Psychological Medicine (2014), **44**, 2223–2229. © Cambridge University Press 2013
doi:10.1017/S0033291713002493

ORIGINAL ARTICLE

The heritability of clinically diagnosed attention deficit hyperactivity disorder across the lifespan

H. Larsson[1]*, Z. Chang[1], B. M. D'Onofrio[2] and P. Lichtenstein[1]

[1] *Department of Medical Epidemiology and Biostatistics, Karolinska Institutet, Stockholm, Sweden*
[2] *Department of Psychological and Brain Sciences, Indiana University, Bloomington, IN, USA*

Background. No prior twin study has explored the heritability of clinically diagnosed attention deficit hyperactivity disorder (ADHD). Such studies are needed to resolve conflicting results regarding the importance of genetic effects for ADHD in adults. We aimed to estimate the relative contribution of genetic and environmental influences for clinically diagnosed ADHD across the lifespan with a specific focus on ADHD in adults.

Method. Information on zygosity and sex was obtained from 59514 twins born between 1959 and 2001 included in the nationwide population-based Swedish Twin Registry. Clinical data for ADHD diagnoses (i.e. stimulant or non-stimulant medication for ADHD) were obtained from the Swedish Prescribed Drug Register (PDR) and from the National Patient Register (i.e. ICD-10 diagnosis of ADHD). Twin methods were applied to clinical data of ADHD diagnoses using structural equation modeling with monozygotic (MZ) and dizygotic (DZ) twins.

Results. The best-fitting model revealed a high heritability of ADHD [0.88, 95% confidence interval (CI) 0.83–0.92] for the entire sample. However, shared environmental effects were non-significant and of minimal importance. The heritability of ADHD in adults was also substantial (0.72, 95% CI 0.56–0.84).

Conclusions. This study shows that the heritability of clinically diagnosed ADHD is high across the lifespan. Our finding of high heritability for clinically diagnosed ADHD in adults indicates that the previous reports of low heritability are best explained by rater effects, and that gene-identification studies of ADHD in adults need to consider pervasiveness (e.g. multiple raters) and developmentally (e.g. childhood-onset criteria) informative data.

Received 19 April 2013; Revised 4 September 2013; Accepted 7 September 2013; First published online 10 October 2013

Key words: ADHD, adults, heritability, twin study.

Introduction

Many twin studies have explored the heritable nature of attention deficit hyperactivity disorder (ADHD) but none of these have been based on clinically diagnosed cases. Such a study is needed to clarify how genetic factors influence ADHD across different levels of severity (Larsson *et al.* 2012) and to resolve inconsistent results regarding the heritability of ADHD in adults (Franke *et al.* 2012).

Twin studies using parent or teacher ratings indicate that continuous measures of ADHD reveal a highly heritable component (~60–90%) (Faraone *et al.* 2005; Burt, 2009; Nikolas & Burt, 2010). The few available twin studies using categorical measures of ADHD (see Table 1) suggest equally high heritability estimates (Sherman *et al.* 1997; Thapar *et al.* 2000; Lichtenstein *et al.* 2010; Larsson *et al.* 2011) but these studies have several limitations. In particular, they applied broad categories containing milder cases that would not meet syndromal criteria for ADHD, and all studies lacked information on the age of onset or impairment criteria used in the DSM and ICD diagnostic definitions of the disorder. Thus, more stringent diagnostic methods and narrow definitions may generate different heritability estimates.

