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The ADHD controversy project: Long-term effects of ADHD medication

Submission date
08/05/2020

Recruitment status
No longer recruiting

Registration date
28/08/2020

Overall study status
Completed

Last Edited
05/03/2026

Condition category
Mental and Behavioural Disorders

[_] Prospectively registered
[X] Protocol
[_] Statistical analysis plan
[X] Results
[_] Individual participant data

Plain English summary of protocol

Background and study aims
Attention-Deficit/Hyperactivity Disorder (ADHD) is among the most common mental disorders in children and adolescents, and it is a strong risk factor for several adverse psychosocial outcomes over the lifespan. Over recent decades there have been substantial increases in clinical diagnosis and medication for ADHD in many countries. Large between- and within-country variations in diagnosis and medication rates have been reported. Due to ethical and practical considerations, few studies have examined the effects of receiving a diagnosis, and there is a lack of research on the effects of medication on long-term outcomes.

This study is a part of a research project titled “the ADHD controversy project” which has four aims organized in four work packages: (WP1) To examine the prognosis of ADHD (with and without medication) compared to patients with other psychiatric diagnoses, patients in contact with public sector child and adolescent psychiatric outpatient clinics (without a diagnosis), and the general population; (WP2) Examine within-country variation in ADHD diagnoses and medication rates by clinics’ catchment area; (WP3) Identify causal effects of being diagnosed with ADHD and (WP4) ADHD medication on long-term outcomes, including emergency visits, comorbidity, education, contact with child welfare services, contact with adult psychiatric health services, employment and income, welfare dependency, crime, self-harm, suicide, and mortality. This trial registration covers WP4 of this project which aim is to identify causal effects of ADHD medication on outcomes, using variation in medication as an instrumental variable (IV).

Who can participate?
The patient sample is all persons in Norway between 5 and 18 years of age that were in contact with child and adolescent psychiatric outpatient clinics in 2009-2011 (i.e. birth cohorts 1991-2006). We will also include a control sample that is a random sample from the general population of equal size to the patient sample. The control sample is defined as individuals in Norway between 5-18 years not in contact with child and adolescent psychiatric outpatient clinics (regardless of reason) during the calendar years 2009-2011.

What does the study involve?
Our comparative analysis of prognosis will be based on survival analysis and mixed-effects models. Our analysis of variation will apply mixed-effects models and generalized linear models.

We have two identification strategies to retrieve the effect of being diagnosed with ADHD and of receiving medication on long-term outcomes. Both strategies rely on using preference-based instrumental variables, which in our project are based on provider preferences for ADHD diagnosis and medication.

What are the possible benefits and risks of participating?
None

Where is the study run from?
All public sector child and adolescent psychiatric outpatient clinics in Norway (BUP centres in Norway).

When is the study starting and how long is it expected to run for?
October 2015 to December 2021

Who is funding the study?
1. The Research Council of Norway
2. The Western Norway Regional Health Authority

Who is the main contact?
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Additional identifiers

Protocol serial number
288585

Study information

Scientific Title
Long-term effects of ADHD medication

Study objectives
H1: There are causal effects of receiving medication for ADHD (for patients on the margin of receiving medication) on a range of long-term outcomes: Emergency visits, comorbidity, education, contact with child welfare services, contact with adult psychiatric health services, employment and income, welfare dependency, crime, self-harm, suicide, and mortality. (Two-tailed hypotheses.)
H0: There are no causal effects of receiving medication for ADHD (for patients on the margin of receiving medication) on these long-term outcomes.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 25/01/2018, Regional Committee for Medical and Health Research Ethics -South-East Norway Committee D (Gullhaugveien 1-3, 0484 Oslo, Norway; +47 22845511; post@helseforskning.etikkom.no), ref: 2017/2150/REK south-east D

Primary study design
Observational

Study design
Observational longitudinal cohort study

Study type(s)
Treatment

Health condition(s) or problem(s) studied
ADHD medication

Interventions
The study is a longitudinal cohort study, where the aim is to answer questions about the effects of ADHD medication on long-term outcomes by studying patients that receive medication due to provider preference.

The study sample consists of individuals between 5-18 years that were in contact (any reason) with child and adolescent psychiatric outpatient clinics in 2009-2011, with follow-up data to 2021. We examine several psychosocial outcomes that to some extent depends on age. For instance, welfare dependency will be measured from age 18, crime from 15 years of age, child welfare service is relevant until 18 and in some special cases until 23 years of age, and adult

psychiatric health services is relevant from 18 years of age. Drop out from education is dependent on track and school system. Mortality, emergency ward visit, the onset of new mental disorder is relevant regardless of age.

To identify the effect of ADHD medication on long-term outcomes, we will use child and adolescent psychiatric outpatient clinics' catchment area variation in medication as an instrumental variable (IV). IV is a common identification strategy in health-services research that exploits the variation induced in the treatment variable (here, ADHD medication prescription) by a plausibly exogenous (as-if random) event or process (i.e., the instrument). The role of the instrument is to "isolate" exogenous variation in the treatment, and hence to remove the endogenous (confounded) variation so that the analysis only uses the exogenous variation to estimate the treatment effect.

