

NUEVOS RESULTADOS CIENTÍFICOS EN TDAH

J. Antoni Ramos-Quiroga [@drramosquioga](#)

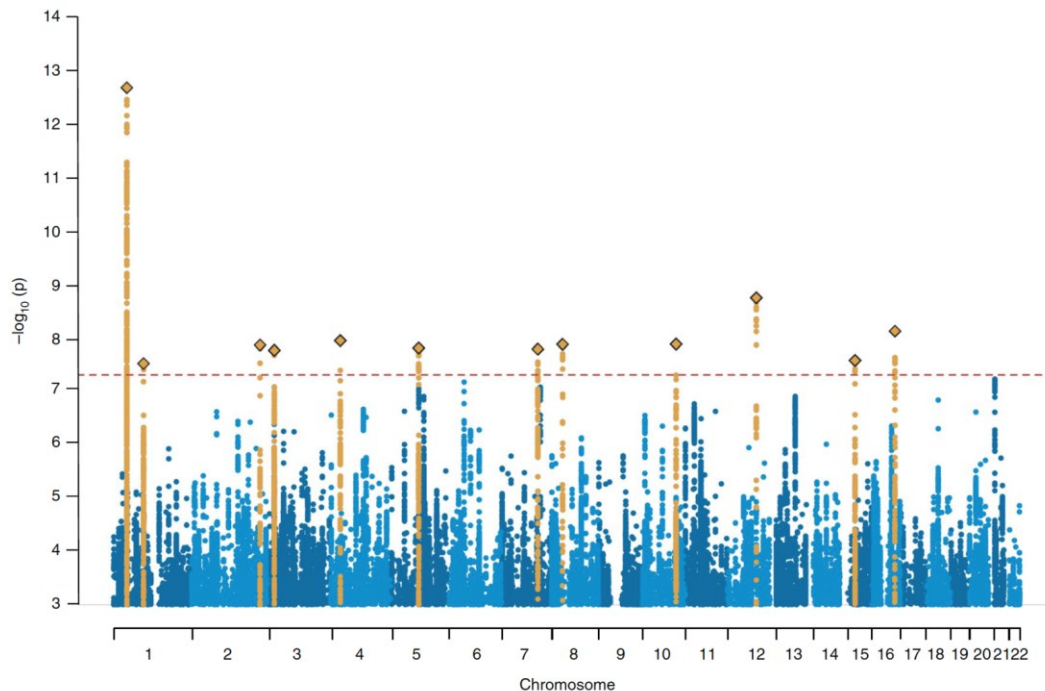
Servicio de Salud Mental



Conflicto de Interés

Interest	Name of organisation
Grants	BGaze, Ferrer, Fundació F.C. Barcelona, Fundació PROBITAS, Instituto Carlos III-EU FP7-H2020, Janssen, Lundbeck, Oryzon, Psious, Nesplora, Roche, Rubió and Shire-Takeda
Honoraria	Biogen, Rubió, Janssen-Cilag, Novartis, Shire, Takeda, Bial, Shionogi, Sincrolab, Novartis, BMS, Medice, Uriach, Technofarma and Raffo
Shares	
Paid positions	
Advisory boards	BGaze, Ferrer, Instituto Carlos III-EU FP7-H2020, Biogen, Novartis, Janssen, Medice, Rubió, Shire-Takeda and Sincrolab
Other involvement	

Estudios genéticos: GWAS



12 loci



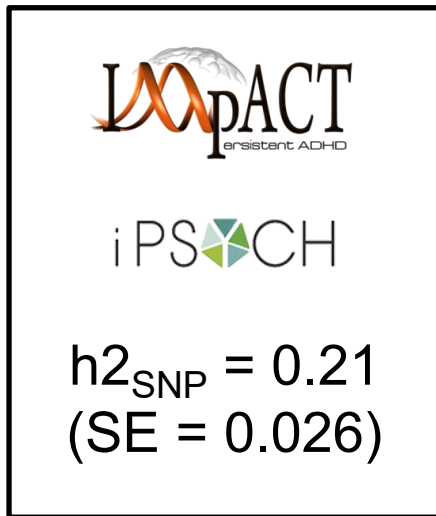
New ADHD meta-analysis
20.183 cases 35.191 controls