Twin studies suggest substantially lower heritability estimates (~30–40%) for ADHD in adults (van den Berg *et al.* 2006; Reiersen *et al.* 2008; Boomsma *et al.* 2010; Larsson *et al.* 2013*a*), but it has been difficult to determine whether the drop in heritability reflects true developmental changes or is related to rater effects (Franke *et al.* 2012). This is because twin studies on ADHD in adults have used self-ratings whereas studies on children have used other informants (i.e. parent and teacher ratings). The few studies on this topic suggest that the heritability of self-rated ADHD is low in both adults and adolescents (Kan *et al.* 2013; Merwood *et al.* 2013), and that the heritability of ADHD in adults is substantial when both parent and self-ratings are combined into a composite index of

* Address for correspondence: Dr H. Larsson, Department of Medical Epidemiology and Biostatistics, Karolinska Institutet, PO Box 281, Stockholm SE-171 77, Sweden.
(Email: Henrik.Larsson@ki.se)

https://doi.org/10.1017/S0033291713002493 Published online by Cambridge University Press

Table 1. *Twin studies exploring the heritability using categorical measures of attention deficit hyperactivity disorder (ADHD)*

Authors	Twin sample	Measure	Informant	% meeting cut-off criteria for ADHD	Heritability (%)
Larsson *et al.* 2011	Population: children/ adolescents; 1450 twin pairs; aged 8–17 years; Swedish	Longitudinal DSM-IV ADHD symptoms	Parents	(i) High trajectory of hyperactivity (ii) High trajectory of inattention	(i) 80 (ii) 72
Lichtenstein *et al.* 2010	Population: 10 895 twin pairs; aged 12 years; Swedish	DSM-IV ADHD symptoms	Parents	1.8	79
Sherman *et al.* 1997	Population: 288 twin pairs; aged 11–12 years; USA	DSM-III-R ADHD symptoms	Teachers and parents, combined	18	79
Thapar *et al.* 2000	Population: 2082 twin pairs; aged 11–12 years; UK	DSM-IV ADHD symptoms	Teachers and parents, combined	–	80

ADHD (Chang *et al.* 2013). Together, these findings suggest that the low heritability for ADHD in adults may be best explained by rater effects. Nevertheless, more rigorously characterized twin samples are required, including clinically stringent measures of ADHD, to more firmly establish the heritability of ADHD in adults.

In the current study we used data from 59 514 twins born between 1959 and 2001 included in the Swedish Twin Register (Lichtenstein *et al.* 2006). Clinical data on ADHD were obtained from Swedish national registers. We aimed to estimate the relative contribution of genetic, shared environmental and non-shared environmental influences for clinically diagnosed ADHD across the lifespan, with a specific focus on ADHD in adults. Based on previously observed similarities between continuous trait measures and broad categorical definitions, we predicted similar heritability estimates for clinically diagnosed ADHD. Based on recent cross-informant twin studies (Chang *et al.* 2013), we also predicted high heritability for ADHD in adults. This is because both cross-informant measures and clinical diagnosis focus on pervasive symptoms.

Method

The Swedish Twin Registry

We obtained data from the nationwide population-based Swedish Twin Registry (Lichtenstein *et al.* 2006). The target population in this study was all twins born in Sweden between 1959 and 2001 (n=89 174). Excluded from the analyses were twin pairs with unknown zygosity (n=21 714), twin pairs in which one twin or both twins had died (n=3250) or emigrated (n=4696) before the start of follow-up in 2001; thus, the final sample of 59 514 twins (29 177 male twins, 49%) represented 67% of the target population. Twin analyses on ADHD in adults were based on a subsample of 37 714 twins (18 092 male twins, 48%) born 1959–1991.

Zygosity was established using DNA testing or standard zygosity questionnaires concerning twin similarity and confusion (Lichtenstein *et al.* 2006). When zygosity was determined based on questionnaire data, only twins with more than 95% probability of being correctly classified were assigned a zygosity. In the twin analyses, 17 026 were monozygotic (MZ), 16 554 were dizygotic (DZ) and 25 934 were opposite-sex DZ twins.

National registers

Data from the Swedish Twin Registry were linked to the population-based Prescribed Drug Register (PDR) and the National Patient Register, using each individual's unique personal identification number.

