pregnancies during the study period. The risk of miscarriage was lowest in women aged 25-29 (10%), and rose rapidly after age 30, reaching 53% in women aged 45 and over. There was a strong recurrence risk of miscarriage, with age adjusted odds ratios of 1.54 (95% confidence interval 1.48 to 1.60) after one miscarriage, 2.21 (2.03 to 2.41) after two, and 3.97 (3.29 to 4.78) after three consecutive miscarriages. The risk of miscarriage was modestly increased if the previous birth ended in a preterm delivery (adjusted odds ratio 1.22, 95% confidence interval 1.12 to 1.29), stillbirth (1.30, 1.11 to 1.53), caesarean section (1.16, 1.12 to 1.21), or if the woman had gestational diabetes in the previous pregnancy (1.19, 1.05 to 1.36). The risk of miscarriage was slightly higher in women who themselves had been small for gestational age (1.08, 1.04 to 1.13).
CONCLUSIONS
The risk of miscarriage varies greatly with maternal age, shows a strong pattern of recurrence, and is also increased after some adverse pregnancy outcomes. Miscarriage and other pregnancy complications might share underlying causes, which could be biological conditions or unmeasured common risk factors.

Introduction
Miscarriage is a common outcome of pregnancy, with most studies reporting 12% to 15% loss among recognised pregnancies by 20 weeks of gestation.[1-6] Quantifying the full burden of miscarriage is challenging because rates of pregnancy loss are high around the time that pregnancies are clinically recognised. As a result, the total rate of recognised loss is sensitive to how early women recognise their pregnancies. There are also differences across countries and studies in distinguishing between miscarriage and stillbirth. Furthermore, the observed miscarriage rate is affected by the competing risk of induced abortion. A general lack of data on induced abortions has made it difficult to determine how seriously this competing risk distorts the estimation of miscarriage rates. Based on national registries or population based cohort studies, the reported risk of miscarriage in Sweden, Finland, and Denmark was between 12.9% and 13.5%.[7-12] A previous Norwegian study included all women treated at one of the main hospitals in Oslo between 2000 and 2002, and estimated a miscarriage rate of 12% when taking into account induced abortions.[8]
Although the cause of most miscarriages is unknown, they presumably result from a complex interplay between parental age, genetic, hormonal, immunological, and environmental factors.[9 10] Genetic factors, including parental chromosomal rearrangements and abnormal embryonic genotypes or karyotypes, could underlie more than half of recurrent miscarriages.[10] Maternal age is the strongest known risk factor. The risk of miscarriage is slightly elevated in the youngest mothers and then rises sharply in older mothers.[7 11] There could be shared underlying risk factors for miscarriage and other adverse pregnancy

BMJ: first published as 10.1136/bmj.l869 on 20 March 2019. Downloaded from http://www.bmj.com/ on 1 November 2021 at Helsebiblioteket gr

ARTICLE OPEN ACCESS

Perinatal Depression and An
With Multiple Sclerosis
A Population-Based Cohort Study

Karine Eid, MD, Øivind Fredvik Torkildsen, MD, PhD, Jan Aarseth, PhD, Heidi Øyen Fle
Trygve Holmøy, MD, PhD, Åslaug Rudjord Lorentzen, MD, PhD, Kjell-Morten Myhr, MD,
Cecilia Simonsen, MD, Cecilie Fredvik Torkildsen, MD, Stig Wergeland, MD, PhD,
Johannes Sverre Willumsen, MD, Nina Øksendal, MD, Nils Erik Gilhus, MD, PhD, and
Marte-Helene Bjørk, MD, PhD