Demontis et al 2018

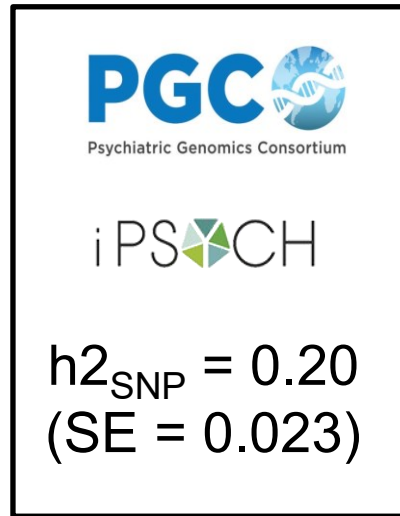
Correlación genética: adultos y niños



Persistent ADHD



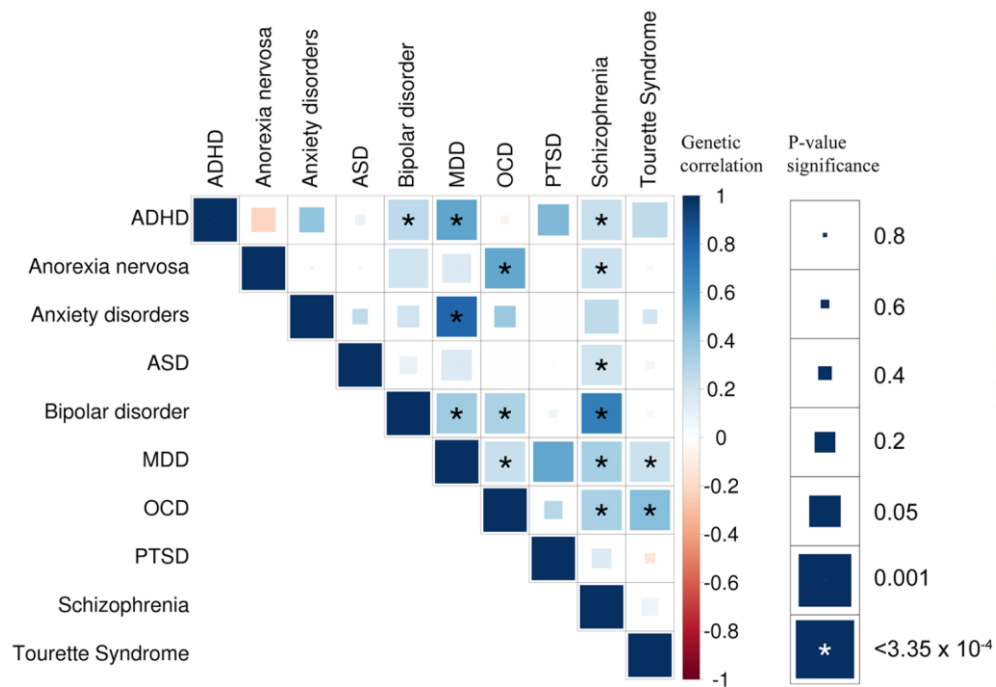
Children ADHD



Genetic correlation = **81%** (SE = 0.085)

P-value = 2.13E-21

Genética y comorbilidad



The Brainstorm Consortium, *Science* **360**, eaap8757 (2018) 22 June 2018

TDAH y consumo de cánnabis



Molecular Psychiatry
https://doi.org/10.1038/s41380-018-0339-3

ARTICLE



Attention-deficit/hyperactivity disorder and lifetime cannabis use: genetic overlap and causality

María Soler Artigas^{1,2,3} · Cristina Sánchez-Mora^{1,2,3} · Paula Rovira^{1,2} · Vanesa Richarte^{2,3,4} · Iris García-Martínez^{1,2} · Mireia Pagerols^{1,2} · Ditte Demontis^{5,6,7} · Sven Stringer⁸ · ADHD Group of the Psychiatric Genomics Consortium, International Cannabis Consortium · Jacqueline M. Vink⁹ · Anders D. Børglum^{5,6,7} · Benjamin M. Neale^{10,11} · Barbara Franke^{12,13,14} · Stephen V. Faraone¹⁵ · Miguel Casas^{1,2,3,4} · Josep Antoni Ramos-Quiroga^{1,2,3,4} · Marta Ribasés^{1,2,3}

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- Evidence of a **causal effect** of ADHD on lifetime cannabis use ($P=5.88 \times 10^{-5}$).
- The odds of cannabis use for ADHD: **7.9** 95% CI (3.72, 15.51)

Table 1 Mendelian randomization results of (a) ADHD as exposure and cannabis use as outcome, and (b) cannabis use as exposure and ADHD as outcome