The Swedish PDR is a national health-care register administered by the National Board of Health and Welfare (NBHW) with data on dispensed pharmaceuticals. Information regarding drug identity according to the Anatomical Therapeutic Chemical (ATC) classification system, quantity and dosage of the prescribed drug, and date of prescription has been registered since July 2005. The PDR covers the entire population of Sweden, and the identity of the patients is available for >99.7% of the population (Wettermark *et al.* 2007).

The National Patient Register, held by the NBHW, has nationwide coverage for psychiatric out-patient care since 2001. Every record has a discharge date, a primary discharge diagnosis and up to seven secondary diagnoses assigned by the treating medical doctor according to ICD-10 (WHO, 1992).

https://doi.org/10.1017/S0033291713002493 Published online by Cambridge University Press

Variables

Twins treated with stimulant or non-stimulant medication for ADHD [methylphenidate (N06BA04); atomoxetin (N06BA09); amphetamine (N06BA01); dexamphetamine (N06BA02)] at any time between July 2005 and July 2010 were identified through the PDR. National guidelines for ADHD medication, issued by the NBHW in 2002, stated that medication should be reserved for cases where other supportive interventions have failed, indicating that pharmacological ADHD treatment probably represents an indicator of the more severe cases of ADHD. The authority to prescribe ADHD drugs in Sweden is restricted to specialist physicians familiar with the treatment of this disorder. In the total sample of 59 514 twins, 730 (1.23%) were treated for ADHD/hyperkinetic disorder at any time between 2005 and 2010.

Twins obtaining a diagnosis of hyperkinetic disorder between 2001 and 2009 were identified through the Patient Register (ICD-10: F90). In the total sample of 59 514 twins, 525 (0.88%) had received a diagnosis of hyperkinetic disorder from out-patient care. A substantial number of these twins (n=392, 74.7%) were treated with stimulant or non-stimulant medication at any time between 2005 and 2010.

To maximize power in the twin model-fitting analyses, the present study applied an 'OR' approach to define clinically diagnosed ADHD, resulting in 863 twins (1.45%) who either met criteria for hyperkinetic disorder at any time between 2001 and 2009 or received stimulant or non-stimulant treatment at any time between 2005 and 2010. We have recently reported high specificity for this register-based definition of ADHD (Larsson *et al.* 2013*b*).

Twin model fitting on ADHD in adults was based on the subsample of 37 714 twins born between 1959 and 1991 (i.e. $\geqslant$18 years old at the end of follow-up) resulting in 241 (0.64%) twins with a clinical diagnosis of ADHD in adults; our definition only considered twins diagnosed with ADHD at age $\geqslant$18 years.

The study was approved by the research ethics committee at Karolinska Institutet, Stockholm, Sweden.

Statistical analyses

The concordance rate (i.e. the risk of ADHD for the cotwin of a twin with ADHD) was calculated as the proportion of individuals belonging to concordantly affected twin pairs out of all twins with the disorder. Correlation of liability (tetrachoric within-twin pair correlation) was also estimated for each sex-zygosity group. Higher concordance rates and correlations of liability in MZ than in DZ twins indicate a genetic contribution to the manifestation of disease. Shared environmental influences were inferred if the DZ correlation was greater than half of the MZ correlation (the DZ correlation higher than expected from sharing 50% of their segregating genes).

Biometric twin analyses were conducted on raw ordinal data using the Mx program (Neale *et al.* 2003) to determine the relative contribution of additive genetic factors (A, heritability) reflecting additive effects of different alleles, shared environmental factors (C) reflecting environmental influences that make twin siblings similar to each other and non-shared environmental factors (E) reflecting non-genetic influences that make twin pairs dissimilar (Rijsdijk & Sham, 2002). In twin models based on ordinal raw data, each individual is coded as having the disease or not, and the threshold (z score) corresponds to the rate of the disease.

The following combinations of variance components were considered in the twin models: ACE and AE. Three sex-limitation models were fitted to the data. The full sex-limitation model allows quantitative and qualitative differences in the parameter estimates between males and females. The common effects sex-limitation model allows quantitative sex differences between males and females, but no qualitative differences. The null model equates all genetic and environmental parameter estimates for males and females, testing the hypothesis that there are no sex differences. Goodness of fit for the different twin models was assessed by Akaike's Information Criterion (AIC); a lower AIC value indicates better fit of the model to the observed data.

