# Sex differences in ADHD trajectories across childhood and adolescence

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# Sex differences in ADHD trajectories across childhood and adolescence

**Running Head: ADHD sex differences**

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**Research Highlights**

- Males and females show differing ADHD developmental trajectories
- Females are more likely than males to show symptom onsets around adolescence
- Early adolescence is a specific window of vulnerability for manifest symptom increases
- Current age of onset diagnostic criteria for ADHD may disadvantage females

**Abstract**

Background: Previous studies have hinted at sex differences in developmental trajectories in ADHD symptoms; however, little is known about the nature or cause of these differences and their implications for clinical practice.

Method: We used growth mixture modelling in a community-ascertained cohort of n=1571 participants to study sex differences in ADHD symptom developmental trajectories across the elementary and secondary school years. Participants were measured at ages 7, 8, 9, 10, 11, 12, 13, and 15.

Results: We found that females were more likely to show large symptom increases in early adolescence while males were more likely to show elevated symptoms from childhood. For both males and females, early adolescence represented a period of vulnerability characterised by relatively sudden symptom increases.

Conclusions: Females affected by hyperactivity/impulsivity may be more likely to be excluded from diagnosis due to current age of onset criteria. More attention should be paid to early adolescence as a period of risk for hyperactivity/impulsivity symptom onset or worsening.

Keywords: ADHD; sex differences; development

Attention-deficit/hyperactivity disorder (ADHD) is characterised by impairing levels of inattention and/or hyperactivity/impulsivity (APA, 2013). In childhood, ADHD is more common in males than in females, with a sex ratio of around 3:1 (Wilcutt, 2012). In adulthood; however, the sex ratio appears to be closer to 1:1 (e.g. Williamson & Johnston, 2015). The decline in ADHD sex ratios with age hints at sex differential developmental trajectories of symptoms. This has potentially important implications for clinical practice, raising the question of whether and how age and sex should collectively be taken into account in diagnosis and treatment. To provide illumination on this issue, we evaluated whether males and females in a community-based sample of n=1571 individuals differed on ADHD symptom trajectories across ages 7 to 15.

A higher prevalence of childhood ADHD in males than females is a consistent finding in ADHD research and is in-keeping with the general tendency for males to show higher levels of externalising or disruptive behaviour (e.g. Martel, 2013; Wilcutt, 2012). While extraneous factors such as referral bias seem to contribute to the higher prevalence of clinically diagnosed ADHD in males, studies in community-based samples have confirmed a sex difference in prevalence (e.g. Gershon & Gershon, 2002).

Taken at face value, the decline in sex ratios in ADHD by adulthood suggest either greater persistence, or later onset, of symptoms in females as compared to males. There are, however, several alternative possibilities that must be addressed. First, it has been noted that the narrowing sex difference could reflect later identification of females with ADHD. Given that females with ADHD show less disruptive behaviour, their issues may be missed by parents and teachers (e.g. Gershon & Gershon, 2002). They may instead self-refer in late adolescence or adulthood due to a subjective sense of impairment, or comorbid conditions such as depression and anxiety (e.g. Williamson & Johnston, 2015). Concerns about age-dependent referral biases are partly addressed by the confirmation of sex ratio declines from

childhood to adulthood in community-based longitudinal samples where ADHD symptoms are assessed at both stages in life (e.g. Agnew-Blais et al., 2015; Caye et al., 2015; Moffit et al., 2015). However, there are currently only a small number of studies that have reported the data needed to support this conclusion.

Another possibility is that males are more likely to lose their ADHD diagnosis because of inadequate hyperactivity/impulsivity diagnostic criteria for adulthood (Williamson & Johnston, 2015). DSM 5 criteria, for example, refer to symptoms such as leaving one's seat in the classroom, climbing excessively, and difficulty playing quietly (APA, 2013). These symptoms are not appropriate markers for adults. As such, individuals with primarily hyperactive/impulsive symptoms are liable to lose their diagnosis with age even if they remain impaired by symptoms. This is in contrast to those with problems primarily in the inattention domain for whom there is no substantive reduction in the 'suitability' of diagnostic criteria with age. Given that females are relatively more affected by inattention (e.g. Biederman et al., 2002), it follows that females could show higher rates of persistence of ADHD symptoms than males for entirely spurious reasons related to the developmental inappropriateness of some diagnostic markers.