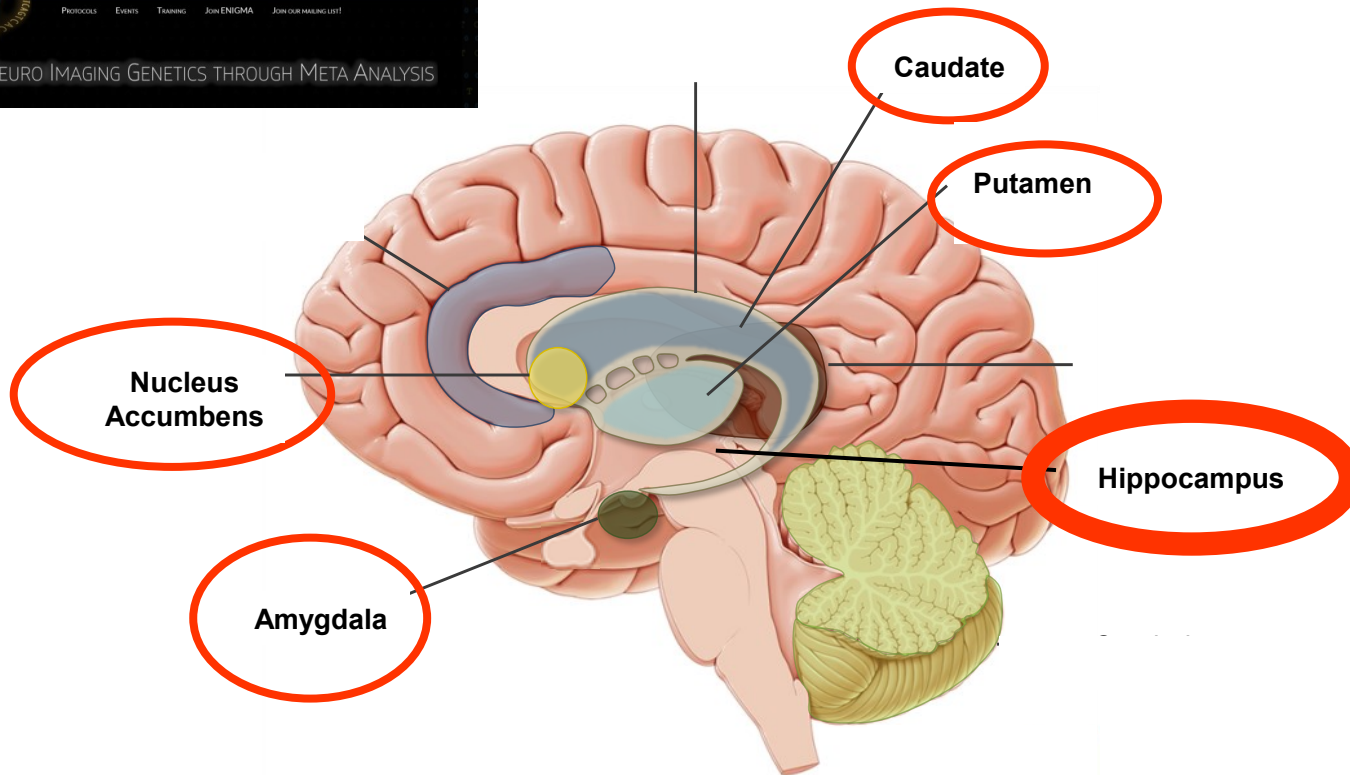
a) Method	OR ^a	OR 95% CI	P-value
Threshold $P < 5 \times 10^{-8}$ (12 variants)			
IVW	1.44	(1.21, 1.72)	5.88E-05
Weighted median	1.58	(1.25, 2.00)	1.13E-04
MR-Egger	1.34	(0.48, 3.77)	5.81E-01
MR-Egger intercept	1.01	(0.92, 1.10)	8.87E-01
MR-PRESSO global test	–	–	2.55E-01
Threshold $P < 5 \times 10^{-6}$ (72 variants)			
IVW	1.14	(1.06, 1.23)	2.61E-04
Weighted median	1.07	(0.96, 1.18)	2.35E-01
MR-Egger	1.19	(0.85, 1.66)	3.04E-01
MR-Egger intercept	1.00	(0.97, 1.02)	8.04E-01
MR-PRESSO global test	–	–	7.42E-01
b) Method	OR ^b	OR 95% CI	P-value
Threshold $P < 5 \times 10^{-6}$ (9 variants)			
IVW	1.07	(0.94, 1.21)	2.92E-01
Weighted median	1.05	(0.96, 1.15)	2.88E-01
MR-Egger	1.29	(0.98, 1.70)	6.64E-02
MR-Egger intercept	0.97	(0.94, 1.01)	1.15E-01
MR-PRESSO global test	–	–	4.42E-01
Threshold $P < 5 \times 10^{-5}$ (70 variants)			
IVW	0.97	(0.93, 1.02)	3.11E-01
Weighted median	0.97	(0.94, 1.01)	1.43E-01
MR-Egger	1.04	(0.94, 1.14)	4.79E-01
MR-Egger intercept	0.99	(0.98, 1.00)	1.78E-01
MR-PRESSO global test	–	–	1.55E-01

P-values < 0.05 are presented in bold

^aOdds of ADHD risk per unit increase in the log OR of cannabis use, except MR-Egger intercept which measures the average pleiotropic effect

^bOdds of cannabis use per unit increase in the log OR of ADHD risk, except MR-Egger intercept which measures the average pleiotropic effect

