CENTRE FOR
FERTILITY AND HEALTH

European Research Council
Established by the European Commission

BIOSFER – A Synergy Grant

Siri E. Håberg
MD PhD
Centre for Fertility and Health
Norwegian Institute of Public Health

Norwegian Centre of Excellence

Norwegian Centre of Excellence

Norwegian Institute of Public Health

Synergy Grant

European Research Council
Established by the European Commission

Are you a researcher that wants to address a research problem so ambitious, that can not be dealt with you and your team alone? The Synergy Grants could be for you!

Synergy Grants can be up to a maximum of **€ 10 million for up to a period of 6 years**
An addition **€ 4 million can be requested** in the proposal for special costs

BIOSFER

Untangling biologic and social causes of low fertility in modern societies

Siri E. Håberg

NIPH
Norwegian Institute of Public Health

Medicine
Female reproduction
Genetics/epigenetics

Cecilia H. Ramlau-Hansen

AARHUS UNIVERSITY

Epidemiology
Semen quality/puberty
Infertility

Mikko Myrskylä

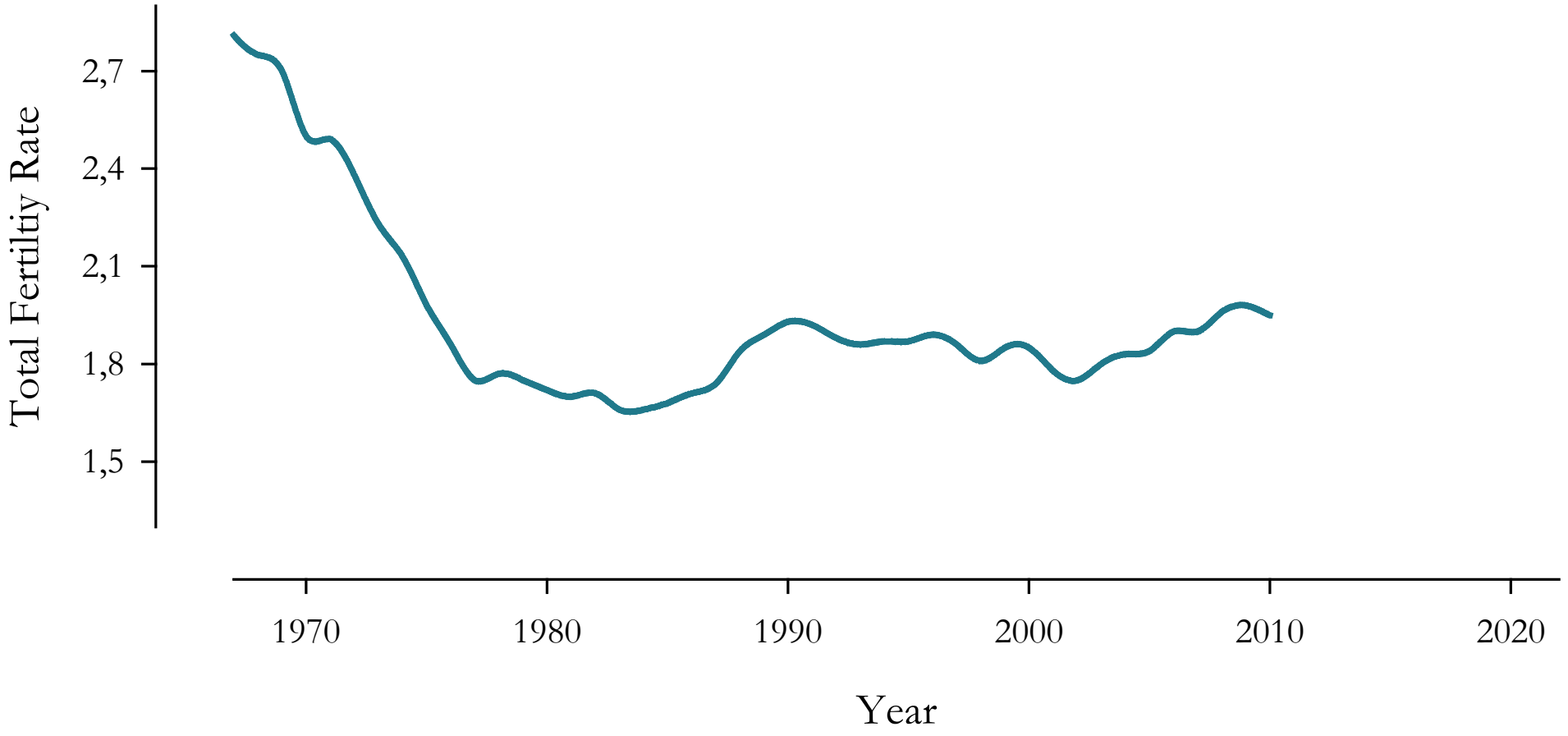
MAX PLANCK INSTITUTE
FOR DEMOGRAPHIC RESEARCH

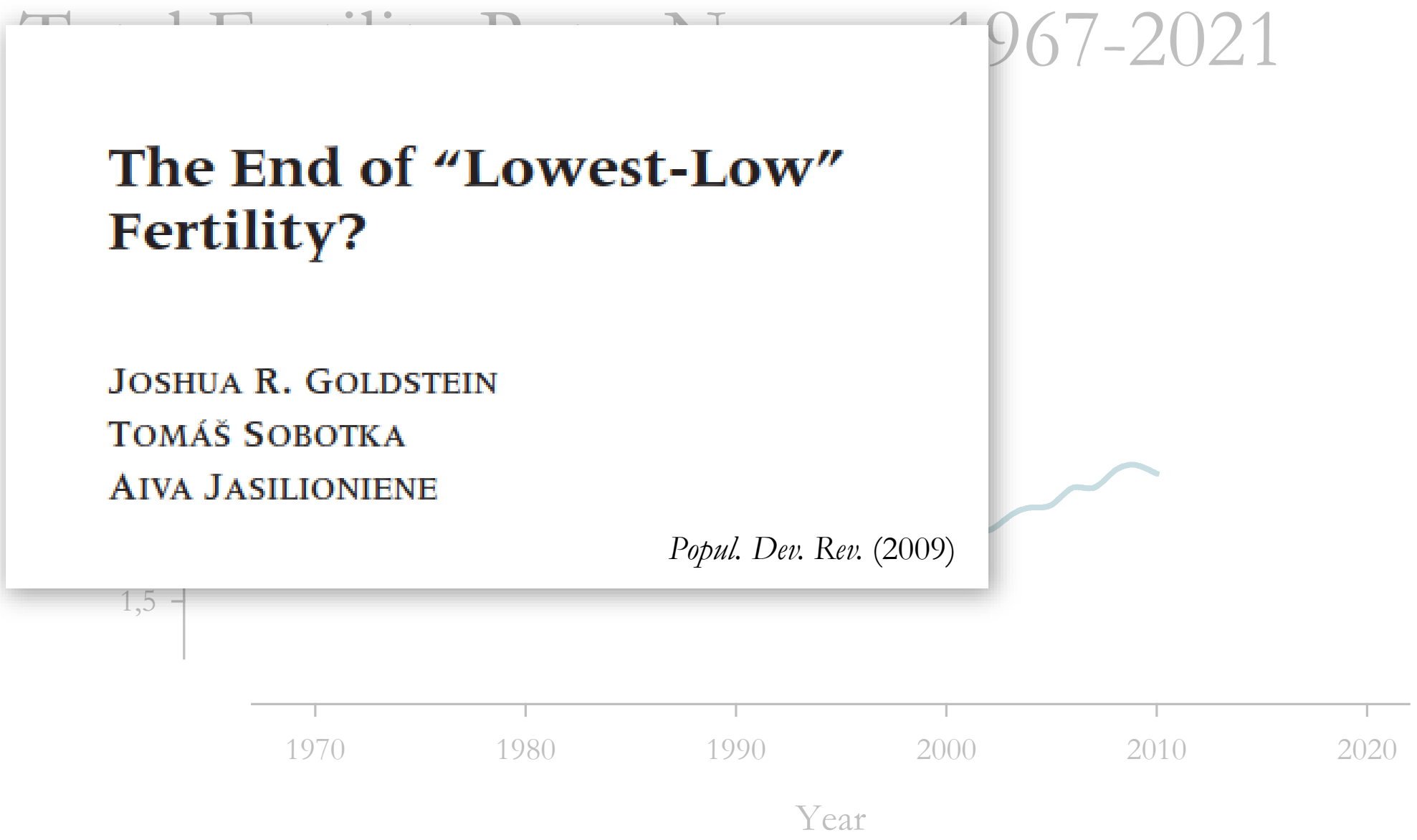
Demography
Social sciences
Statistics

BIOSFER

Untangling biologic and social causes of low fertility in modern societies

Total Fertility Rate, Norway 1967-2021





The End of "Lowest-Low" Fertility?

JOSHUA R. GOLDSTEIN
TOMÁŠ SOBOTKA
AIVA JASILIONIENE

Popul. Dev. Rev. (2009)

The En
Fertilit

JOSHUA R.
TOMÁŠ SOE
AIVA JASILI

1,5

1970

2020

Year

Vol 460|6 August 2009|doi:10.1038/nature08230 nature

nature LETTERS

Advances in development reverse fertility declines

Mikko Myrskylä[1], Hans-Peter Kohler[1] & Francesco C. Billari[2]

During the twentieth century, the global population has gone through unprecedented increases in economic and social development that coincided with substantial declines in human fertility and population growth rates[1,2]. The negative association of fertility with economic and social development has therefore become one of the most solidly established and generally accepted empirical regularities in the social sciences[1–3]. As a result of this close connection between development and fertility decline, more than half of the global population now lives in regions with below-replacement fertility (less than 2.1 children per woman)[4]. In many highly developed countries, the trend towards low fertility has also been deemed irreversible[5–9]. Rapid population ageing, and in some cases the prospect of significant population decline, have therefore become a central socioeconomic concern and policy challenge[10]. Here we show, using new cross-sectional and longitudinal analyses of the total fertility rate and the human development index (HDI), a fundamental change in the well-established negative relationship between fertility and development as the global population entered the twenty-first century. Although development continues to promote fertility decline at low and medium HDI levels, our analyses show that at advanced HDI levels, further development can reverse the declining trend in fertility. The previously negative development–fertility relationship has become J-shaped, with the HDI being positively associated with fertility among highly developed countries. This reversal of fertility decline as a result of continued economic and social development has the potential to slow the rates of population ageing, thereby ameliorating the social and economic problems that have been associated with the emergence and persistence of very low fertility.

