Issue 3, March 2015

ADDUCE NEWSLETTER

ATTENTION DEFICIT HYPERACTIVITY DISORDER DRUGS USE CHRONIC EFFECTS

WHAT IS ADDUCE ?

ADDUCE is an EU-network, set up in response to the EU-7th Framework call, in which the long-term effects of stimulant medication on growth, the neurological and cardiovascular system and psychiatric states will be investigated in individuals with ADHD. Multiple pharmaco-epidemiological research methods will be used to achieve this aim. The project relies on experts in the fields of ADHD, drug safety, neuropsychopharmacology and cardiovascular research.
Recently, an amendment for project extension has been approved.

The ADDUCE website is open to everyone:

www.ADHD-ADDUCE.org

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

(Coghill, D. et al.)

Study design

CHILDREN (6-17 Y)	COUNTRIES	MEASURES
ADHD + MPH	 	growth and development
ADHD - MPH		cardiovascular system
Non-ADHD	 	neurological system
		psychiatric symptoms

2 year follow up

Recruitment has now been finalized

Many thanks to all participants!

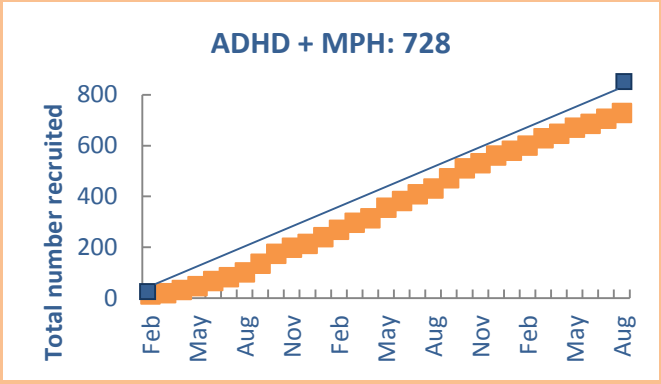
Let's keep up the good work:

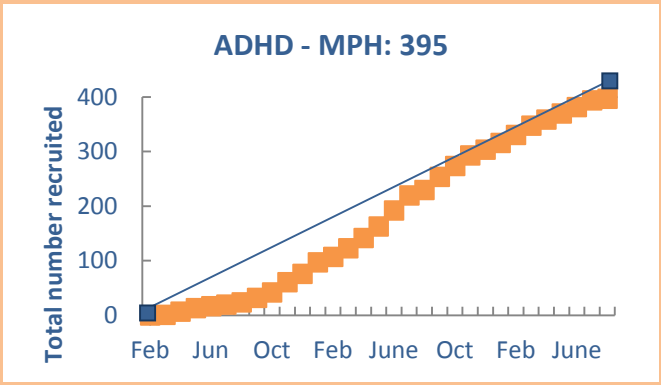
continue follow up: each visit is important!

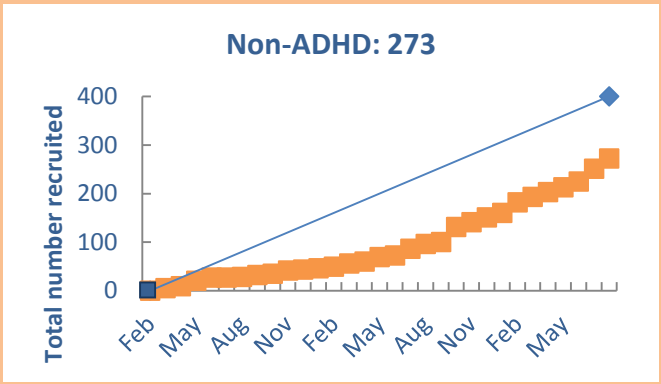
enter data into the e-CRF as soon as possible after each visit

Final recruitment status

actual recruitment target recruitment







	ADHD + MPH	ADHD-MPH	Non-ADHD	TOTAL
Germany	132	18	34	**184**
Hungary	246	188	109	**543**
Italy	149	183	30	**362**
UK	201	6	100	**307**
TOTAL	**728**	**395**	**273**	**1396**
Needed	800	400	400	1600
% recruited	91.0	99.3	68.0	87.4

Source: Inglis, S.

Spin-off: UK questionnaire on negative effects of MPH on mood and cognition (Kovshoff, H. et al.)

In a subgroup of 45 patients, relevant specific cognitive, motivational, and mood-related adverse events following long term MPH use (more than one year of consecutive use) were reported by 91% of the participants. These covered three main domains including Cognition: Attention/ Concentration, Changes in thinking, Reduced creativity, Sensory overload, Memory, and Slower Processing Speed; Motivation: Loss of intrinsic motivation for goal directed activities, Lack of effort/engagement in daily tasks and Increased focus on rewards/incentives; and Mood: Dampening of Spontaneity/Flat affect, Mood dysregulation, Increased anxiety/ Feeling edgy and External locus of control.

The views and experiences described were transformed in items for a questionnaire which can be used to systematically assess for the presence of adverse cognitive and motivational side effects of methylphenidate.

Through this, clinicians can identify adverse effects which may require further exploration, and tailor support/treatment accordingly. Identification of negative experiences of medication early on may be predictive of adherence and patient satisfaction with treatment and ultimately lead to improved ADHD-related clinical practice in the long term.

Spin-off: UK neuroimaging study (Johnston, B. et al.)

To test whether it is possible to predict response to methylphenidate, brain structure and function in children has been investigated at the University of Dundee. The study involved one brain scan in medication-naïve children between 10 and 17 years old. The follow up data that are collected through the main ADDUCE study will be used to differentiate treatment response.

The brain scanning has now been finished and the analyses of the data are ongoing.

Spin-off: Italian bone imaging study
(Zuddas, A. et al.)