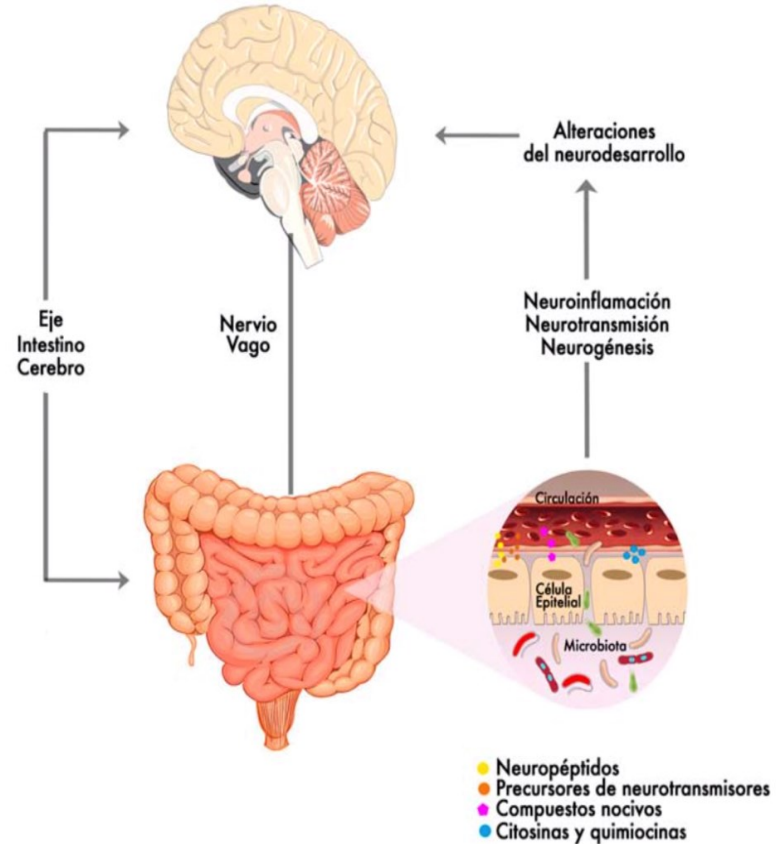
Estructuras subcorticales



Eje intestino-cerebro

El eje intestino-cerebro en el trastorno por déficit de atención/hiperactividad: papel de la microbiota

Vanesa Richarte, Karina Rosales, Montserrat Corrales, Mariano Bellina, Christian Fadeuilhe, Eva Calvo, Pol Ibáñez, Cristina Sánchez-Mora, Marta Ribasés, Josep A. Ramos-Quiroga



Microbiota intestinal

Translational Psychiatry

www.nature.com/tp

ARTICLE OPEN

 Check for updates

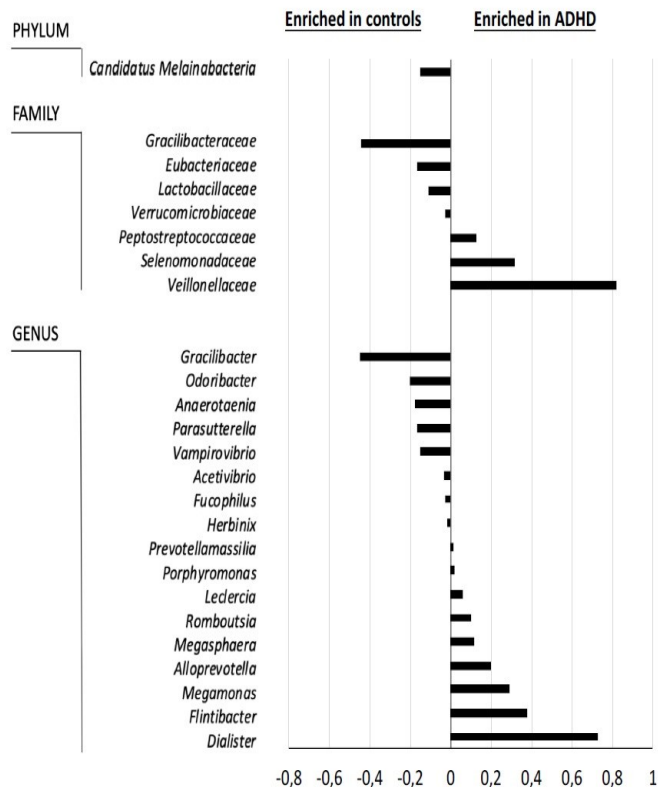
Gut microbiota signature in treatment-naïve attention-deficit/hyperactivity disorder

Vanesa Richarte^{1,2,3}, Cristina Sánchez-Mora^{1,2,4}, Montserrat Corrales^{1,2,3}, Christian Fadeuilhe^{1,2,3}, Laura Vilar-Ribó ^{1,2,4}, Lorena Arribas^{1,4}, Estela Garcia⁴, Silvia Karina Rosales-Ortiz^{4,5}, Alejandro Arias-Vasquez^{6,7}, María Soler-Artigas ^{1,2,4,8}, Marta Ribasés ^{1,2,4,8}  and Josep Antoni Ramos-Quiroga ^{1,2,3,4} 

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Resultados

TDAH en la edad adulta



Diferencias en la abundancia relativa de diversos taxones microbianos en la muestra de pacientes en comparación con los individuos control



A nivel de **familia**, diferencias en Selenomonadaceae, Veillonellaceae y Gracilibacteraceae.

A nivel de **genero**, diferencias en la abundancia relativa de *Dialister*, *Megamonas*, *Anaerotaenia* y *Gracilibacter*.