The cross-country association between total fertility rate (TFR) Information). The TFR is shown for years 1975 and 2005 relative to the lowest TFR that was observed while a country's HDI was within the window of 0.85–0.9. The reference year is the first year in which this lowest TFR is observed. A line is then used to connect the HDI–TFR

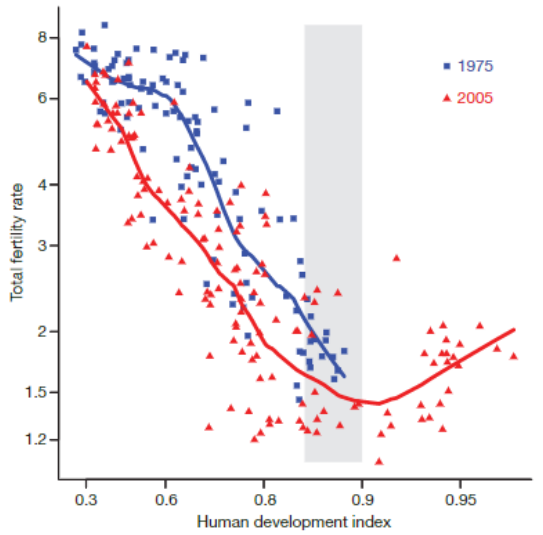


Figure 1 | Cross-sectional relationship between TFR and HDI in 1975 and 2005. The TFR reflects the number of children that would be born to a woman during her lifetime if she experienced the age-specific fertility rates

The En
Fertilit

JOSHUA R.
TOMÁŠ SOB
AIVA JASIL

Vol 460|6 August 2009|doi:10.1038/nature08230 nature

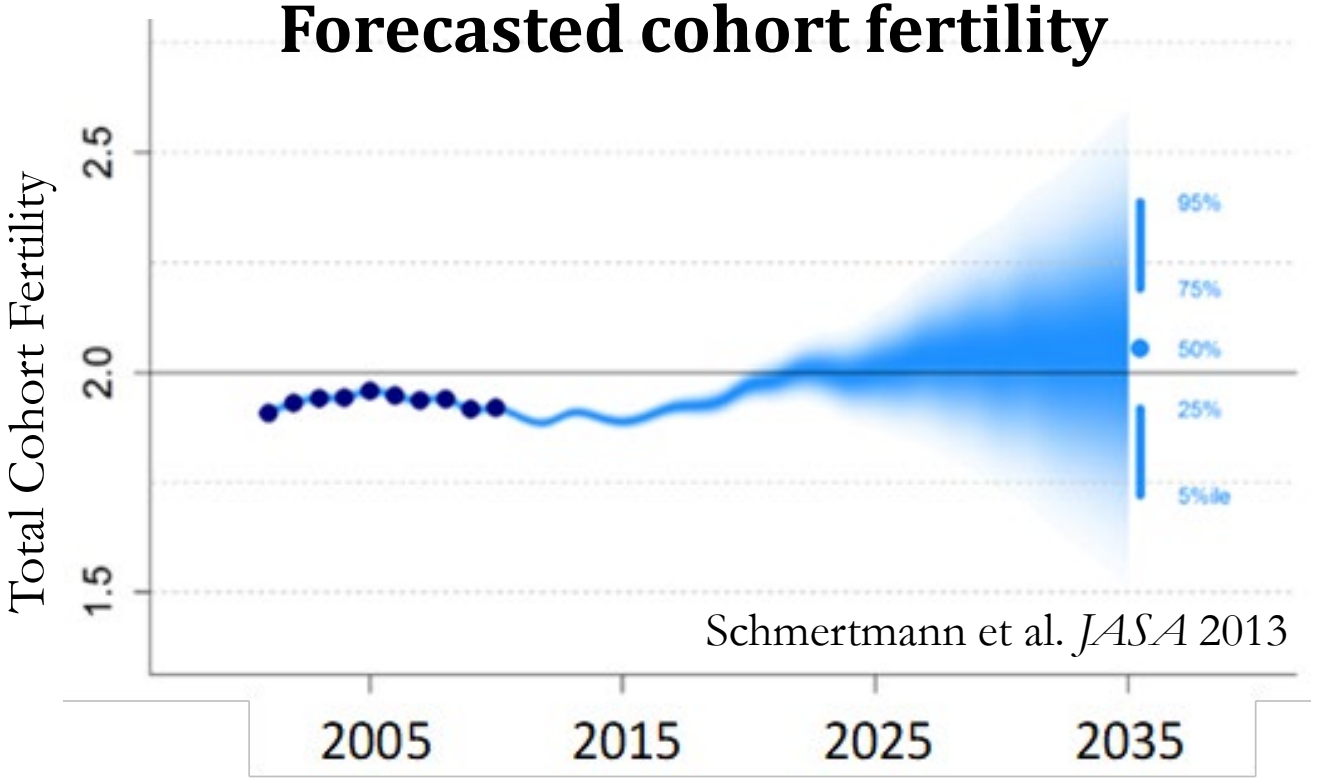
nature LETTERS

Advances in development reverse fertility declines

Mikko Myrskylä[1], Hans-Peter Kohler[1] &

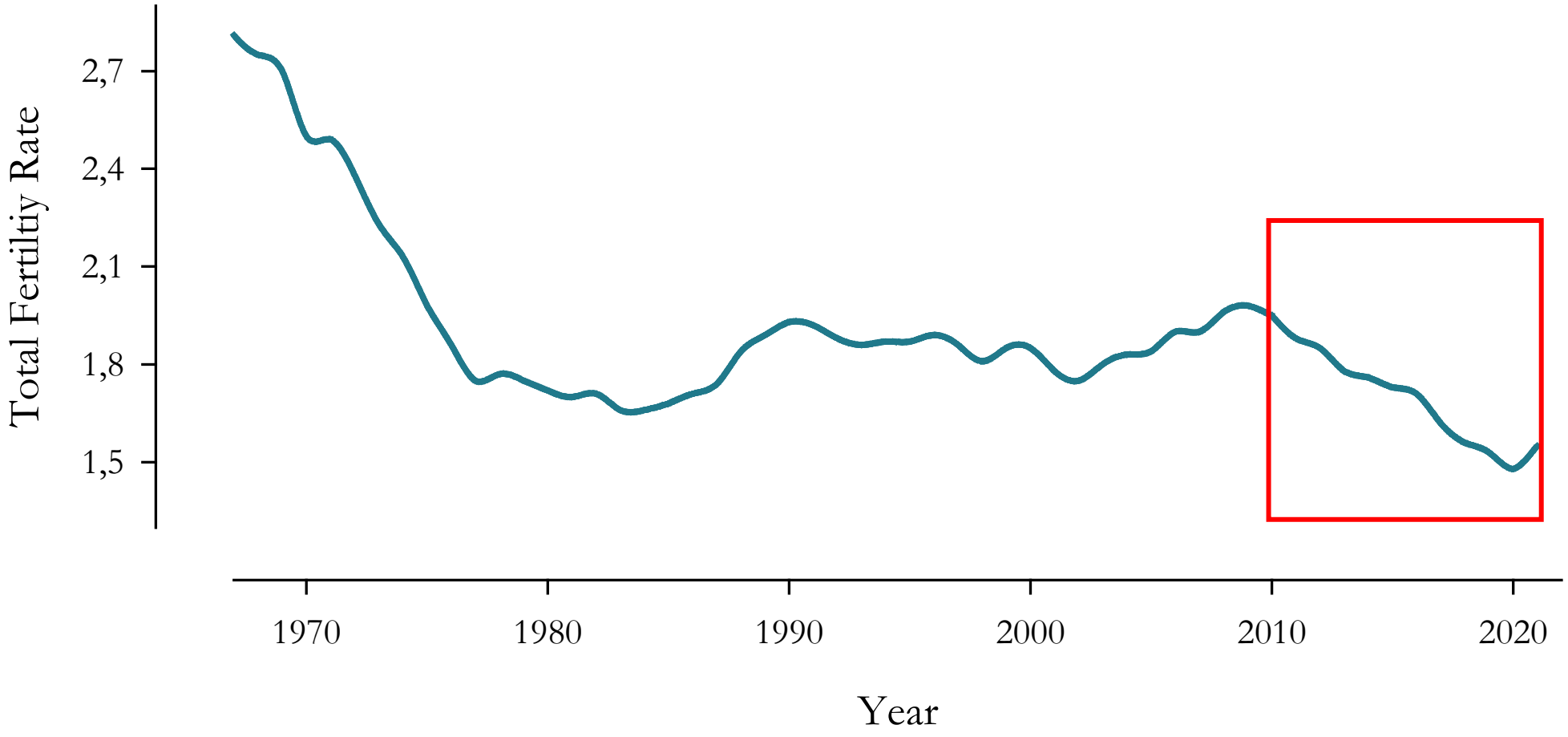
During the twentieth century, the global pop
through unprecedented increases in economic a
ment that coincided with substantial declines
and population growth rates[1,2]. The negative ass
with economic and social development has the
of the most solidly established and generally a
regularities in the social sciences[1–3]. As a re
connection between development and fertility
half of the global population now lives in reg
replacement fertility (less than 2.1 children per
highly developed countries, the trend towards lo
been deemed irreversible[5–9]. Rapid population a
cases the prospect of significant population decli
become a central socioeconomic concern and
Here we show, using new cross-sectional and lon
of the total fertility rate and the human develop
a fundamental change in the well-established
ship between fertility and development as the
entered the twenty-first century. Although devel
to promote fertility decline at low and mediu
analyses show that at advanced HDI levels, fu
can reverse the declining trend in fertility. The p
development–fertility relationship has become
HDI being positively associated with fertili
developed countries. This reversal of fertility
of continued economic and social development h
slow the rates of population ageing, thereby
social and economic problems that have bee
the emergence and persistence of very low ferti
The cross-country association between total