The quantitative genetic models were performed under the usual assumptions of the classical twin designs: random mating, no gene–environment interaction, and equal environments of MZ and DZ twin pairs (Rijsdijk & Sham, 2002).

Results

Concordance rates and tetrachoric correlations for the full sample (59 514 twins born 1959–2001) are shown in Table 2. Tetrachoric DZ correlations were half of the MZ correlations, suggesting genetic, but not shared environmental, influences on ADHD. MZ correlations were less than 1, suggesting non-shared environmental influences (including measurement error). Tetrachoric twin correlations were similar for males and females, indicating a lack of quantitative sex differences in the genetic and environmental contribution. In addition, twin correlations were similar for same-sex DZ and opposite-sex DZ twins, suggesting no qualitative sex differences (Table 2).

Table 3 displays the age-adjusted model-fitting results of ACE and AE sex-limitation models compared to the saturated model using the full twin

https://doi.org/10.1017/S0033291713002493 Published online by Cambridge University Press

Table 2. *Concordance rates and tetrachoric correlations with 95% confidence intervals (CIs) for clinical diagnosis of attention deficit hyperactivity disorder (ADHD) in 59 514 Swedish twins, by sex and zygosity*

					Opposite-sex twins	
	MZM	DZM	MZF	DZF	Case = Male	Case = Female
No. of concordant affected pairs	35	13	11	5	29	29
No. of discordant pairs	55	139	38	68	277	100
Concordance rate (95% CI)	0.56 (0.45–0.66)	0.16 (0.09–0.25)	0.37 (0.21–0.54)	0.13 (0.04–0.26)	0.17 (0.12–0.24)	0.37 (0.27–0.47)
Tetrachoric correlation (95% CI)	0.90 (0.84–0.94)	0.48 (0.33–0.61)	0.81 (0.68–0.90)	0.50 (0.28–0.67)	0.49 (0.40–0.58)	

MZM, Monozygotic male; MZF, monozygotic female; DZM, dizygotic male; DZF, dizygotic female.

sample (59 514 twins born 1959–2001). In all these models, thresholds were equated across twin 1 and twin 2, for MZ and DZ twins, but not across males (z score = 1.46) and females (z score = 2.06). The AE null model had the lowest AIC value; that is, a model that constrained the genetic and environmental parameter estimates to be equal across sex, and excluded variance in liability due to the shared environmental factor, provided the most parsimonious fit of the data. This best-fitting model estimated the heritability and non-shared environment contribution as 0.88 [95% confidence interval (CI) 0.83–0.92] and 0.12 (95% CI 0.08–0.17) respectively.

Similar results were obtained when refitting all twin models using an 'AND' approach (i.e. clinically diagnosed ADHD defined as meeting criteria for hyperkinetic disorder and received stimulant/non-stimulant treatment). The best-fitting model (the AE null model) estimated the heritability and non-shared environment contribution as 0.89 (95% CI 0.82–0.94) and 0.11 (95% CI 0.06–0.18) respectively. Similar genetic and environmental parameter estimates were also obtained when the twin modeling was restricted to either ADHD cases identified through ICD diagnoses (A = 0.89, 95% CI 0.83–0.93; E = 0.11, 95% CI 0.07–0.17) or pharmacological ADHD treatments (A = 0.88, 95% CI 0.83–0.92; E = 0.12, 95% CI 0.08–0.17), providing converging evidence across different outcome definitions (Table 3).

Heritability of ADHD in adults

Analyses were also conducted on the 37 714 twins born between 1959 and 1991 to estimate the heritability of ADHD in adults. These twins were on average 23.0 years old at the start of the register follow-up. Importantly, we only considered twins diagnosed with ADHD at age $\geqslant$18 years. The best-fitting model (the AE null model) estimated the heritability and non-shared environment contributions as 0.72 (95% CI 0.56–0.84) and 0.28 (95% CI 0.16–0.44) respectively.