Developmental inappropriateness of diagnostic criteria is an important issue in its own right; however, there are reasons to question its impact on sex ratio declines with age. In one community-based longitudinal study, for example, a sex ratio decline was observed but was attributable to females having a later onset rather than a greater persistence of symptoms into adulthood (Agnew-Blais et al., 2015). Similarly, in studies analysing retrospectively reported ADHD symptoms in childhood and adulthood, no sex difference in persistence has been observed (Kessler et al., 2005; Ebejer et al., 2012).

Finally, the shifting sex ratio could reflect sex differences in symptom distributions. One proposed explanation for later symptom onsets refers to an interaction with environmental demands and supports. Symptoms may remain 'subthreshold' in supportive childhood environments but may tip over into the clinical range with increasing autonomy and life demands (e.g. Faraone & Biederman, 2016). It has been suggested that males show greater variance in ADHD symptom liability; specifically, that males are over-represented at both the highest and lowest levels (e.g. Arnett et al., 2015). This could mean that there are more females with symptoms just below diagnostic thresholds in early childhood, which move into the clinical range as academic, social and other life challenges intensify. Again, this may be especially relevant for inattention symptoms which may be minimally disruptive in early childhood, but problematic later in life when academic and occupational performance comes to play a more central role. This concern can be addressed by community-based longitudinal studies using continuous measurement scales for ADHD symptoms, as opposed to binary classifications based on meeting versus not meeting diagnostic criteria.

A useful statistical approach for studying group differences in developmental trajectories in continuously-measured ADHD symptoms is growth mixture modelling. Growth mixture modelling summarises individual developmental trajectories over time using a small number of categories defined by patterns of symptom growth/decline over time. Only a few studies have examined sex differences in ADHD symptom developmental trajectories in non-clinical samples. Döpfner et al. (2014) examined developmental trajectories of parent-reported ADHD symptoms over ages 7 to 19. For both inattention and hyperactivity symptoms, three categories were judged optimal. These were characterised by high versus moderate versus low levels, all with small declines in severity over time. They found that boys were over-represented in trajectory groups characterised by high levels of ADHD symptoms. Given the age range studied, this was generally in line with the observation that

males are more affected by ADHD prior to adulthood; however, it did not reveal any sex differences in ages of onset or peak ages of symptoms.

Malone et al. (2010) examined developmental trajectories across grades 3 to 9 (ages 6/7 to 13/14) based on parent-reported ADHD symptoms. Trajectories could be summarised in terms of three categories which they labelled 'minimal', 'concave' and 'convex'. The minimal group showed low levels of ADHD symptoms while the concave and convex groups showed higher levels. The convex group peaked in symptom levels in grade 6, while the concave group peaked in grade 3, showing a minimum at grade 6 and a slight rebound by grade 9. Males were over-represented in the 'concave' class relative to the 'minimal' class; however, the 'convex' class did not differ in gender composition to the 'minimal' class. Thus, males were relatively more likely to show an early-peaking trajectory and females to show an early adolescence-peaking trajectory.

Using the current sample, Murray, Eisner, Obsuth & Ribeaud (2017) examined developmental trajectories in inattention and hyperactivity/impulsivity symptoms across ages 7 to 15 based on teacher assessments. Their study had a particular focus on identifying predictors of early versus late onset symptoms. They judged a four-class growth mixture solution to be optimal for both inattention and hyperactivity/impulsivity dimensions. Classes were highly similar across the dimensions and could be characterised as: 'high stable', 'low increasing', 'high decreasing' and 'low stable'. These labels describe initial symptom levels (high/low) and trajectories over time (stable/decreasing/increasing). They found that males were more likely to be in the 'low increasing' category with later onsets as compared to the low stable category but the sex difference in membership in the 'low increasing' versus 'high stable' categories was not significant. The non-significant trend in the latter comparison was for relatively more females in the late onset compared with high stable group. These data thus hinted at possible later onsets for females.