In this study, participants are evaluated by an accurate auxological assessment and pubertal staging performed by an expert paediatric endocrinologist to evaluate adverse effects of MPH on growth and development. Furthermore, it is explored whether the application of bone age monitoring might be a helpful tool to study adverse developmental effects of MPH and might add value to the routine measures of growth. Bone age is regarded as a gold standard to evaluate the "growing power" of an individual and represents a major tool to calculate expected final height.
Bone age is monitored in 40 medicated ADHD patients, aged 6 to 12, and compared to 40 same age not medicated ADHD subjects at the University of Cagliari. This is done by an X-ray of the left wrist at baseline, and after 1 and 2 years. As this is the first study to investigate the effects of MPH on bone age, it should be considered exploratory. Descriptive results will be reported to document the proportion of patients with height deficit who also have a variation in bone maturation rate.
At present, the baseline data are being analysed and preliminary results are expected soon.

Three years or longer use of MPH and effects on 24-hours blood pressure measures and left ventricular mass using echocardiogram in children and adults with ADHD

(Buitelaar, J. et al.)

Objective

The goal of this study is to determine whether the long-term use of MPH (> 3 years) increases the blood pressure and causes left ventricular hypertrophy (LVH) in children and adults with ADHD.

Study design

Participants

Children and adolescents with ADHD (12-25 years) of whom 2/3 are using MPH for more than 3 years and 1/3 not using MPH will participate in the study.

Assessment

GENERAL ASSESSMENT

Demographics
Family developmental, medical and psychiatric history
Physical health
Developmental history
School/SES
Lifestyle, physical exercise
Medication history
Substance Misuse Questionnaire (SUQ)
ADHD DSM-IV rating scale
CGI-S, CGAS, GAF
YSR (Youth Self-Report) / ASR (Adult Self-Report)

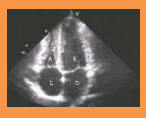
PHYSICAL ASSESSMENT

General physical examination: height, weight, BMI, blood pressure and vital signs

Cardiac examination

Echocardiography to detect left ventricular hypertrophy (LVH)

24 hours blood pressure measurement



Since the end of 2014, the allowed **age range** in the study has been extended from 15 - 25 years to **12 - 25 years** old in The Netherlands, United Kingdom and Hungary.

How to participate in the ADDUCE cardiovascular study?

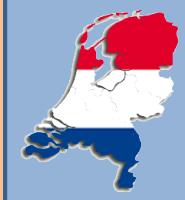
More than 100 people have already participated in this study, but we want to include as many children and adults as possible!

At the moment we are recruiting in Barcelona, Budapest, Groningen and Nijmegen. Recruitment in London and Dundee will start soon.

February 2015	ADHD + MPH	ADHD - MPH	TOTAL
NL – Nijmegen	33	18	51
NL – Groningen	13	1	14
UK – London	0	0	0
UK – Dundee	0	0	0
Spain – Barcelona	9	7	16
Hungary – Budapest	12	15	27
TOTAL	**67**	**41**	**108**

Do you want to help us to gather more knowledge about the cardiovascular effects of the use of stimulants in AD(H)D?

Are you *diagnosed with ADHD*?
Are you *between 12 and 25 years* old?
Are you *using MPH for more than 3 years* OR did you *never take any ADHD medication*?
Please *contact* one of the study *coordinators* in your country!
Participants can enroll *until September 2015*.



Nijmegen:
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Leonie Hennissen (leonie.hennissen@radboudumc.nl)

Groningen:
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Tips and tricks for recruitment and retention

(Inglis, S.)

Recruitment methods for the ADHD groups:

Engaging the clinicians is very important. Experience learns that participants with ADHD are mainly recruited through the clinicians who deliver the clinical care to the ADHD patients. It could also be of help to put up some posters in the clinics to advertise the study. Further, it may be useful to visit local ADHD parent support groups and communicate with them via social media.

How to motive participants to stay in the studies?

Text reminders can be used to remind participants about their next appointment. It is also valuable to mail out appointment letters so that families have a written record of their appointment.

Please make sure that your methods for recruitment and retention are in your protocol and have been approved by your local ethics committee.

What about the results of the studies?

Publication rules

Two types of papers will result from the ADDUCE studies: CORE papers and SPIN-OFF papers. Before a manuscript (both types) is submitted to a journal or any other medium for its publication, it must be sent to the ADDUCE Editorial Board (AEB) for formal approval (marina.danckaerts@uzleuven.be). Proposal for papers or other publication output will be submitted for approval in a one page format, available on the ADDUCE website (www.ADHD-ADDUCE.org). The proposal should specify the proposed authors, the title, the scientific background, the specific questions or hypotheses to be addressed and the proposed methods of analysis. Once approved by the AEB and subsequent to the preparation of the needed data files, the working group for each project will have two months to complete their analyses and provide a summary report to the AEB. They will have an additional two months to prepare a good draft of the manuscript. Papers accepted for publication will be sent as pre-publication reports to the EMA a month before publication, in order for the EMA to determine whether a public announcement regarding the research would be warranted.

Publications

Murray, M.L., Insuk, S., Banaschewski, T., Neubert, A.C., McCarthy, S., Buitelaar, J.K., Coghill, D., Dittmann, R.W., Konrad, K., Panei, P., Rosenthal, E., Sonuga-Barke, E.J., & Wong, I.C.K. (2013). An inventory of European data sources for the long-term safety evaluation of methylphenidate. *European Child & Adolescent Psychiatry, 22*, 605-618

In preparation

Several systematic reviews regarding the effects of MPH are being prepared. Also, a methodological paper about the ADDUCE project is in preparation. Further, some empirical studies on the effects of MPH on cognition, emotion and mood, and on the risk of seizure and the risk of self-harm are in the process of writing.