Forecasted cohort fertility



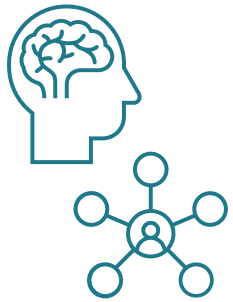
Schmertmann et al. *JASA* 2013

Total Fertility Rate, Norway 1967-2021



Psychological factors

Social factors



Fertility intentions

Psychological factors

Social factors

Fertility intentions

FERTILITY

FECUNDITY

Psychological factors

Social factors

Fertility intentions

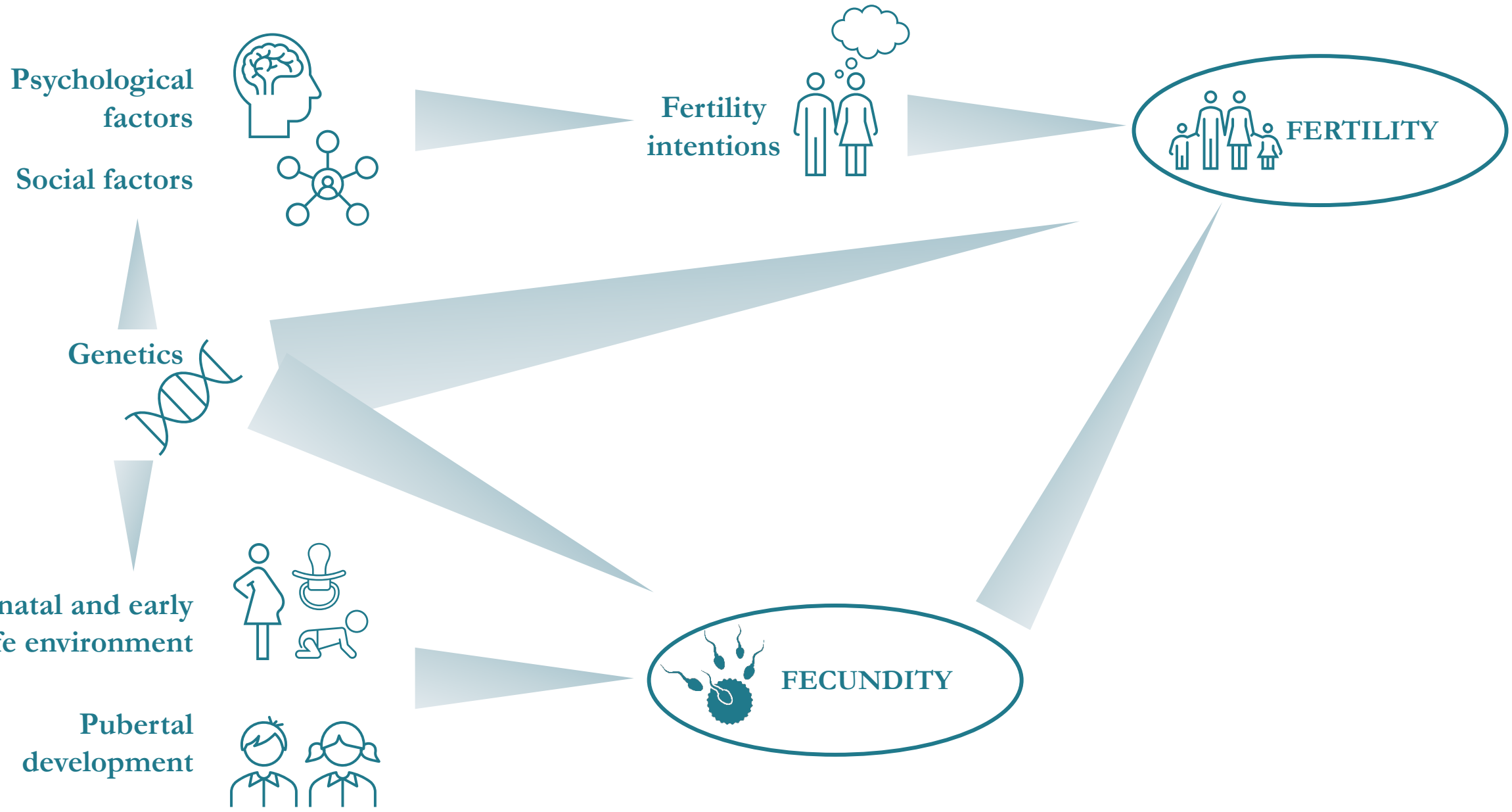
FERTILITY

Prenatal and early life environment

Pubertal development

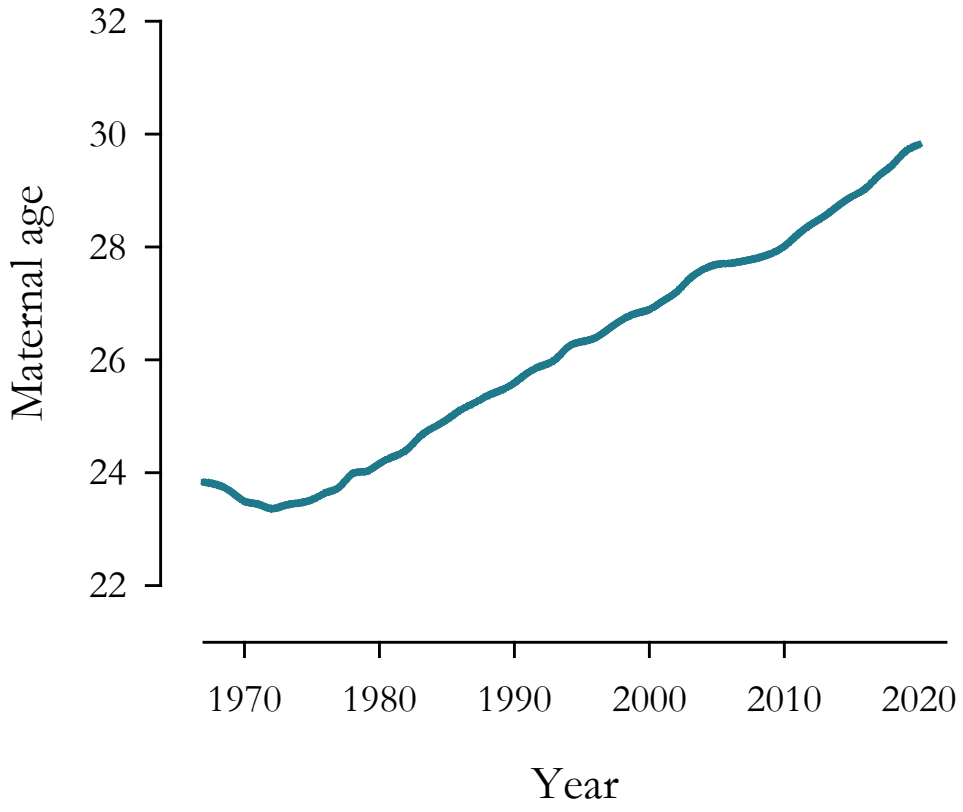
FECUNDITY

BIOSFER


Psychological factors
Social factors
Genetics
Prenatal and early life environment
Pubertal development
Fertility intentions
FERTILITY
FECUNDITY