The above-mentioned growth mixture studies yielded evidence indicative of sex differences in ADHD developmental trajectories; however, they only examined sex differences in the likelihood of being in certain trajectory classes estimated in combined samples of males and females. They did not examine whether males and females show different sets of trajectory classes altogether. Robbers et al. (2011) examined trajectories of parent-reported attention problems across ages 6 to 12 for males and females separately. They found very similar results across boys and girls. Here, developmental trajectories for both sexes could be described by three classes: 'stable low', 'low increasing' and 'high decreasing'. Similarly, Van Lier et al. (2007) fit growth mixture models to parent-reported ADHD symptom data across ages 4 to 18 for males and females separately. They found that in spite of significant sex differences in overall symptom levels, developmental trajectories were similar across males and females. For both sexes, ADHD symptoms could be characterised by four classes: 'near zero', 'low', 'moderate' and 'high' with almost identical class prevalences in males versus females. They also found no significant differences in the shape of the latter trajectory across males and females; however graphical displays of the four trajectory classes suggested that each female class was characterised by slightly lower levels of symptoms than the corresponding male class.

Taken together, the evidence from community samples provides a mixed picture on whether there are substantively important sex differences in developmental trajectories for ADHD. Some studies have suggested that females may be more likely to have a later onset, especially around puberty, while others have suggested no sex differences. Importantly, no previous study of this type has been specifically focussed on characterising sex differences in trajectories; rather, each tested sex differences as a secondary or preliminary analysis. As such, previous studies may not have been optimally calibrated to detect and interpret sex differences. In this study we, therefore, specifically focus on sex differences in

developmental trajectories and evaluate whether males and females can be characterised by different sets of developmental trajectory classes. In particular, we sought to establish whether females are more likely to have trajectories characterised by later symptom onsets.

## Method

### Participants

Participants were from the ongoing Zurich Project on Social Development from Childhood to Adulthood (z-proso). Z-proso is a longitudinal cohort study of psychosocial development with a particular focus on externalising problems. The first wave of z-proso was in 2004 when participants were aged 7 and entering school. Those due to attend one of 56 schools in Zurich (selected using a stratified random sampling procedure) were invited to participate via their parents. Parents provided informed consent on behalf of their child until age 11, after which point the participants themselves provided consent. Of the N=1675 target sample, n=1571 contributed data to the current study (761 females and 810 males). Given ascertainment methods and high participation rates, the sample can be considered broadly representative of the underlying same-aged Zurich population, with a slight under-representation of participants with parents from immigrant backgrounds. Given the composition of the Zurich population, the sample is diverse in ethnic and socioeconomic terms. Further information on the sample and z-proso in general can be found at: http://www.jacobscenter.uzh.ch/en/research/zproso/aboutus.html. Details of recruitment, assessment, measurement and attrition are also provided in previous publications (Eisner & Ribeaud, 2007; Eisner, Murray, Eisner, Ribeaud, 2018).

Data used in the current study were collected from teachers when the participants were aged 7 (median age =7.45), 8 (median= 8.23), 9 (median = 9.21), 10 (median= 10.70), 11 (median= 11.60), 12 (median= 12.63), 13 (median= 13.88) and 15 (median= 15.68).

Variable-specific sample sizes at each wave are provided in Table 1. From baseline the sample size decreased with drop-out but increased again at age 13 at the point at which consent to participate was in the hands of the participants themselves, rather than their parents. A comprehensive analysis of attrition is reported in Eisner et al., (2018). This study found that, in a multiple regression and after correction for multiple comparisons there was no significant relation between ADHD symptom levels and drop-out. However, in bivariate analyses higher teacher-reports of ADHD symptoms were significantly associated with drop-out before age 11 (OR=1.20, $p<.001$). We thus used full information maximum likelihood (FIML) estimation to deal with missingness. FIML provides unbiased parameter estimates provided that data are (conditionally) missing at random (MAR).

**Ethical Considerations**

Given the minimally intrusive nature of the study design, questions and interventions, as well as the focus on social science research questions, the relevant Ethics Committee of the Canton of Zurich issued, based on the Swiss Human Research Act, a "declaration of no objection" for the z-proso project. It states that the project falls outside the remit of the Ethics Committee of the Canton of Zurich, and furthermore declared z-proso as ethically unproblematic.