Neurology® 2021;96:e2789-e2800. doi:10.1212/WNL.0000000000012062

Abstract
Objective
To assess the occurrence of perinatal depression and anxiety in wome diagnosis of multiple sclerosis (MS).
Methods
A total of 114,629 pregnant women were included in the Norwegian Mothe Cohort study (1999–2008). We assessed depression and anxiety by questi after pregnancy. Women with MS were identified from national health re records and grouped into (1) MS diagnosed before pregnancy (n = 140) or pregnancy with (2) symptom onset before pregnancy (n = 98) or (3) s pregnancy (n = 308). Thirty-five women were diagnosed with MS in the The reference group (n = 111,627) consisted of women without MS.
Results
Women with MS diagnosed before pregnancy had an adjusted odds ratio of 2.0 (95% confi dence interval, 1.2–3.1) for depression in the third trimester. Risk factors were adverse so cioeconomic factors and history of psychiatric disease and physical/sexual abuse. The risk of anxiety was not increased. Women diagnosed with MS in the postpartum period had especially high risk of postpartum depression. Women with MS symptom onset within 5 years after pregnancy had increased risk of both depression and anxiety during pregnancy, whereas women with more than 5 years until symptom onset did not.

Early Childhood Research Quarterly
Contents lists available at
Early Childhood Rese
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Predicting selection into ECEC of higher qual
The role of parental education and income

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Mari Vaage Wang[a], Ragnhild Eek Brandlistuen[a]

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Keywords:
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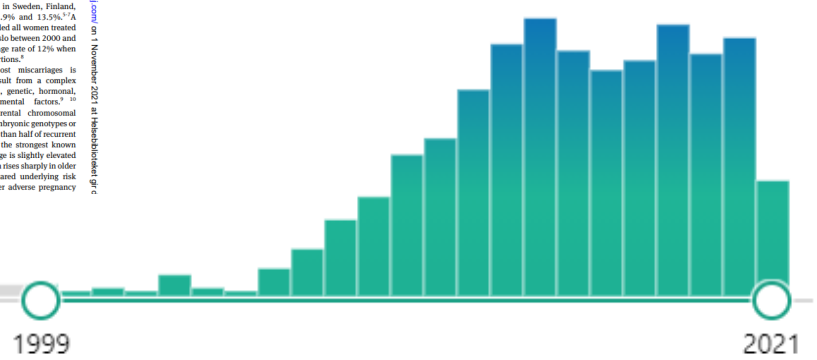
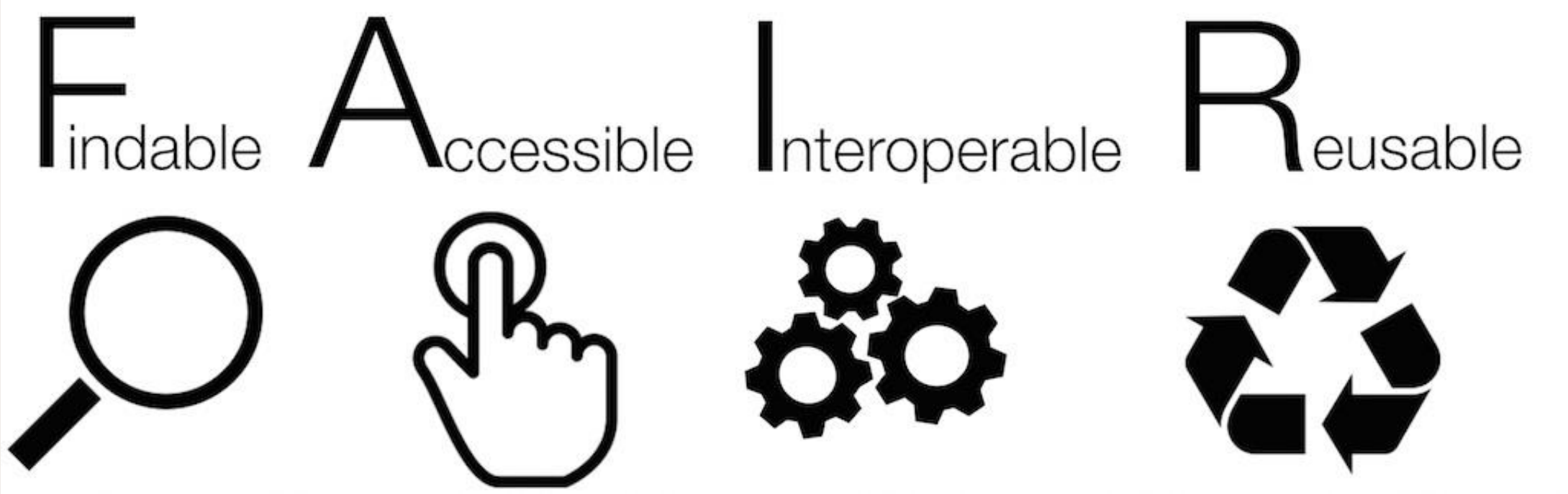
Disadvantaged children
Universal ECEC
MoBa