Mortalidad asociada a TDAH

Danish Birth Cohort from first birthday or 1995-2013

- Using Danish National Registers a cohort of **1.92 million** included **32,061 with ADHD**. Follow-up 24.9 million person-years
- Mortality rate per 10,000 person years; ADHD 5.85 and non-ADHD 2.21:
 - Fully adjusted MRR for **ADHD cohort 2.07**, 95% CI 1.7-2.5; $p < 0.0001$
 - **MRR varied by age of diagnosis:** <6 years **1.86**, 6-17 **1.58**, >18 years **4.25**
 - **Accidents** were most common cause of death 42/79 where known cause

ADHD is associated with significantly increased mortality rates for natural and unnatural causes of death. Mortality rates are higher in females.

Guías y consensos

NICE National Institute for Health and Care Excellence

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Home > NICE Guidance > Conditions and diseases > Mental health and behavioural conditions > Attention deficit disorder

Attention deficit hyperactivity disorder: diagnosis and management

NICE guideline (NG87) | Published date: March 2018 | Last updated: September 2019

European Psychiatry 56 (2019) 14–34

Contents lists available at ScienceDirect

European Psychiatry

Journal homepage: <http://www.europsy-journal.com>

Original article

Updated European Consensus Statement on diagnosis and treatment of adult ADHD

J.J.S. Kooij^{a,b,*}, D. Bijlenga^{a,b}, L. Salerno^{a,b}, R. Jaeschke^{a,b}, I. Bitter^{a,b}, J. Balázs^{a,b}, J. Thome^{a,b}, G. Dom^{a,b}, S. Kasper^{a,b}, C. Nunes Filipe^{a,b}, S. Stes^{a,b}, P. Mohr^{a,b}, S. Leppämäki^{a,b}, M. Casas Brugué^{a,b}, J. Bobes^{a,b}, J.M. McCarthy^{a,b}, V. Richarte^{a,b}, A. Kjems Philipsen^{a,b}, A. Pehlivanidis^{a,b}, A. Niemela^{a,b}, B. Sty^{a,b}, B. Semerciz^{a,b}, B. Bolea-Alamanac^{a,b}, D. Edvinsson^{a,b}, D. Baeyens^{a,b}, D. Wynchank^{a,b}, E. Sobanski^{a,b}, A. Philipsen^{a,b}, F. McNicholas^{a,b}, H. Caci^{a,b}, I. Mihailescu^{a,b}, I. Manor^{a,b}, I. Dobrescu^{a,b}, J. Krause^{a,b}, J. Fayyad^{a,b}, J.A. Ramos-Quiroga^{a,b}, K. Foeken^{a,b}, F. Rad^{a,b}, M. Adamou^{a,b}, M. Ohlmeier^{a,b}, M. Fitzgerald^{a,b}, M. Gill^{a,b}, M. Lensing^{a,b}, N. Motavalli Mukaddes^{a,b}, P. Brudkiewicz^{a,b}, P. Gustafsson^{a,b}, P. Tani^{a,b}, P. Oswald^{a,b}, P.J. Carpentier^{a,b}, P. De Rossi^{a,b}, R. Delorme^{a,b}, S. Markovska Simoska^{a,b}, S. Pallanti^{a,b}, S. Young^{a,b}, S. Bejerot^{a,b}, T. Lehtonen^{a,b}, J. Kustow^{a,b}, U. Müller-Sedgwick^{a,b}, T. Hirvikoski^{a,b}, V. Pironti^{a,b}, Y. Ginsberg^{a,b}, Z. Félégházy^{a,b}, M.P. Garcia-Portilla^{a,b}, P. Asherson^{a,b}

Guía de Práctica Clínica sobre las Intervenciones Terapéuticas en el Trastorno por Déficit de Atención con Hiperactividad (TDAH)

GUÍAS DE PRÁCTICA CLÍNICA EN EL SNS
MINISTERIO DE SANIDAD, SERVICIOS SOCIALES E IGUALDAD

INSTITUTO DE SALUD CAROLINA
guíasalud.es
IMS Instituto Argentino de Ciencias de la Salud

INTERNATIONAL CONSENSUS STATEMENT OF ADOLESCENTS

European
Addiction
Research

Research Article

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DOI: 10.1159/000508385

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Published online: July 7, 2020



International Consensus Statement for the Screening, Diagnosis, and Treatment of Adolescents with Concurrent Attention-Deficit/Hyperactivity Disorder and Substance Use Disorder

