Issue 2, February 2013

ADDUCE NEWSLETTER

ATTENTION DEFICIT DRUGS USE CHRONIC EFFECTS

WHAT IS ADDUCE ?

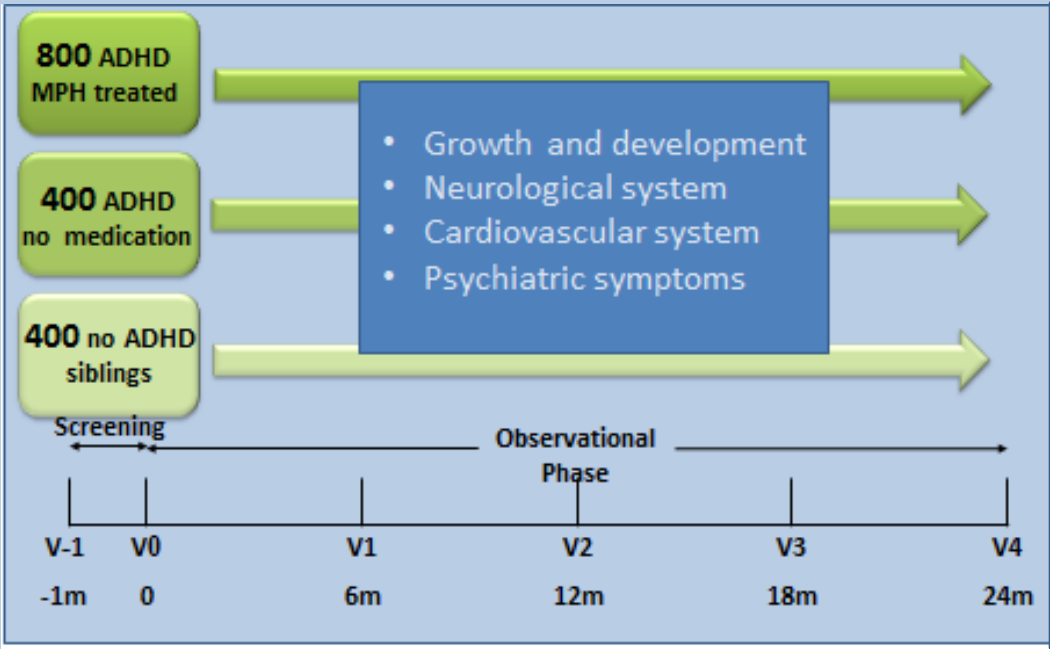
ADDUCE is an EU-network, established in response to the EU-7th Framework call, focusing on the safety of treatment of ADHD in children and adolescents. More specifically, the long-term effects of stimulants on growth, the neurological system, psychiatric states and the cardiovascular system will be investigated. The ADDUCE team will use multiple pharmaco-epidemiological research methods to achieve this aim. The consortium hosts experts in the fields of ADHD, drug safety, neuropsychopharmacology and cardiovascular research.

www.ADHD-ADDUCE.org

A 24-month prospective open-label observational cohort pharmacovigilance study of methylphenidate use

(Coghill,D., Wong, I. & Neubert,A.)

Overview of the study:



Inclusion criteria ADHD:

- Clinical diagnosis
- 6-17 years
- No previous MPH or other ADHD medication
- All physical and psychiatric comorbidities allowed
- All other medication allowed (except AMF or ATX)

Inclusions criteria Non ADHD: (of both ADHD groups)
- child matched for age, gender & socio economic status
- mean SNAP IV < 1.5 – normal SDQ score

ADDUCE open label study: main recruitment sites and recruitment status

Country	ADHD + MPH	ADHD - MPH	Sibs - ADHD
Hungary	111	59	31
Germany	22	NA	0
UK	82	NA	11
Italy	18	18	3

Assessments

Individual and Family Medical & Psychiatric history
Developmental history + Learning history
Medication history
SNAP-IV (ADHD – Oppositional Defiant Disorder symptoms)
CGI-S, CGI-I, C-GAS (Impairment & Severity)
SDQ (General Psychopathology)
SCQ (Social Communication)
DCDQ-07 (Developmental Coordination Disorder)
Growth: height, weight, waist circumference, BMI, height velocity Standard Deviation Score, target height (based on parental height), predictive height (Tanner-Whitehouse method), pubertal maturation
Cardiovascular: inspection, palpation, auscultation, blood pressure, pulse
Psychiatric:

- Mood & feelings questionnaire (Parent & Child)
- Columbia suicide severity Rating Scale
- PLikS: Psychosis-like symptoms
- Yale global tics severity Rating Scale
- DAWBA : tics, rapidly changing mood, awkward & troublesome behaviour
- Substance use questionnaire

Neurological:

- AIMS: abnormal involuntary mood scale
- CSHQ: child's sleep habits questionnaire

The UK neuroimaging arm

UK participants between 10-17 years will be invited to participate in structural and functional neuroimaging. Applying new Support Vector Machines' analyses, it will be tested whether reliable identification is feasible – at an individual level and prior to exposure to methylphenidate - of those who will subsequently fail to respond to medication (expected rate 30%) or, who will experience significant intolerance or adverse reactions (expected rate 20% - with overlap)

Bone-age measures

In a subsample of 70 Italian children measures of bone-age will be taken to explore whether this "gold standard" measure of "growing power" would add any additional clinical value to measuring height and weight in children on medication.