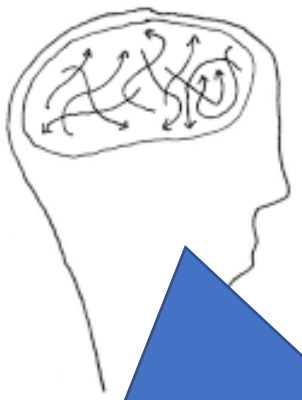
ABSTRACT
There is consensus about the posit on children's development, partic limited knowledge exists on the a potential socioeconomic selection heavily subsidized, and regulated ECEC. Furthermore, we explore th relationship quality. Our concept different quality aspects is for pare Study linked with teacher-reporte by registry data at ECEC and muni degree income, predict child atten Further, higher parental SES and structural quality (i.e., developmental material, staff competence and stability) predict better student-teacher relationship quality in terms of higher level of closeness and less conflict. These findings suggest that ambitions of universal equal access to high quality ECEC are not



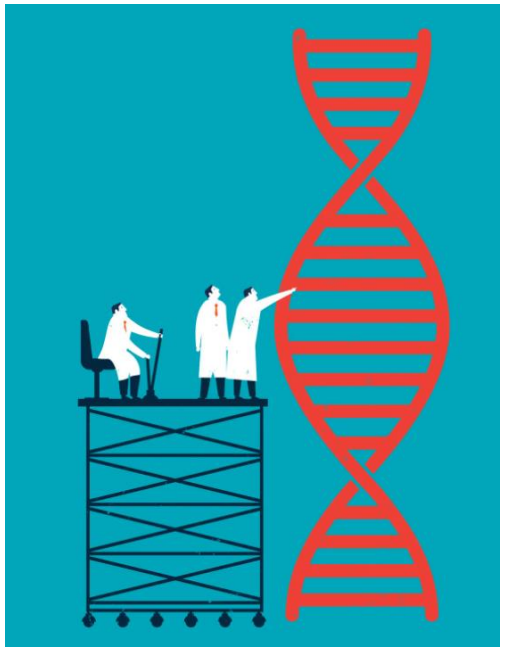
FAIR principles

«Open as possible, closed as necessary»





Nusha Ashjaee / Verywell



The most important discoveries lie ahead

phenotools

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Lorentz Irgens, Leiv Bakketeig, Johs Wiik, Bodolf Hareide, Per Magnus, Camilla Stoltenberg, Ragnhild Nordengen, Kari Kveim Lie, Rolv Terje Lie, Stein Emil Vollset, Kjell Haug, Grete Tell, Pat Schreuder, Kjersti Skjold Rønningen (biobank), Helle Meltzer, Ragnhild Hovengen, Jorid Eide, Arild Sunde and Elin Alsaker, (built up systems for tracking, data cleaning and storage)

It requires risk taking, immense endurance, tolerance for uncertainty, considerable personal stamina, stubbornness and visionary capacities to lead such projects.

Helen Pearson, The life project: The Extraordinary Story of Our Ordinary Lives. London, England: Allen Lane; 2016

Scientific advisory board

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Brandlistuen

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Pål Surén

Anne Lise
Brantsæter

Børge Sivertsen

It takes a village..

… and funding

- The Ministry of Health and Care Services
- The Norwegian Institute of Public Health (NIPH)
- <u>Projects and partners:</u>
  - Norwegian Minestry of Education and Research
  - The Research Council of Norway
  - National Institutes of Health
  - European research council (ERC)
  - Studies – such as (ABC-studien NIH)

NORWEGIAN MINISTRY OF HEALTH AND CARE SERVICES

NORWEGIAN MINISTRY OF EDUCATION AND RESEARCH

The Research Council of Norway

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Norwegian Institute of Public Health

NIPH

Norwegian Institute of Public Health

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Thank you!