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Geurt van de Glind^{d,e} Tobias Banaschewski^f Csaba Barta^{g,h} Alex Begemanⁱ Miguel Casas^j
Cleo L. Crunelle^k Constanza Daigre Blanco^{l,n} Søren Dalsgaard^o Zsolt Demetrovics^p
Jacomine den Boer^l Geert Dom^q Valsamma Eapen^r Stephen V. Faraone^s Johan Franck^t
Rafael A. González^{u,v} Lara Grau-López^{l,n,t} Annabeth P. Groenman^{w,x} Malin Hemphälä^t
Romain Ickic^{y,z,A} Brian Johnson^s Michael Kaess^{B,C} Máté Kapitány-Fövényi^{D,E}
John G. Kasinathan^F Sharlene S. Kaye^G Falk Kiefer^H Maija Konstenius^t Frances R. Levin^I
Mathias Luderer^J Giovanni Martinotti^K Frieda I.A. Matthys^L Gergely Meszaros^M
Franz Moggi^N Ashmita P. Munasur-Naidoo^{O,P} Marianne Post^Q Sharon Rabinovitz^R
J. Antoni Ramos-Quiroga^{m,n,s,T} Regina Sala^U Abu Shafi^V Ortal Slobodin^W Wouter G. Staal^{X,Y}
Rainer Thomasius^Z Ilse Truter^a Michiel W. van Kernebeek^β Maria C. Velez-Pastrana^Y
Sabine Vollstädt-Klein^H Florence Vorspan^{Z,δ,ε,ζ} Jesse T. Young^{θ,ι,κ} Amy Yule^λ
Wim van den Brink^{e,μ} Vincent Hendriks^{a,ξ}

INTERNATIONAL CONSENSUS STATEMENT OF ADOLESCENTS



Statements	Consensus reached in round No.
<i>Pharmacological treatment of comorbid ADHD and SUD</i>	
20 Despite the lack of evidence for the efficacy of pharmacotherapy in adolescents with concurrent ADHD and SUD, it is recommended that pharmacological treatment of ADHD, particularly with psychostimulants, should be considered for this group	1
21 Each adolescent with concurrent ADHD and SUD and his/her parents should receive information about the option of pharmacotherapy for ADHD and its preconditions and monitoring	1
22 Before starting stimulant pharmacotherapy in adolescents with concurrent ADHD and SUD, it is important that the adolescents are abstinent or have reduced/stabilized their substance use. If this is not the case, the clinician should consider non-stimulant pharmacotherapy (e.g., atomoxetine, guanfacine, or bupropion)	No consensus reached
23 Before starting psychostimulant treatment, the clinician should communicate that treatment will only be continued if it has a demonstrably favorable effect in terms of reduced ADHD symptoms and/or improved functioning	1
24 Pharmacological treatment in adolescents with concurrent ADHD and SUD should preferably be embedded in psychosocial treatment	2
25 If the clinician suspects psychostimulant medication misuse or diversion, this is an urgent reason to discuss, and if necessary, terminate psychostimulant treatment and consider non-stimulant treatment. To minimize the risk of misuse and diversion of stimulant medication, it is best to prescribe long-acting instead of short-acting psychostimulants, to avoid long-term and repeat prescriptions and to carefully monitor progress and possible problems	3
26 Pharmacological treatment of ADHD requires careful titration and monitoring of its effect and possible adverse effects. Higher doses of psychostimulants may be required in patients with ADHD and concurrent SUD than in those without SUD for a favorable effect on both the ADHD symptoms and reduction of substance use	1
27 First-line pharmacotherapy of ADHD in adolescents with concurrent ADHD and SUD consists of long-acting psychostimulants (e.g., methylphenidate, lisdexamfetamine, dexamphetamine, and mixed amphetamine salts). As second-line pharmacological treatments atomoxetine, guanfacine XR or bupropion can be considered	3
28 Although comparable at the population level, the efficacy and tolerability of long-acting methylphenidate, (lis)dexamphetamine and extended-release mixed amphetamine salts may differ between individuals. It is, therefore, recommended to test the effect with one of these stimulant medications in a patient with concurrent ADHD and SUD, and, in case of nonresponse at an adequate dose, switch to the next stimulant medication	1
29 An electrocardiogram is needed before initiating psychostimulant treatment only in adolescents with ADHD and SUD who have a (family) history, symptoms or signs of cardiac disease, and/or who use a medication or illicit drug (e.g., cocaine and amphetamine) that may increase cardiac risk. Heart rate and (systolic) blood pressure should be monitored throughout the course of pharmacological ADHD treatment in all adolescents with concurrent ADHD and SUD	2
30 In adolescents with ADHD and SUD treated with psychostimulants or atomoxetine, growth and weight should be monitored	2

INTERNATIONAL CONSENSUS STATEMENT OF ADOLESCENTS



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30 In adolescents with ADHD and SUD treated with psychostimulants or atomoxetine, growth and weight should be monitored	2

Metanálisis en red

Articles

Comparative efficacy and tolerability of medications for attention-deficit hyperactivity disorder in children, adolescents, and adults: a systematic review and network meta-analysis



Samuele Cortese, Nicoletta Adamo, Cinzia Del Giovane, Christina Mohr-Jensen, Adrian J Hayes, Sara Carucci, Lauren Z Atkinson, Luca Tessari, Tobias Banaschewski, David Coghill, Chris Hollis, Emily Simonoff, Alessandro Zuddas, Corrado Barbui, Marianna Purgato, Hans-Christoph Steinhausen, Farhad Shokraneh, Jun Xia, Andrea Cipriani