BIOSFER

Maternal age at first birth, Norway 1970-2020



Psychological factors

Social factors

Fertility intentions

FERTILITY

Age

Egg count

Prenatal and early life environment

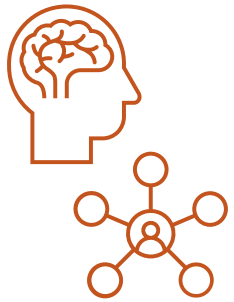
Pubertal development

FECUNDITY

BIOSFER

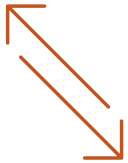
Psychological factors

Social factors



Fertility intentions

FERTILITY



Age

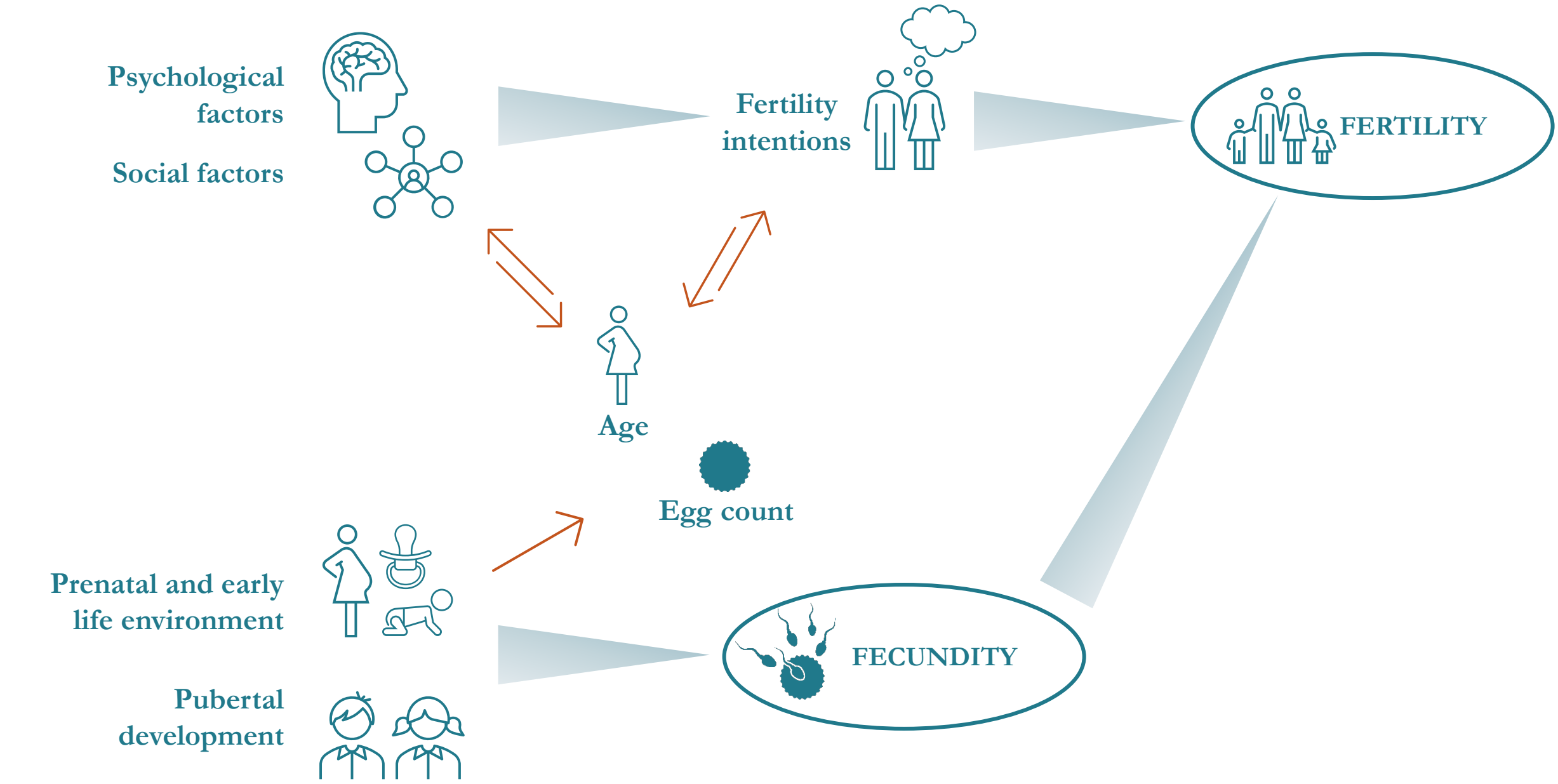
Egg count

Prenatal and early life environment

Pubertal development

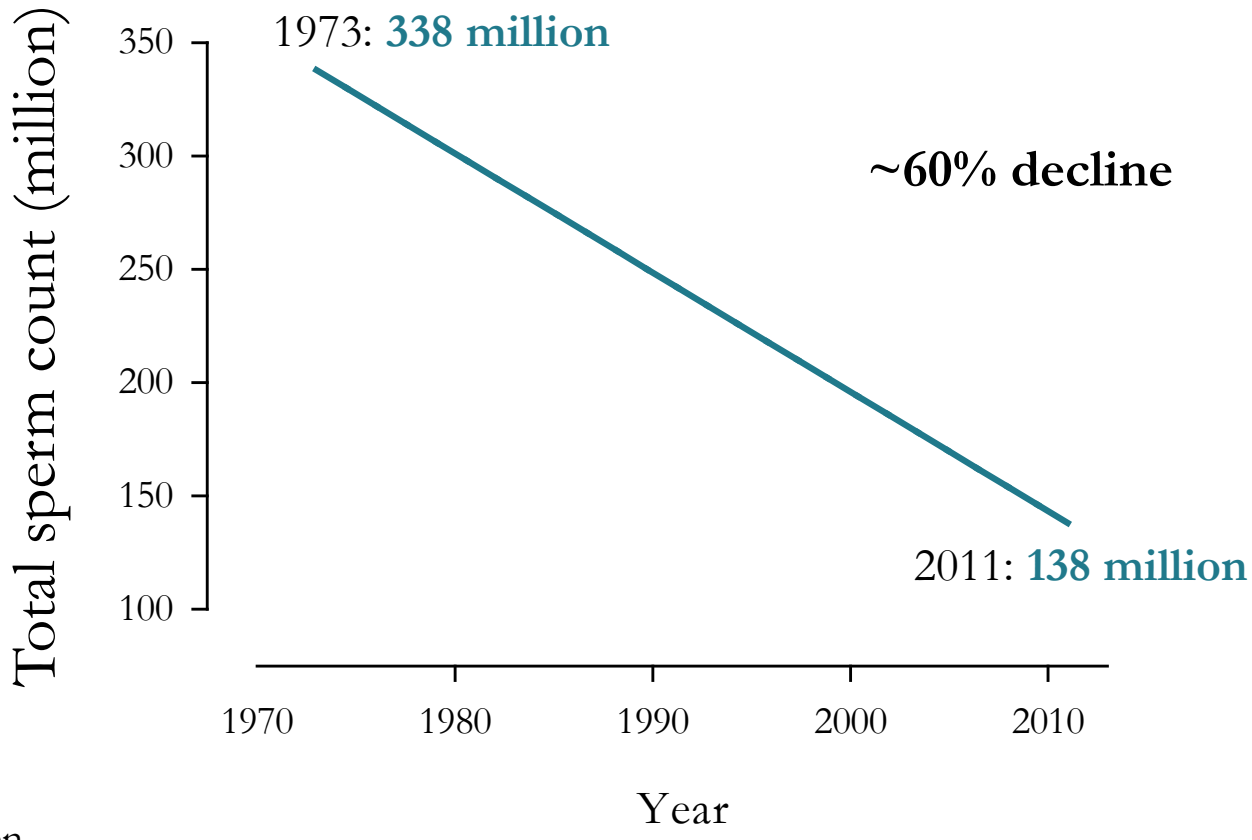
FECUNDITY

BIOSFER


Psychological factors
Social factors
Fertility intentions
FERTILITY
Age
Egg count
Prenatal and early life environment
Pubertal development
FECUNDITY

BIOSFER

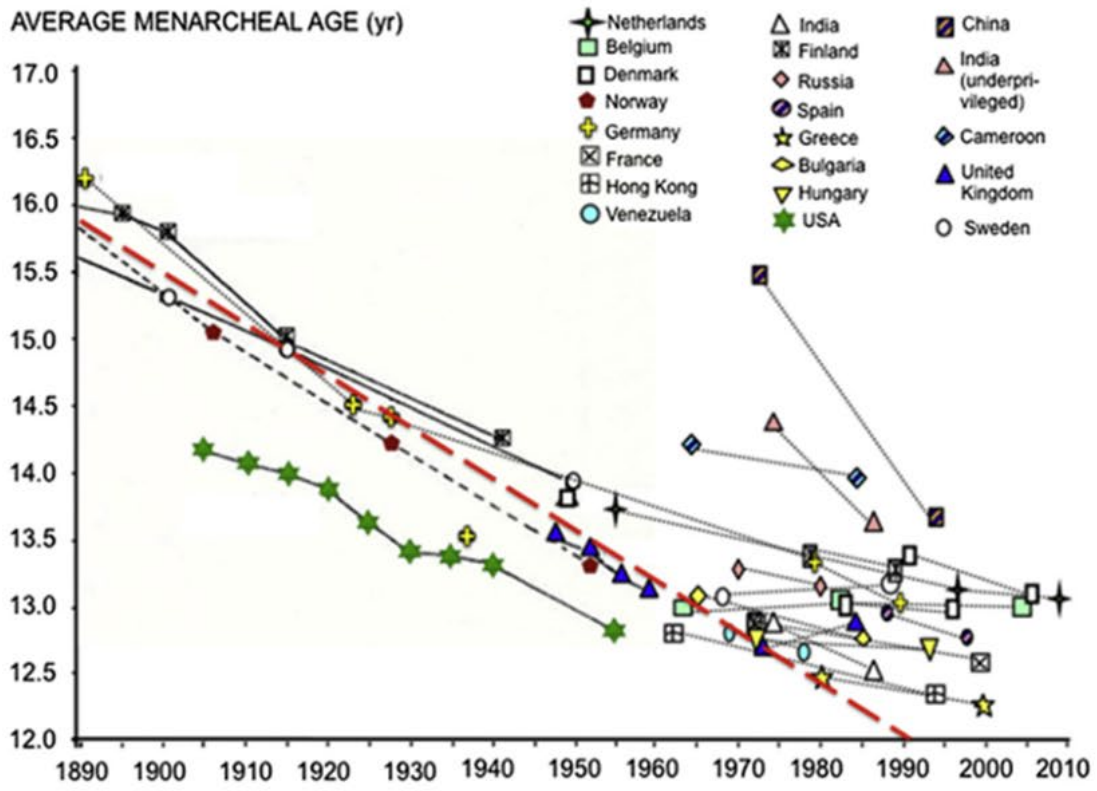
Is semen quality declining?