Discussion

This study showed that the heritability of clinically diagnosed ADHD is high across the lifespan. The finding of high heritability for clinically diagnosed ADHD in adults suggests that the previous reports of low heritability are best explained by rater effects and that gene-identification studies of ADHD in adults should not rely only on self-ratings.

In this study, using data from representative national registers, we estimated the heritability of clinically diagnosed ADHD at 88%. Our result is in line with the large number of twin studies using continuous trait measures of ADHD based on parent or

https://doi.org/10.1017/S0033291713002493 Published online by Cambridge University Press

Table 3. *Model-fitting results of univariate analysis of attention deficit hyperactivity disorder (ADHD)*

	Fit of model compared to saturated model				
Model	−2LL	df	χ^2	Δdf	AIC
Saturated model	8092.5	59489	–	–	–
1. ACE univariate					
Full sex-limitation model[a]	8112.0	59505	19.5	16	−12.5
Common effects sex-limitation model[b]	8112.0	59506	19.5	17	−14.5
Null model[c]	8113.5	59509	21.0	20	−19.0
2. AE univariate					
Full sex-limitation model[a]	8112.5	59507	20.0	18	−16.0
Common effects sex-limitation model[b]	8112.5	59508	20.0	19	−18.0
Null model[c]	**8113.7**	**59510**	**21.3**	**21**	**−20.7**

−2LL, Likelihood fit statistic; df, degrees of freedom; χ^2, the difference in –2LL between the saturated and restricted models; Δdf, difference in df between the saturated and restricted models; AIC, Akaike's Information Criterion.

Best-fitting model indicated in bold.

[a] The full sex-limitation model allows quantitative and qualitative differences in the parameter estimates between males and females.

[b] The common effects sex-limitation model allows quantitative sex differences between males and females, but no qualitative differences.

[c] The null model equates all genetic and environmental parameter estimates for males and females, testing the hypothesis that there are no sex differences.

teacher ratings (Faraone *et al.* 2005; Burt, 2009), and the few studies that have explored the genetic impact on categorically defined ADHD (Sherman *et al.* 1997; Thapar *et al.* 2000; Lichtenstein *et al.* 2010; Larsson *et al.* 2011). There are noteworthy differences between the present study and these prior twin studies, in particular related to differing assessment methodologies. In the present study subjects were diagnosed using ICD-10. These diagnoses are performed by clinicians, and thus based on structured interviews covering age of onset of the impairing symptoms and presence of impairment in multiple settings, whereas prior twin studies were based on quantitative measures of ADHD symptoms without addressing the childhood criteria and not systematically assessing the impairment in multiple settings criteria. Nevertheless, remarkably similar heritability estimates for ADHD were obtained across studies, suggesting strong genetic effects in ADHD regardless of whether the assessment used continuous trait measures, broad categorical definitions or narrow diagnostic definitions, which in turn provides further support for ADHD as a quantitative extreme of genetic and environmental factors operating dimensionally throughout the distribution of ADHD symptoms (Levy *et al.* 1997; Chen *et al.* 2008; Larsson *et al.* 2012).