Our identification strategies exploit as-if random variation in providers' preference to prescribe ADHD medication to patients with ADHD across Norwegian public sector child and adolescent psychiatric outpatient clinics.

Intervention Type
Drug

Phase
Not Applicable

Drug/device/biological/vaccine name(s)
Psychostimulants for ADHD (ATC-codes N06B, CO2, CO2A), melatonine (ATC-codes N05, N05B), antidepressants (ATC-code N06A), antiepileptics (ATC-code N03A)

Primary outcome(s)
We have nine primary outcomes (point 1a, 3a … to 9b), and one overall primary outcome for the general prognosis, measured at age 21. The primary outcome for general prognosis is the avoidance of all primary adverse outcomes among those as listed below, measured as dichotomy until age 21. The secondary outcome is the number of adverse outcomes among those listed below. The specific primary and secondary outcomes for ADHD medications are:

1. Emergency ward visits, measured anytime
1.1. Primary: Emergency ward visit for severe injury
1.2. Secondary: Any contact with emergency department. Analyses for type of and severity of injury. Measured for anytime.
2. Child welfare and protection services (Barnevernet), measured at any time during the period where services are available by law.
2.1. Primary: Any intervention from the child welfare and protection services (in Norwegian: Barnevernet)
2.2. Secondary: Type of contact, type of interventions (voluntary or involuntary), specifically for parental guideline and foster care.
3. Contact with adult psychiatric health services anytime from the age of 18
3.1. Primary: Any contact
3.2. Secondary: Type of contact
4. Onset of other mental disorder, measured anytime during follow-up
4.1. Primary: Onset of other mental disorders > 2 years after initial contact with public sector child and adolescent psychiatric outpatient clinic in 2009-2011
4.2. Secondary analyses for types of diagnosis

5. Educational attainment, measures to be included at age-appropriate time-points.
5.1. Primary: Non-completion of high-school, 5 years after planned start of high-school.
5.2. Secondary outcomes for average grades level at primary school, enrollment to high-school, delayed high-school completion, non-completion of high school, grades from high-school at completion, enrollment into higher education after high-school, dropout from higher education.
6. Welfare dependency measured at age-appropriate time-points.
6.1. Primary: Award of work assessment allowance (WAA, in Norwegian AAP)
6.2. Secondary outcomes for receipt of any welfare benefits more than 1G over one year. Secondary outcomes for types of benefits (unemployment benefits, social benefits of 0.5G or more, sickness absence, work assessment allowance with more than 1 year duration, disability benefits for life), NEET (Not in Education, Employment or Training anytime from 15/16 onwards for 1 year or more).
7. Crime measures to be included at age-appropriate time-points
7.1. Primary: Any criminal charge (regardless of conviction)
7.2. Secondary: Type of crime
8. Self-harm, measured at any time during the follow up
8.1. Primary: Any type of self-harm
8.2. Secondary: Any type of secondary self-harm
9. Mortality, measured at any time during the follow up
9.1. Primary: Any mortality
9.2. Secondary: Cause of death in categories of suicide, injuries and other

Key secondary outcome(s)
As specified above

Completion date
31/12/2021

Eligibility

Key inclusion criteria
The patient sample is all persons in Norway between 5 and 18 years of age that were in contact with child and adolescent psychiatric outpatient clinics in 2009-2011 (i.e. birth cohorts 1991-2006). We will also include a control sample that is a random sample from the general population of equal size to the patient sample. The control sample is defined as individuals in Norway between 5-18 years not in contact with child and adolescent psychiatric outpatient clinics (regardless of reason) during the calendar years 2009-2011.

We have four different sample definitions:
1. All patients diagnosed with ADHD in 2009-2011, regardless of referral reason
2. All patients referred to child and adolescent outpatient clinics from GP's with suspicion of ADHD in 2009-2011, regardless of whether the patient was diagnosed with ADHD
3. All patients in contact with child and adolescent outpatient clinics for any reason in 2009-2011, regardless of whether the patient was diagnosed with ADHD
4. All individuals in child and adolescent outpatient clinics catchment area in 2009-2011

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Mixed

Lower age limit
5 Years

Upper age limit
18 Years

Sex
All

Total final enrolment
0

Key exclusion criteria
Does not meet inclusion criteria

Date of first enrolment
01/01/2009

Date of final enrolment
31/12/2011

Locations

Countries of recruitment
Norway

Study participating centre
All public sector child and adolescent psychiatric outpatient clinics in Norway (BUP centres in Norway)
Norway
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Study participating centre
Haukeland University Hospital
Center for Research and Education in Forensic Psychiatry
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Sponsor information

Organisation
Haukeland University Hospital

ROR
https://ror.org/03np4e098

Funder(s)

Funder type
Government

Funder Name
The Research Council of Norway

Funder Name
The Western Norway Regional Health Authority

Results and Publications

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Not expected to be made available

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article		27/06/2023	06/09/2023	Yes	No
Results article		19/09/2024	01/09/2025	Yes	No
Results article		05/03/2026	05/03/2026	Yes	No
Protocol article		19/01/2021	22/01/2021	Yes	No
Study website		11/11/2025	11/11/2025	No	Yes