Meta analysis:
185 studies / 42 935 men

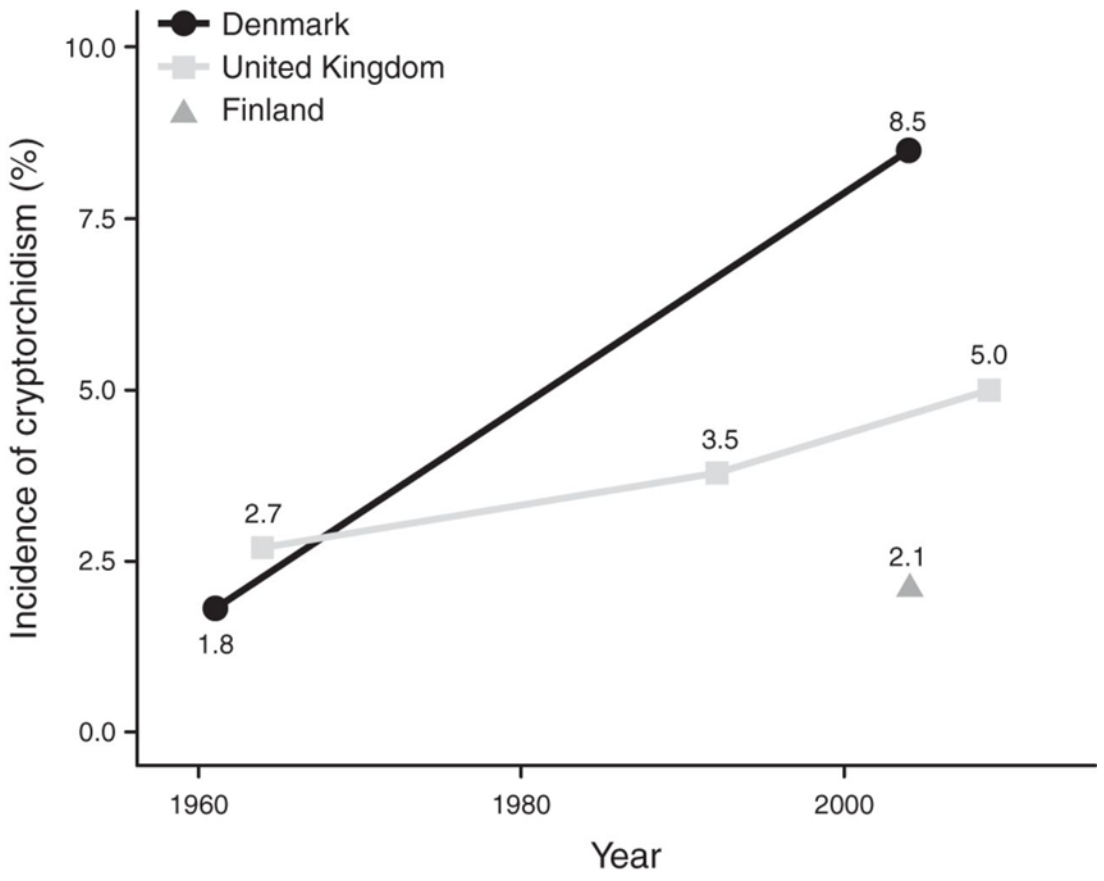
Figure modified from Levine et al, *Hum. Rep. Up.* 2017

Decreasing age at first menstruation?



Parent et al., *Front Neuroendocrinol* 2015

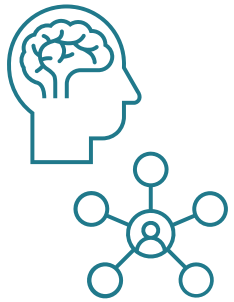
Increasing number with undescended testicles?



Skakkebaek NE et al. *Physiol Rev* 2016

Psychological factors

Social factors



Genetics

Prenatal and early life environment

Pubertal development

Fertility intentions

Diet

Smoking

Alcohol

Age

Semen quality

Egg count

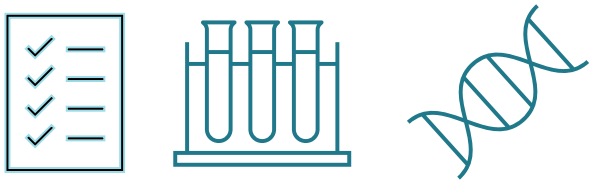
FECUNDITY

FERTILITY

BIOSFER

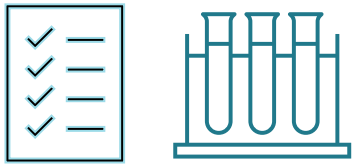
Data Sources

114 000 young adults (born 1999-2009) + parents



Danish National Birth Cohort

100 000 young adults (born 1996-2003) + parents



The Puberty Cohort

&

The Fetal Programming of Semen Quality Cohort

New Data

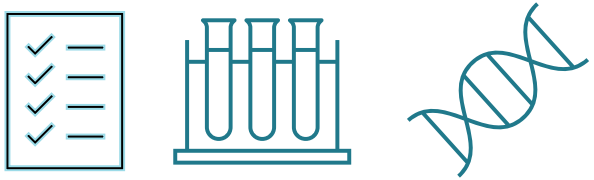
Questionnaires
Clinical Examination
Pregnancy Planner Cohort
Randomized Controlled Trial