One novel finding of this study was that clinically diagnosed ADHD in adults was highly heritable. This finding is in line with a recent cross-informant twin study reporting that the heritability of ADHD in 19- to 20-year-olds was 78%, when both parent and self-ratings were combined into a composite index of ADHD symptoms to adjust for rater bias (Chang *et al.* 2013), and also with prior family studies suggesting a high familial loading on ADHD in adults (Biederman *et al.* 1995, 1996; Faraone *et al.* 2000; Faraone, 2004), but is inconsistent with twin studies of self-rated ADHD in adults (van den Berg *et al.* 2006; Reiersen *et al.* 2008; Boomsma *et al.* 2010; Larsson *et al.* 2013*a*). One possible explanation of previous reports of low heritability for ADHD in adults is the increased contribution of measurement error (reflecting accuracy of the measures) associated with the use of self-ratings (Franke *et al.* 2012; Chang *et al.* 2013; Kan *et al.* 2013; Merwood *et al.* 2013). Another explanation is that the clinical diagnosis of ADHD in adults reflects persistence of the childhood disorder (i.e. childhood onset), whereas cross-sectional self-ratings may also reflect adult-onset ADHD-like symptoms (i.e. phenocopies) involving different genetic and environmental processes. Taken together, this indicates that self-ratings may not be the best measure to use in gene-identification studies of ADHD in adults and that other factors such as childhood onset, pervasiveness and impairment should be taken into account.

Limitations

This study had some limitations. First, it was not possible to classify ADHD cases according to the

https://doi.org/10.1017/S0033291713002493 Published online by Cambridge University Press

three DSM-IV ADHD subtypes (i.e. combined, primarily hyperactive-impulsive and primarily inattentive type) as they were not recorded across the registers. However, prior twin research does suggest similar heritability estimates for the inattentive and hyperactive-impulsive component of ADHD (Larsson *et al*. 2006; Nikolas & Burt, 2010).

Second, the validity of the non-standardized register diagnoses has not been explored using comparisons with research diagnoses based on independent semi-structured interviews and/or medical records. Although our own validity checks of ADHD support high specificity for the register-based diagnosis, we could not rule out false negatives (i.e. individuals with ADHD who had never been recorded in any registers). This is because the Patient Register provided coverage of out-patient care after 2001 and the PDR provided data on twins treated with stimulant or non-stimulant medication after 2005. However, bias due to such outcome misclassification most probably applies equally to MZ and DZ pairs and would therefore not introduce a significant upward bias of the heritability estimate.

Third, the ascertainment of ADHD cases was based predominantly on ICD-10 diagnosis of hyperkinetic disorder and prescribed medication unique for the treatment of ADHD. The ICD-10 definition of ADHD is stricter than that in DSM-IV, and the Swedish national guidelines for medication of ADHD state that medication should be reserved for cases where other supportive interventions have failed, indicating that our measure most probably represents an indicator of the more severe cases of ADHD. Thus, generalizations should be made with caution.

Fourth, even with a nationwide twin cohort born 1959–2001, the absolute numbers of clinically diagnosed concordant or discordant twin pairs remained limited, resulting in wide CIs and limited power to detect shared environmental influences. Point estimates, especially for ADHD in adults, should therefore be interpreted with caution.

Conclusions

We have demonstrated that heritability estimates for clinically diagnosed ADHD are high across the lifespan. This indicates that the previous reports of low heritability for ADHD symptoms in adults are best explained by rater effects giving rise to measurement error, rather than by distinct developmental changes in the importance of non-shared environmental factors.

Acknowledgments

This research was supported by grants from the Swedish Council for Working Life and Social Research and from the Swedish Research Council (2010-3184; 2011-2492) and National Institute of Child Health and Human Development (HD061817). All authors had full access to all the data in the study. H. Larsson takes responsibility for the integrity of the data and the accuracy of the data analysis.

Declaration of Interest

None.

References

Biederman J, Faraone S, Milberger S, Curtis S, Chen L, Marrs A, Ouellette C, Moore P, Spencer T (1996). Predictors of persistence and remission of ADHD into adolescence: results from a four-year prospective follow-up study. *Journal of the American Academy of Child and Adolescent Psychiatry* **35**, 343–351.

Biederman J, Faraone SV, Mick E, Spencer T, Wilens T, Kiely K, Guite J, Ablon JS, Reed E, Warburton R (1995). High risk for attention deficit hyperactivity disorder among children of parents with childhood onset of the disorder: a pilot study. *American Journal of Psychiatry* **152**, 431–435.