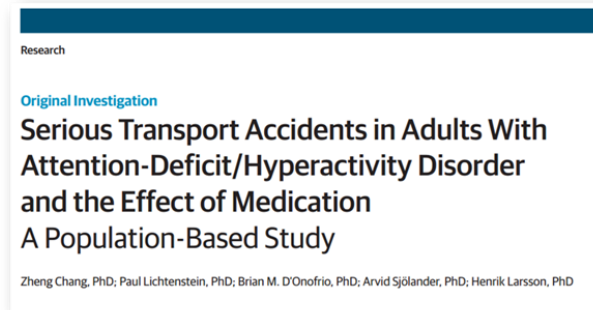
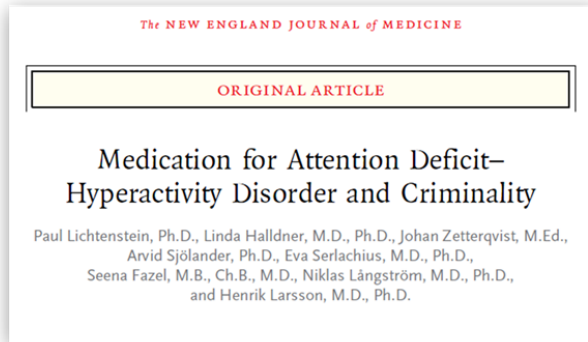
Summary

Background The benefits and safety of medications for attention-deficit hyperactivity disorder (ADHD) remain controversial, and guidelines are inconsistent on which medications are preferred across different age groups. We aimed to estimate the comparative efficacy and tolerability of oral medications for ADHD in children, adolescents, and adults.

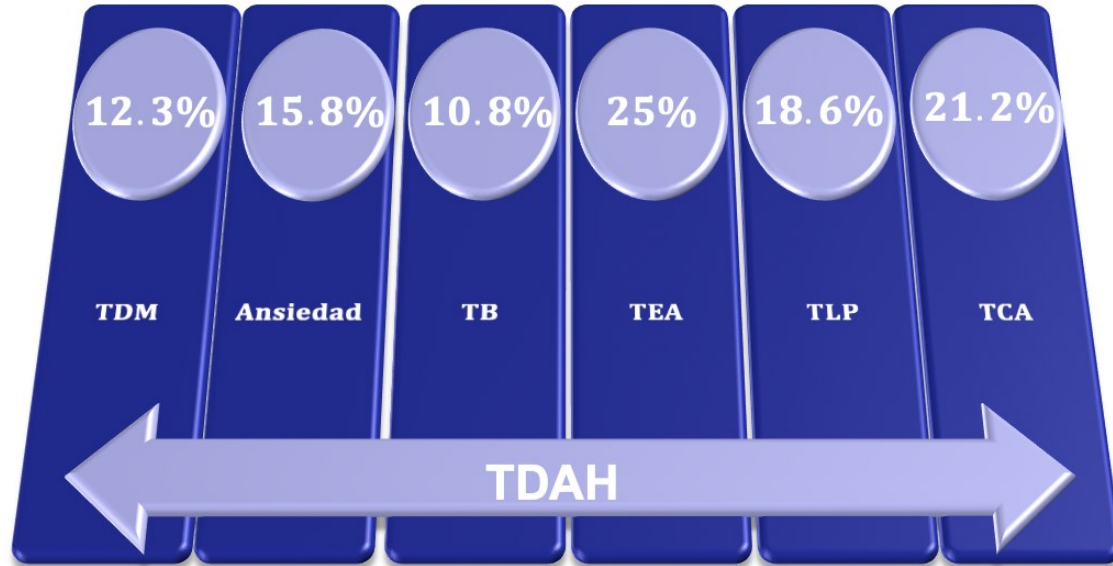
Lancet Psychiatry 2018;
5: 727–38

Published Online
August 7, 2018
[http://dx.doi.org/10.1016/
S2215-0366\(18\)30269-4](http://dx.doi.org/10.1016/S2215-0366(18)30269-4)

Estudios de registros poblacionales



TDAH en psiquiatría general



Deberdt W et al. 2015
Kessler R et al. 2006

The Prevalence and Treatment of ADHD in Spain: A Retrospective Cohort Analysis

Jose Antonio Ramos-Quiroga^{1,2,3,4}  Vanesa Richarte^{1,2,3,4}, Isabel Soto⁵, Maria Targhetta⁶, John Ward⁷, and Núria Perulero⁵

Journal of Attention Disorders

1–9

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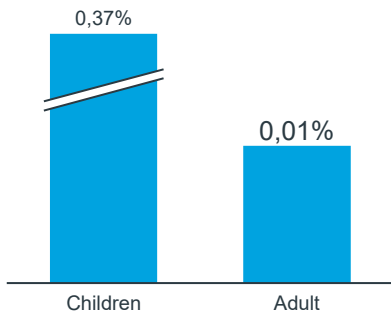
journals.sagepub.com/home/jad