Data Sources

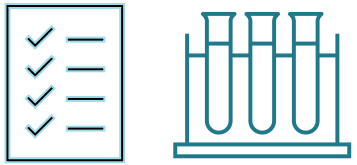
New Data

Danish and Norwegian Administrative Registers

114 000 young adults (born 1999-2009) + parents



100 000 young adults (born 1996-2003) + parents



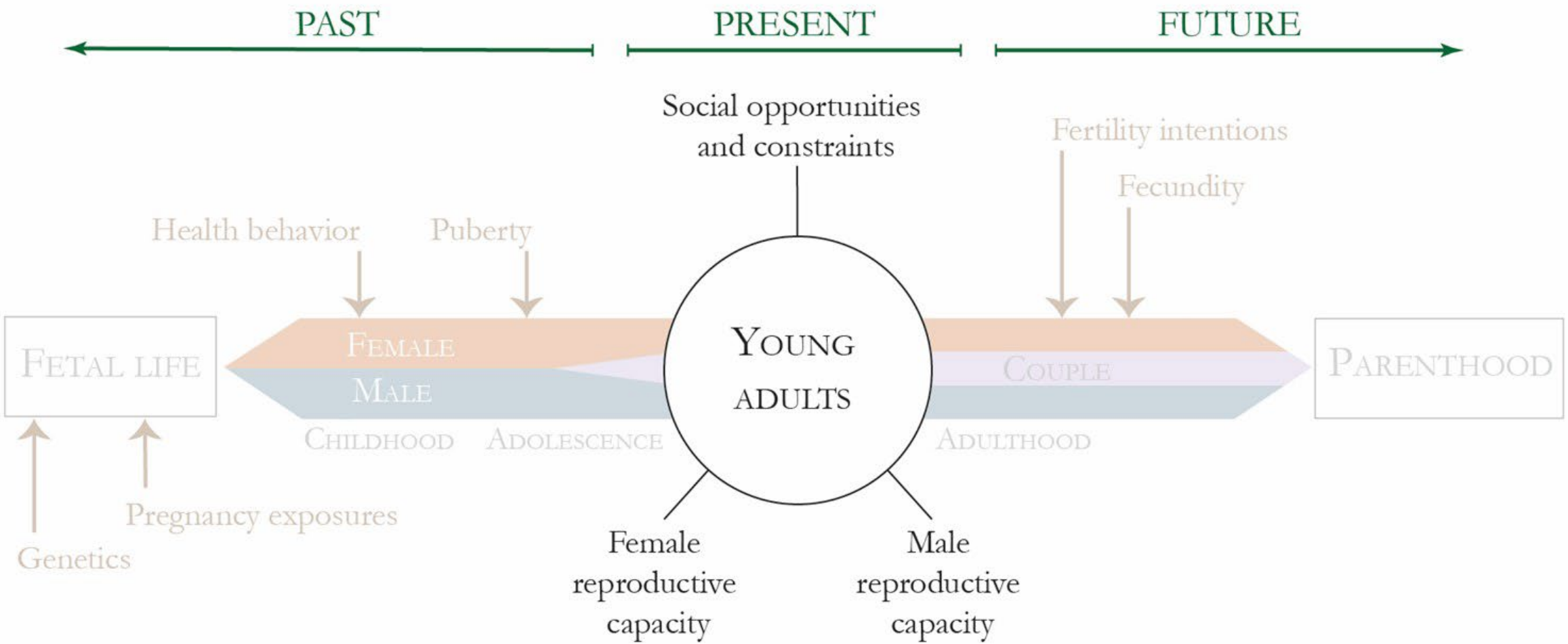
The Puberty Cohort

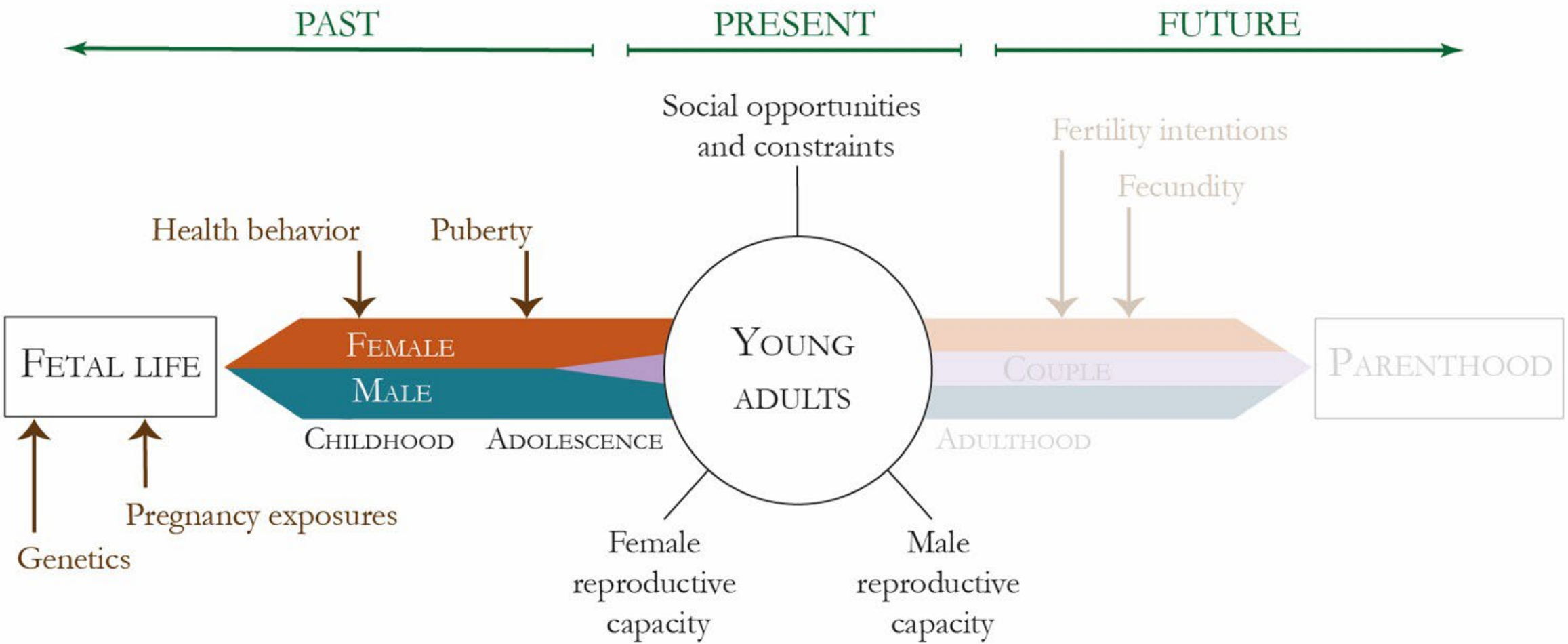
&

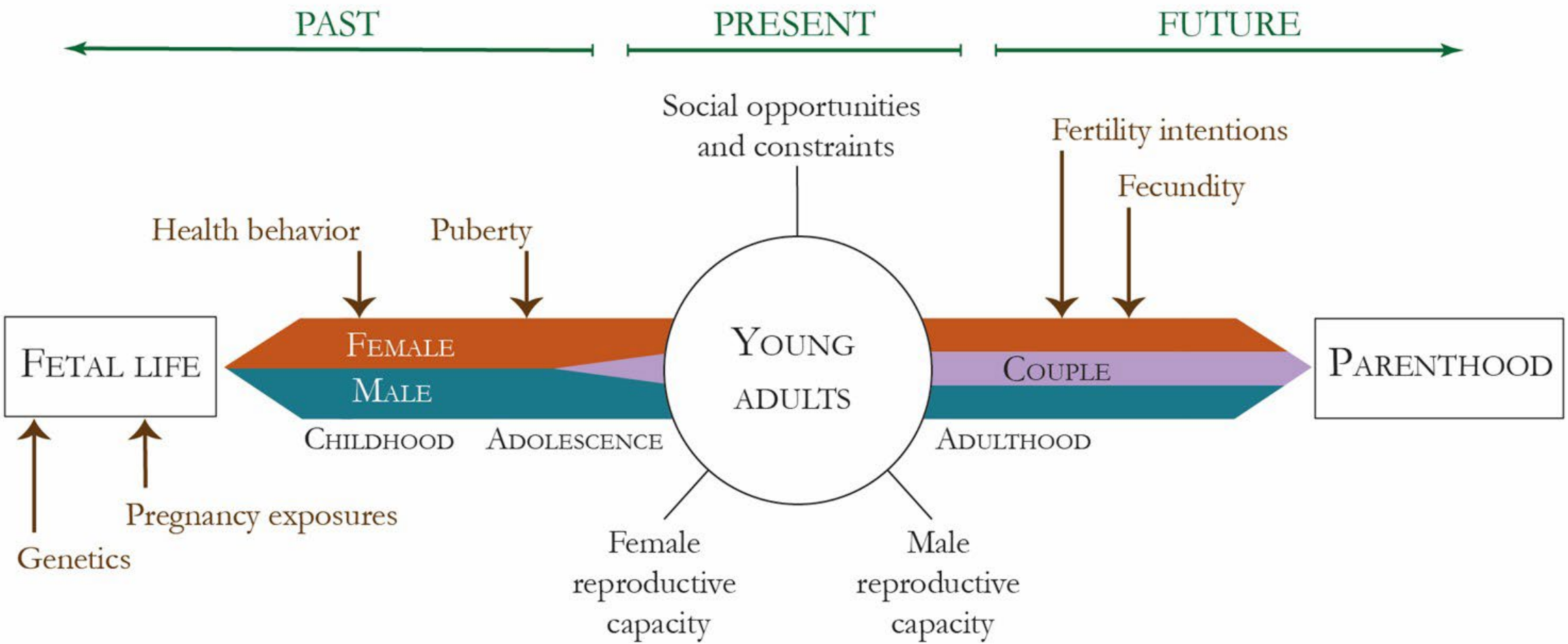
The Fetal Programming of Semen Quality Cohort

Questionnaires
Clinical Examination
Pregnancy Planner Cohort
Randomized Controlled Trial

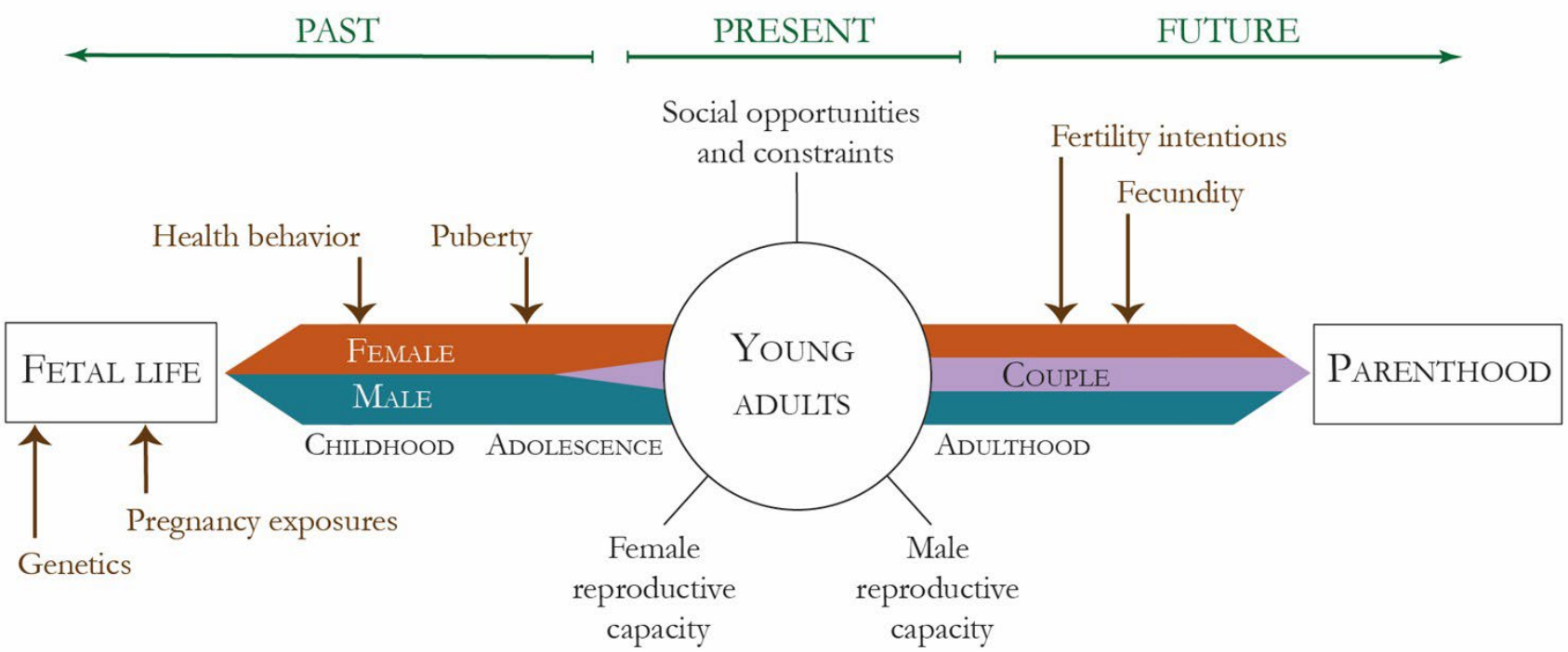
Entire Population


PAST
PRESENT
FUTURE
Social opportunities and constraints
Fertility intentions
Fecundity
Health behavior
Puberty
FETAL LIFE
FEMALE
MALE
YOUNG ADULTS
COUPLE
PARENTHOOD
CHILDHOOD
ADOLESCENCE
ADULTHOOD
Genetics
Pregnancy exposures
Female reproductive capacity
Male reproductive capacity


PAST
PRESENT
FUTURE
Social opportunities and constraints
Fertility intentions
Fecundity
Health behavior
Puberty
FETAL LIFE
FEMALE
MALE
YOUNG ADULTS
COUPLE
PARENTHOOD
CHILDHOOD
ADOLESCENCE
ADULTHOOD
Genetics
Pregnancy exposures
Female reproductive capacity
Male reproductive capacity


PAST
PRESENT
FUTURE
Social opportunities and constraints
Fertility intentions
Fecundity
Health behavior
Puberty
FETAL LIFE
FEMALE
MALE
YOUNG ADULTS
COUPLE
PARENTHOOD
CHILDHOOD
ADOLESCENCE
ADULTHOOD
Genetics
Pregnancy exposures
Female reproductive capacity
Male reproductive capacity