Boomsma DI, Saviouk V, Hottenga JJ, Distel MA, de Moor MH, Vink JM, Geels LM, van Beek JH, Bartels M, de Geus EJ, Willemsen G (2010). Genetic epidemiology of attention deficit hyperactivity disorder (ADHD index) in adults. *PLoS One* **5**, e10621.

Burt SA (2009). Rethinking environmental contributions to child and adolescent psychopathology: a meta-analysis of shared environmental influences. *Psychological Bulletin* **135**, 608–637.

Chang Z, Lichtenstein P, Asherson PJ, Larsson H (2013). Developmental twin study of attention problems: high heritabilities throughout development. *JAMA Psychiatry* **70**, 311–318.

Chen W, Zhou K, Sham P, Franke B, Kuntsi J, Campbell D, Fleischman K, Knight J, Andreou P, Arnold R, Altink M, Boer F, Boholst MJ, Buschgens C, Butler L, Christiansen H, Fliers E, Howe-Forbes R, Gabriels I, Heise A, Korn-Lubetzki I, Marco R, Medad S, Minderaa R, Muller UC, Mulligan A, Psychogiou L, Rommelse N, Sethna V, Uebel H, McGuffin P, Plomin R, Banaschewski T, Buitelaar J, Ebstein R, Eisenberg J, Gill M, Manor I, Miranda A, Mulas F, Oades RD, Roeyers H, Rothenberger A, Sergeant J, Sonuga-Barke E, Steinhausen HC, Taylor E, Thompson M, Faraone SV, Asherson P (2008). DSM-IV combined type ADHD shows familial association with sibling trait scores: a sampling strategy for QTL linkage. *American Journal of Medical Genetics. Part B, Neuropsychiatric Genetics* **147B**, 1450–1460.

Faraone SV (2004). Genetics of adult attention-deficit/hyperactivity disorder. *Psychiatric Clinics of North America* **27**, 303–321.

Faraone SV, Biederman J, Monuteaux MC (2000). Toward guidelines for pedigree selection in genetic studies of attention deficit hyperactivity disorder. *Genetic Epidemiology* **18**, 1–16.

https://doi.org/10.1017/S0033291713002493 Published online by Cambridge University Press

Faraone SV, Perlis RH, Doyle AE, Smoller JW, Goralnick JJ, Holmgren MA, Sklar P (2005). Molecular genetics of attention-deficit/hyperactivity disorder. *Biological Psychiatry* **57**, 1313–1323.

Franke B, Faraone SV, Asherson P, Buitelaar J, Bau CH, Ramos-Quiroga JA, Mick E, Grevet EH, Johansson S, Haavik J, Lesch KP, Cormand B, Reif A (2012). The genetics of attention deficit/hyperactivity disorder in adults, a review. *Molecular Psychiatry* **17**, 960–987.

Kan KJ, Dolan CV, Nivard MG, Middeldorp CM, van Beijsterveldt CE, Willemsen G, Boomsma DI (2013). Genetic and environmental stability in attention problems across the lifespan: evidence from the Netherlands Twin Register. *Journal of the American Academy of Child and Adolescent Psychiatry* **52**, 12–25.

Larsson H, Anckarsater H, Rastam M, Chang Z, Lichtenstein P (2012). Childhood attention-deficit hyperactivity disorder as an extreme of a continuous trait: a quantitative genetic study of 8,500 twin pairs. *Journal of Child Psychology and Psychiatry and Allied Disciplines* **53**, 73–80.

Larsson H, Asherson P, Chang Z, Ljung T, Friedrichs B, Larsson JO, Lichtenstein P (2013*a*). Genetic and environmental influences on adult attention deficit hyperactivity disorder symptoms: a large Swedish population-based study of twins. *Psychological Medicine* **43**, 197–207.

Larsson H, Dilshad R, Lichtenstein P, Barker ED (2011). Developmental trajectories of DSM-IV symptoms of attention-deficit/hyperactivity disorder: genetic effects, family risk and associated psychopathology. *Journal of Child Psychology and Psychiatry and Allied Disciplines* **52**, 954–963.