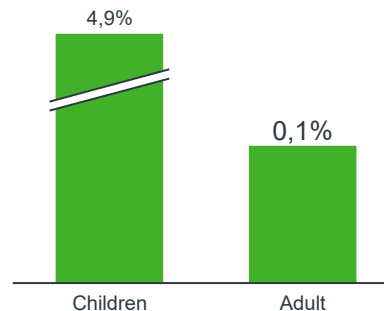
Epidemiología: análisis por edad y género

ADHD prevalence and incidence

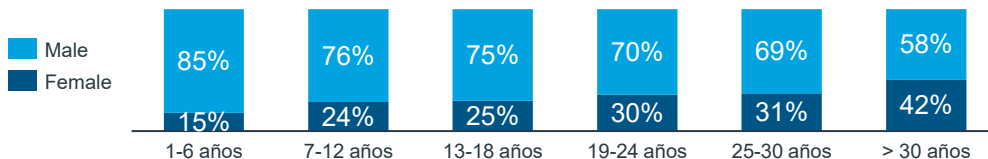
Incidence (New patients diagnosed per year)



Prevalence (Prevalent patients in the database)



Age and Gender distribution at diagnosis



Análisis total pacientes diagnosticados TDAH

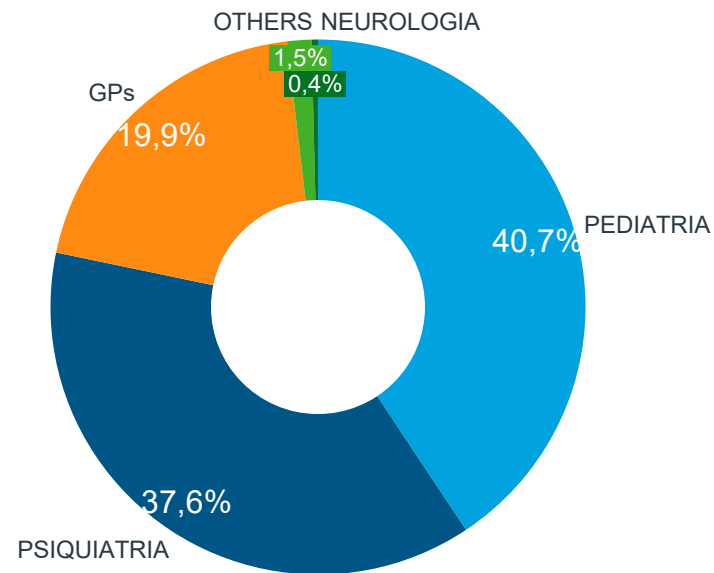
1. Distribución por género



2. Distribución por rango de edad



3. Especialidad que realiza el diagnóstico

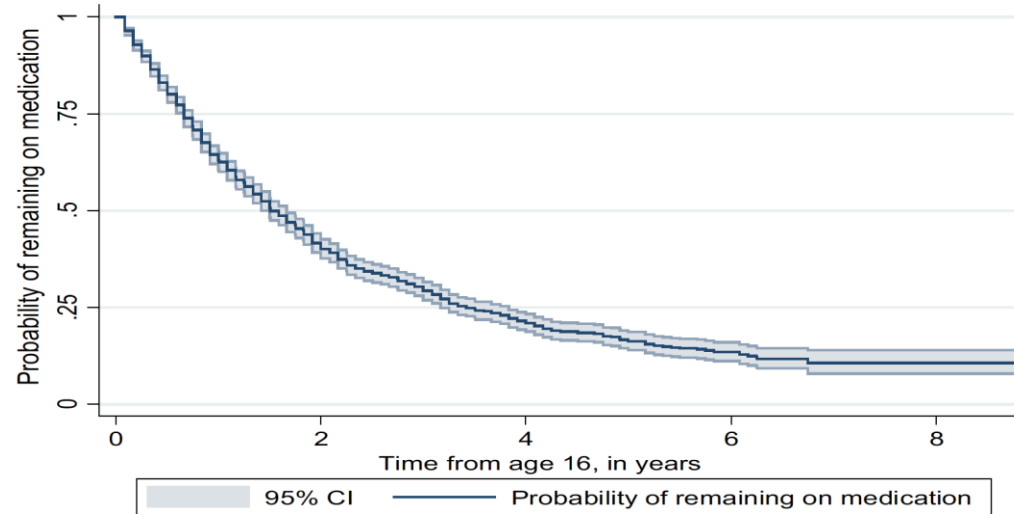


*ICD-9 Incluidos: 314.0 – 314.9

Población de referencia de la base es de 1,17 millones

Falta de continuidad de tratamiento

Fig. 1 The probability of remaining on ADHD medication over time for young people prescribed medication at age 16 (Kaplan–Meier plot, *shaded area* represents 95% confidence intervals)



Conclusiones



NICE National Institute for Health and Care Excellence

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Attention deficit hyperactivity disorder: diagnosis and management

NICE guideline [NG87] Published date: March 2018 Last updated: September 2019

Conclusiones

¿ A qué estamos esperando?

Agradecimientos



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Servicio de Salud Mental