BIOSFER - SYNERGY



BIOSFER - IMPACT

BIOSFER gives fundamental information on what determines fertility today

BIOSFER - IMPACT

BIOSFER gives fundamental information on what determines fertility today

BIOSFER paves the way for an integrative study of fertility

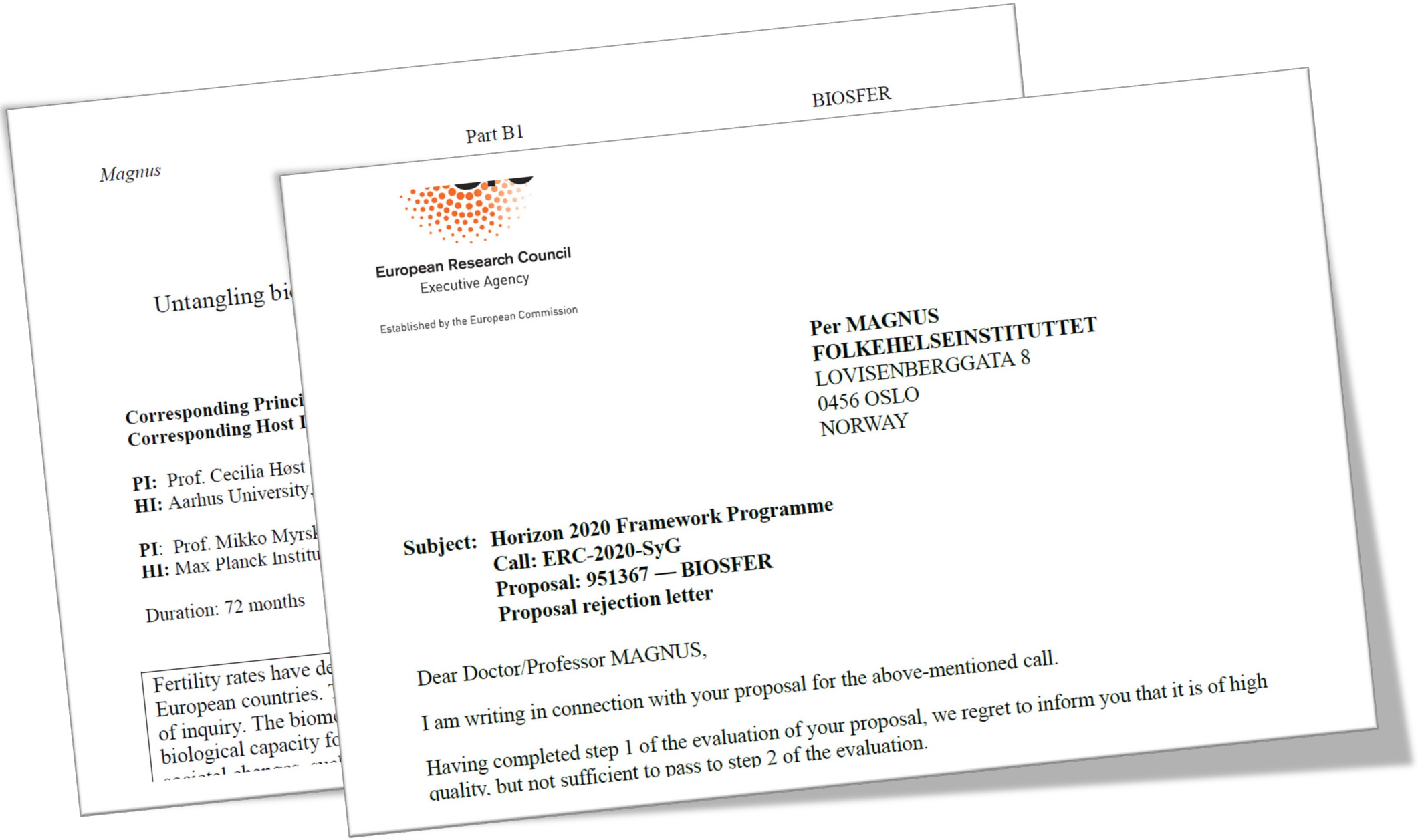
BIOSFER - IMPACT

BIOSFER gives fundamental information on what determines fertility today

BIOSFER paves the way for an integrative study of fertility

BIOSFER creates timely understanding on how modern societies shape formative years for fertility

The application process



Magnus

Part B1

BIOSFER

Untangling bi

Corresponding Princi
Corresponding Host I

PI: Prof. Cecilia Høst
HI: Aarhus University

PI: Prof. Mikko Myrsk
HI: Max Planck Institu

Duration: 72 months

Fertility rates have de
European countries.
of inquiry. The biome
biological capacity fo

European Research Council
Executive Agency

Established by the European Commission

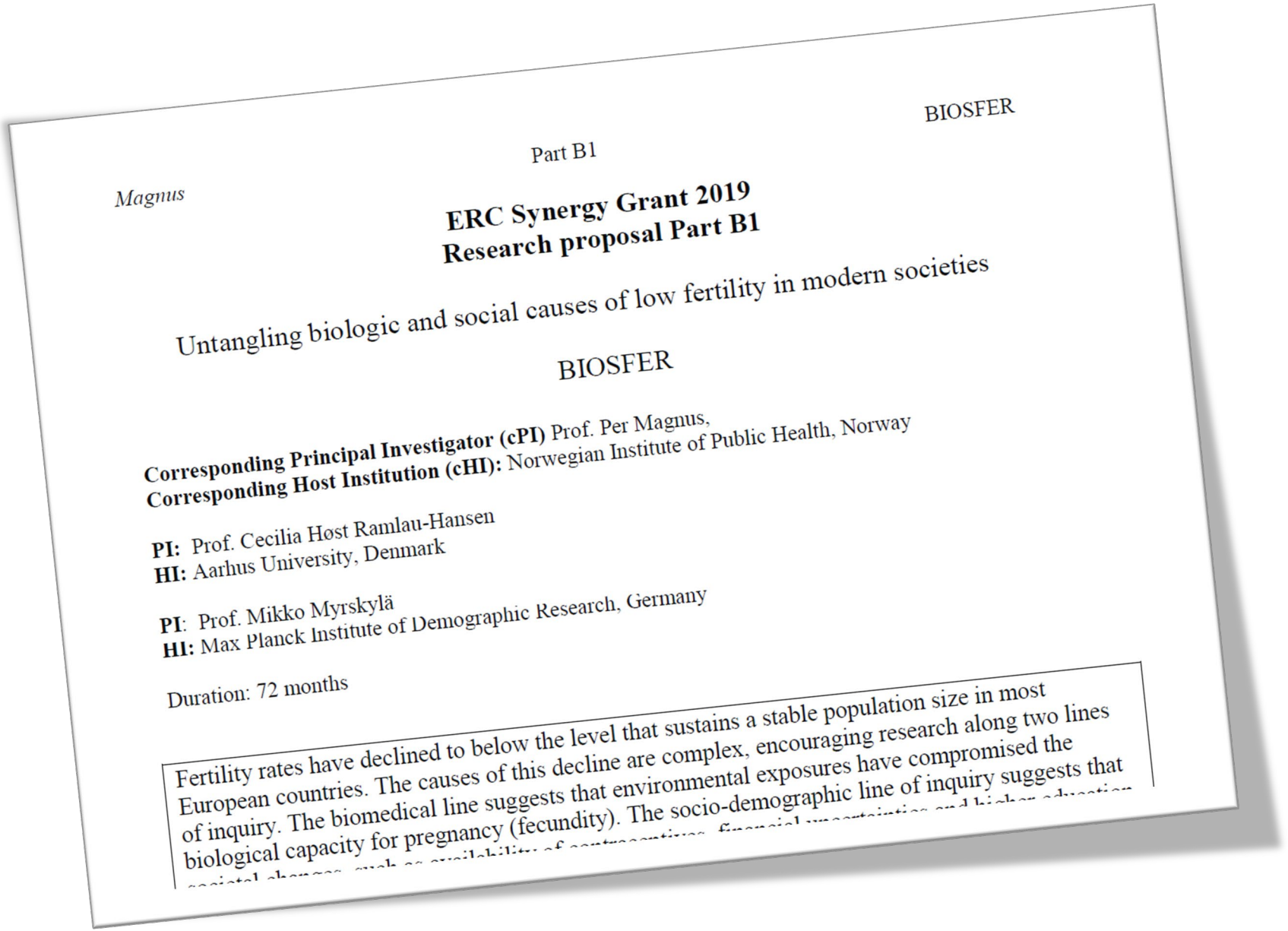
Per MAGNUS
FOLKEHELSEINSTITUTTET
LOVISENBERGGATA 8
0456 OSLO
NORWAY

Subject: Horizon 2020 Framework Programme
Call: ERC-2020-SyG
Proposal: 951367 — BIOSFER
Proposal rejection letter

Dear Doctor/Professor MAGNUS,

I am writing in connection with your proposal for the above-mentioned call.

Having completed step 1 of the evaluation of your proposal, we regret to inform you that it is of high quality, but not sufficient to pass to step 2 of the evaluation.