Summary of study WP3:

A 24-month prospective open-label observational cohort pharmacovigilance study of methylphenidate use

This cohort study will enroll a total of 1600 children and adolescents (6-17 years) of whom 800 are about to start with methylphenidate treatment for ADHD and 800 controls. Half of the controls will be children and adolescents with ADHD not taking medication and the other half will be siblings of children with ADHD, not having a diagnosis of ADHD. The study will be fully naturalistic, so children with any other additional physical or mental health problems will be allowed to participate and all other medication (except medication for ADHD in present or past) is permitted. Only the siblings should be free of psychiatric problems. Measures will be taken 6-monthly over a period of 2 years in order to study eventual impact of methylphenidate on psychiatric, growth, neurological and cardiovascular outcome measures (see "Assessments"). Two centers from Northern Europe (Dundee [UK] and Mannheim [Germany]), one from Southern Europe (Cagliari [Italy]), and one from New Europe (Budapest [Hungary]) act as main sites, but in most countries several additional satellite sites will be involved. Recruitment has started first in the UK, then in Hungary and recently also in Germany and Italy.

How to participate in this study ?

If you have been diagnosed with ADHD
And you are between 6-17 years old
And you would like to start taking medication
Or you have not taken medication so far
And you live near one of the study centers
You can contact the study coordinators:

UK

Dundee

Dr. David Coghill : d.r.coghill@dundee.ac.uk
Dr. Sarah Inglis : s.k.inglis@dundee.ac.uk

HUNGARY

Budapest

Dr. Julia Gadoros : gadorosju@gmail.com
Dr. Andrea Biro : dr.biro.andi@gmail.com

ITALY

Cagliari

Prof.Alessandro Zuddas : azuddas@unica.it
Dr. Sara Carucci: sara.carucci@gmail.com
M. Piredda: mariangela.piredda@gmail.com

GERMANY

Mannheim

Prof.Dittman: ralf.dittmann@zi-mannheim.de
Prof.Banaschewski : tobias.banaschewski@zi-mannheim.de
Ruth Berg: Ruth.Berg@zi-mannheim.de

Information brochures for children, adolescents and parents can be downloaded from the website:
http://www.adhd-adduce.org/page/view/113/English
http://www.adhd-adduce.org/page/view/115/Hungarian

WP 8: Three years use of methylphenidate and effects on 24-hours blood pressure measures and left ventricular mass using echocardiograms in late adolescents and adults with ADHD

This study will use a cross-sectional design to compare two groups of adolescent and young adult (15-25 years) patients with ADHD (DSM-IV, any subtype): 800 subjects treated with methylphenidate for > 3 years, and a matched group of 400 subjects with ADHD who have never been treated with methylphenidate. Any comorbidity and any co-medication will be allowed.

Main study parameters/endpoints: (1) Hypertension defined on the basis of 24-hour blood pressure measures as systolic and/or diastolic blood pressure of a positive value ≥ 1.65 (equivalent to the 95th percentile), and (2) Left ventricular mass measured by echocardiography.

Primary Objective: To determine whether the long-term use of methylphenidate (> 3 years) increases the blood pressure and causes left ventricular hypertrophy (LVH) identified by echocardiography.

Secondary Objectives:

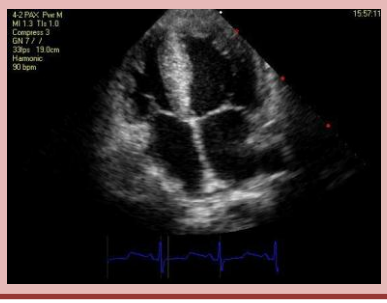
1) To explore the role of potential mediators, moderators and confounders e.g. age, sex, socioeconomic status, family functioning, co-medication, negative lifestyle factors, weight and familial cardiovascular risk, in the relationship between methylphenidate treatment and the effects on blood pressure and echocardiogram.
2) To describe the dose-response relationship (dosage, duration of treatment, discontinuation vs. continued use) between methylphenidate exposure and the effects on blood pressure and echocardiogram.

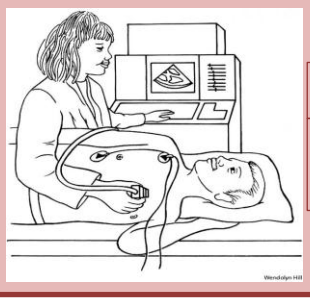
Recruitment sites: at least 4 adult ADHD clinics in Europe (Nijmegen, London, Nottingham, and Barcelona).

Exclusion criteria: treatment with dexamphetamine or atomoxetine

Inclusion criteria: DSM-IV clinical ADHD diagnosis, confirmed by a structured interview. At least 50% of participants being treated continuously for 3 years with a minimum effective dose of 0.5 mg methylphenidate /kg/day (drug holidays may be included). Adherence is measured by self-report.

Procedure: All participants will be seen at a screening visit, a baseline visit for comprehensive face-to-face assessments, and a visit for the echocardiography, and for obtaining ambulatory 24-hours blood pressure measurements. All measures are non-invasive procedures.





Echocardiography

24-hour Blood Pressure measurement

The ADDUCE website is open to everyone. More information on ADHD and its treatment is available as well as on the ADDUCE project and its consortium.

ADDUCE investigators can obtain a personal login to enter the contributors' part and find all the deliverables and core documents of the project there.
Contact kathy.puttemans@uzleuven.be for your login

ADDUCE CONTRIBUTORS
Attention Deficit Hyperactivity Drugs Use Chronic Effects

Visit the ADDUCE website at:
www.adhd-adduce.org

For questions about this newsletter: marina.danckaerts@uzleuven.be