Larsson H, Lichtenstein P, Larsson JO (2006). Genetic contributions to the development of ADHD subtypes from childhood to adolescence. *Journal of the American Academy of Child and Adolescent Psychiatry* **45**, 973–981.

Larsson H, Ryden E, Boman M, Langstrom N, Lichtenstein P, Landen M (2013*b*). Risk of bipolar disorder and schizophrenia in relatives of people with attention-deficit hyperactivity disorder. *British Journal of Psychiatry* **203**, 103–106.

Levy F, Hay DA, McStephen M, Wood C, Waldman I (1997). Attention-deficit hyperactivity disorder: a category or a continuum? Genetic analysis of a large-scale twin study. *Journal of the American Academy of Child and Adolescent Psychiatry* **36**, 737–744.

Lichtenstein P, Carlstrom E, Rastam M, Gillberg C, Anckarsater H (2010). The genetics of autism spectrum disorders and related neuropsychiatric disorders in childhood. *American Journal of Psychiatry* **167**, 1357–1363.

Lichtenstein P, Sullivan PF, Cnattingius S, Gatz M, Johansson S, Carlstrom E, Bjork C, Svartengren M, Wolk A, Klareskog L, de Faire U, Schalling M, Palmgren J, Pedersen NL (2006). The Swedish Twin Registry in the third millennium: an update. *Twin Research and Human Genetics* **9**, 875–882.

Merwood A, Greven CU, Price TS, Rijsdijk F, Kuntsi J, Mcloughlin G, Larsson H, Asherson PJ (2013). Different heritabilities but shared etiological influences for parent, teacher and self-ratings of ADHD symptoms: an adolescent twin study. *Psychological Medicine* **43**, 1973–1984.

Neale MC, Boker SM, Xie G, Maes HH (2003). *Mx Statistical Modeling*. Department of Psychiatry, VCU Box 900126: Richmond, VA 23298.

Nikolas MA, Burt SA (2010). Genetic and environmental influences on ADHD symptom dimensions of inattention and hyperactivity: a meta-analysis. *Journal of Abnormal Psychology* **119**, 1–17.

Reiersen AM, Constantino JN, Grimmer M, Martin NG, Todd RD (2008). Evidence for shared genetic influences on self-reported ADHD and autistic symptoms in young adult Australian twins. *Twin Research and Human Genetics* **11**, 579–585.

Rijsdijk FV, Sham PC (2002). Analytic approaches to twin data using structural equation models. *Briefings in Bioinformatics* **3**, 119–133.

Sherman DK, McGue MK, Iacono WG (1997). Twin concordance for attention deficit hyperactivity disorder: a comparison of teachers' and mothers' reports. *American Journal of Psychiatry* **154**, 532–535.

Thapar A, Harrington R, Ross K, McGuffin P (2000). Does the definition of ADHD affect heritability? *Journal of the American Academy of Child and Adolescent Psychiatry* **39**, 1528–1536.

van den Berg SM, Willemsen G, de Geus EJ, Boomsma DI (2006). Genetic etiology of stability of attention problems in young adulthood. *American Journal of Medical Genetics. Part B, Neuropsychiatric Genetics* **141B**, 55–60.

Wettermark B, Hammar N, Fored CM, Leimanis A, Otterblad Olausson P, Bergman U, Persson I, Sundstrom A, Westerholm B, Rosen M (2007). The new Swedish Prescribed Drug Register – opportunities for pharmacoepidemiological research and experience from the first six months. *Pharmacoepidemiology and Drug Safety* **16**, 726–735.

WHO (1992). *The ICD-10 Classification of Mental and Behavioural Disorders: Clinical Descriptions and Diagnostic Guidelines*. World Health Organization: Geneva.

https://doi.org/10.1017/S0033291713002493 Published online by Cambridge University Press