BIOSFER

Part B1

Magnus

ERC Synergy Grant 2019
Research proposal Part B1

Untangling biologic and social causes of low fertility in modern societies

BIOSFER

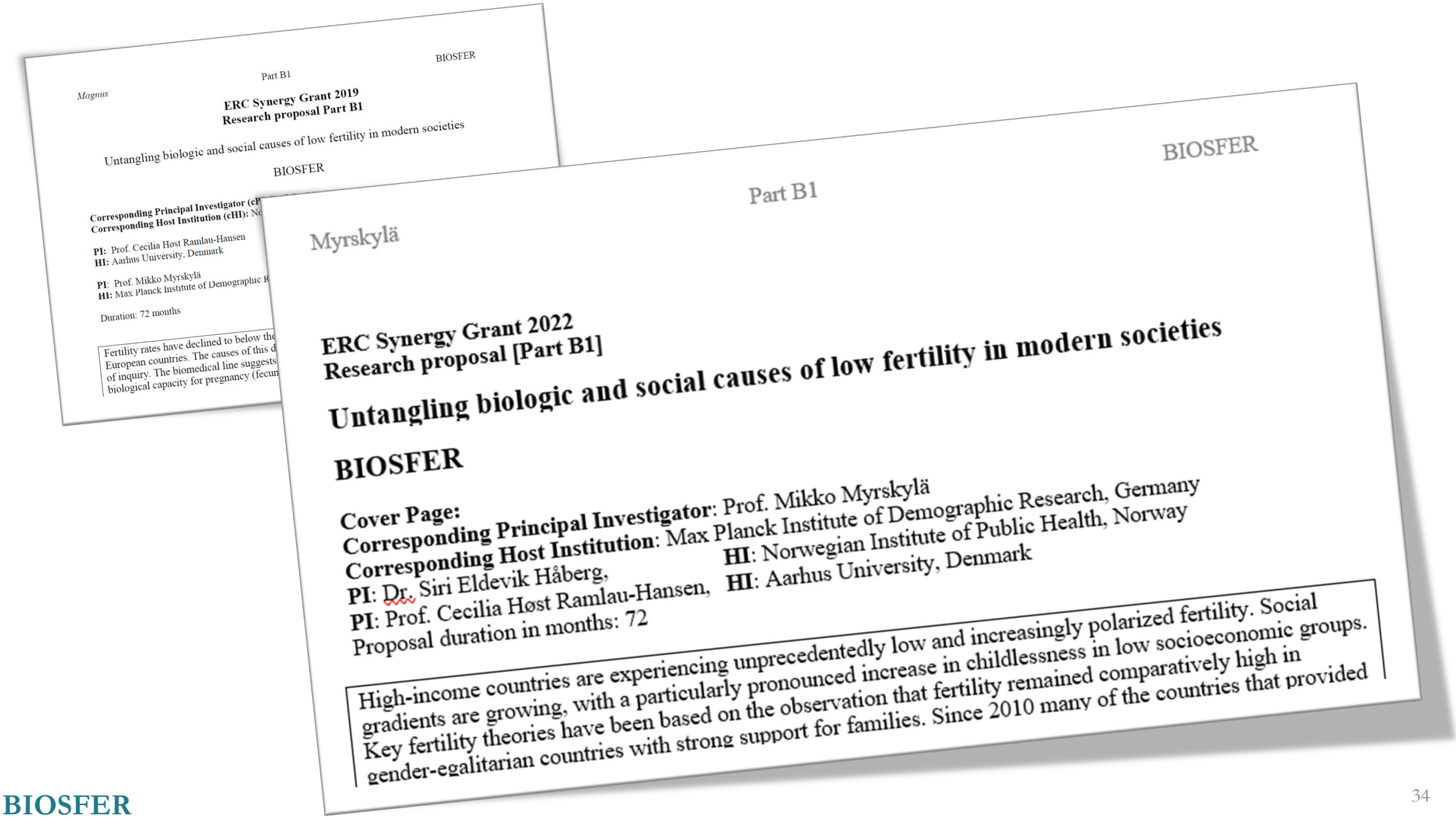
Corresponding Principal Investigator (cPI) Prof. Per Magnus,
Corresponding Host Institution (cHI): Norwegian Institute of Public Health, Norway

PI: Prof. Cecilia Høst Ramlau-Hansen
HI: Aarhus University, Denmark

PI: Prof. Mikko Myrskylä
HI: Max Planck Institute of Demographic Research, Germany

Duration: 72 months

Fertility rates have declined to below the level that sustains a stable population size in most European countries. The causes of this decline are complex, encouraging research along two lines of inquiry. The biomedical line suggests that environmental exposures have compromised the biological capacity for pregnancy (fecundity). The socio-demographic line of inquiry suggests that


Magnus
Part B1
BIOSFER
ERC Synergy Grant 2019
Research proposal Part B1
Untangling biologic and social causes of low fertility in modern societies
BIOSFER
Corresponding Principal Investigator (cP
Corresponding Host Institution (cHI): No
PI: Prof. Cecilia Høst Ramlau-Hansen
HI: Aarhus University, Denmark
PI: Prof. Mikko Myrskylä
HI: Max Planck Institute of Demographic R
Duration: 72 months
Fertility rates have declined to below the
European countries. The causes of this d
of inquiry. The biomedical line suggests
biological capacity for pregnancy (fecun
Myrskylä
Part B1
BIOSFER
ERC Synergy Grant 2022
Research proposal [Part B1]
Untangling biologic and social causes of low fertility in modern societies
BIOSFER
Cover Page:
Corresponding Principal Investigator: Prof. Mikko Myrskylä
Corresponding Host Institution: Max Planck Institute of Demographic Research, Germany
PI: Dr. Siri Eldevik Håberg,
PI: Prof. Cecilia Høst Ramlau-Hansen,
HI: Norwegian Institute of Public Health, Norway
HI: Aarhus University, Denmark
Proposal duration in months: 72
High-income countries are experiencing unprecedentedly low and increasingly polarized fertility. Social
gradients are growing, with a particularly pronounced increase in childlessness in low socioeconomic groups.
Key fertility theories have been based on the observation that fertility remained comparatively high in
gender-egalitarian countries with strong support for families. Since 2010 many of the countries that provided

The application process

Step 1 Nov 2021
Step 2 March 2022

Step 3
Sept 2022

360 applications → 100 invited for interview

European Research Council
Established by the European Commission

POTENTIAL QUESTIONS:

1. Scandinavian fertility is the most studied topic in all of demogr
   m€ investment into this thoroughly studied topic?
2. Who decides whether fertility trends are good or bad? Economis
   perspective than environmentalists. Individuals may have a diffe
   communities. Who are you serving with this project?
3. The proposal repeatedly makes reference to limitations in existi
   This raises the expectation that the project will contribute to the
   development/improvement of theories on the topic.
4. What is a good theory (in general and in the specific case of the
5. You argue from the life course perspective but then plan to stud
   adults. How is this compatible with the life course perspective?
   stage over the course of individuals life; we invest in important
   elements such as timing and duration).
6. The studies are performed in two Nordic countries with differen
   How does BIOSFER argue that observations of differences in p
   result of differences in "national spirits", but can be generalized
   regions?
7. Power and the ability to achieve the stated cohort sizes: taking i
   rate in FEPOS and that some families have been non-respondin
   DNBC, are the cohort sizes realistic? What about loss during fo
   completely clear whether numbers of cohort members are invita
   (Suggest to be as detailed as you can for this at the presentation
   prepare a slide that you have ready, if you get questions)
8. If you are interested in the association between stress levels and
   with unsuccessful attempts to conceive why are you not using d
9. Is it possible that unsuccessful attempts might also increase uni
10. Is it possible that stress leads to infertility (biological question)?
11. Data from fertility clinics are based on a very selected population. We are interested in the whole trajectory before couples take this step as part of couples separate before undergoing a treatment or decide against a medically assisted reproduction.
12. We aim to unpack the existing heterogeneity of couples and to observe whether the individual stress levels increase and if so, when it starts increasing (timing and duration)

SCIENTIIFIC – SYNERGY – Siri (Mikko/Cecilia)
Fertility cannot be explained by social factors alone or biology alone.
The factors interact and influence each other in unknown ways.
Theories failed within social science so far.

PRACTICAL SYNERGY – Siri (Mikko)
Common data – accessible to all
Common PHDs and post docs – joint supervision
Bi-weekly teams meetings in smaller working groups
Yearly camps (did we say how many weeks)?
Longer stays at each other institutions for all levels of researchers

The research teams described under each PI will not work in isolation

- Mentoring will take place across teams
- Supervision networks will be developed across disciplines
- Frequent online-meetings dedicated to in-depth presentations of results and their ramifications (frequency not defined in proposal)
- PI strategy meetings (digital) to oversee progress (frequency not defined in proposal)
- In-person YEARLY scientific workshops with the complete teams and the coordination staff at each HI ("synergy camps") – held either at the His or at an external venue. Dedicated to discussions, practical work on each others' data sets, coordination between the cohorts etc.
- Short term research stays, for individual researchers or groups of researchers, at each others' physical premises (frequency and duration not defined in the proposal)

Major breakthrough findings/results?
SUMMARY – overall impact: Cecilia

- BIOSFER will provide a novel bio-social framework for understanding the life-course


erc
European Research Council
Established by the European Commission
WHERE EXCELLENCE
MEETS CREATIVITY

The application process

Step 1 Nov 2021 Step 2 March 2022	Step 3 Sept 2022	Announced Oct 2022

360 applications → 100 invited for interview → 29 funded

European Research Council
Established by the European Commission

Fra: European Commission <EC-N
Sendt: torsdag 13. oktober 2022
Til: Siri Eldevik Håberg <SiriEldevil
Emne: For Information - BIOSFER
Viktighet: Høy

Europa / Fun

Dear Madam/Sir,

The Evaluation Result Letter is av
Log on to the Funding & Tenders

Regards,
Grant Management Services

Please do not reply to this messa

lick on Action > Follow-up.

Subject: Horizon Europe (HORIZON)
Call: ERC-2022-SYG
Project: 101071773 — BIOSFER
Evaluation result information letter

Dear Applicant,

I am writing in connection with your proposal for the above-mentioned call.

We are pleased to inform you that your proposal has been favourably evaluated and that you will be contacted soon, to be invited for grant preparation.

Please find enclosed the evaluation report (ER). It is based on the comments and opinion of independent experts that participated in the evaluation.

In order to ensure compliance with fundamental ethical principles, your proposal may have to undergo an ethics review. If this is the case, we will contact you as soon as the results of this review are known (or if we need more information from you).

⚠ Please note that this letter does **NOT** constitute a **formal commitment for funding**.

I would be grateful if you could inform everyone involved in your proposal of this letter.

Yours sincerely,

Where are we now after 14 months?

- Data collection in progress
- 20 PhDs/Post Docs working on BIOSFER papers
- 20 published papers, 19 submitted papers, 40 in progress
- First reporting coming up

- More work, and more FUN than expected
- The SYNERGY really works!!