**Measures**

Inattention and hyperactivity/impulsivity symptoms were measured using the teacher-report version of the *Social Behavior Questionniare* (SBQ; Tremblay et al., 1991). The measure includes four inattention items, and four hyperactivity/impulsivity items. Items have a five-point response scale which runs from *never* to *very often.* They were administered in paper and pencil format to each participant's teacher as part of a larger questionnaire on child psychosocial functioning. Most youth had the same teacher across ages 7, 8, 9 before

switching to a different teacher who taught them across ages 10, 11, 12. At ages 13 and 15, participants were in high school. The potential effects of the teacher changes were examined in growth curve analyses by Murray, Eisner, Obsuth & Ribeaud (2017). In that study, it was found that there were excess correlations between data provided by the same informant (i.e. between the data at ages 7, 8 and 9 and between the data at ages 10, 11 and 12). Residual covariances were thus included between scores provided by the same informant at different waves, resulting in an improvement in model fit. The study also plotted the raw mean scores across time to assess whether there was any qualitative shift in responses corresponding to the teacher changes. The study found no evidence for such as shift.

The psychometric properties of the SBQ in the current sample have been analysed in several previous publications (e.g. Murray, Eisner & Ribeaud, 2017; Murray, Obsuth, Eisner & Ribeaud 2017). These have provided evidence for the reliability and validity of the ADHD items as administered in z-proso.

The SBQ ADHD items were used to obtain latent inattention and hyperactivity/impulsivity estimates. This utilised a longitudinal confirmatory factor model in which ADHD was specified as an oblique factor model with inattention and hyperactivity/impulsivity latent factors formed of four items each. Scaling and identification were achieved by fixing the means and latent variances of the inattention and hyperactivity/impulsivity factors at baseline to 0 and 1 respectively and fixing the loading and intercept of the first item of each factor equal across measurement waves. Residual covariances between the same item measured at different waves were freely estimated. Models were fit with maximum likelihood estimation in *Mplus 7.13* (Muthen & Muthen, 2012). Factor scores were estimated from this model all had determinancies >.90.

**Statistical Procedure**

**Latent growth curve models.**

We began by comparing the average inattention and hyperactivity/impulsivity developmental trajectories for males and females using a multi-group latent growth curve model. We used the factor scores obtained using the longitudinal factor model described in the 'Measures' section. Residual covariances between hyperactivity/impulsivity (or inattention) between scores at ages 7,8, and 9 and between scores at ages 10, 11 and 12 were freely estimated to take account of the fact that common raters provided the data within these two sets of waves. We used a $\chi^2$difference test on cross-group equality constraints to test whether males and females differed significantly on intercept factor means and slope factor means.

**Growth mixture models.**

We next fit growth mixture models (GMMs) to the ADHD factor scores (obtained as described in the 'Measures' section) for each sex separately. Given the evidence that inattention and hyperactivity/impulsivity symptoms are dissociable in their developmental trajectories (Arnold et al., 2014) and that sex differences may vary by subtype (e.g. Lahey et al., 1994), GMMs were also fit separately to the inattention versus hyperactivity/impulsivity scores. Again, residual covariances between hyperactivity/impulsivity (or inattention) scores across waves where the same rater provided data were freely estimated. Factor variances and covariances were fixed equal across classes. We began by determining the optimal number of classes to retain. We fit models with between 1 and 6 classes. We fit a set of models with linear growth parameters only and a set of models with both linear and quadratic growth parameters, giving 12 models per dimension for each gender.

As not all models in the set were nested, the Lo-Mendall-Rubin (LMR) test was used to determine whether a model with *k*-1 classes should be rejected in favour of a model with *k*

classes for the set of linear models and the set of linear + quadratic models separately. AIC, BIC and saBIC provided supplemental model fit comparison information. They were used to compare non-nested models differing in whether they included both linear and quadratic growth versus linear growth only. Parameter estimates were also examined to determine whether best-fitting models made substantive sense. After selecting optimal class solutions for inattention and hyperactivity/impulsivity for males and females, we compared them descriptively in lieu of a direct multi-group model, which is not currently possible.

## Results

### Hyperactivity/impulsivity

A multi-group latent growth curve model with linear and quadratic growth and no cross-group equality constraints fit well to the hyperactivity/impulsivity scores ($\chi^2$ (42) =226.812, $p$<.001; CFI=.98, TLI=.97, RMSEA=.075, SRMR=.04). The intercept, linear slope and quadratic slope factor means for males were: 0.19, -0.42, and 0.09 respectively. The corresponding factor means for females were: -0.27, -0,61, and 0.29. These average gender trajectories are shown in Figure 1. Adding cross-group equality constraints on the intercept and linear and slope factor means resulted in a significant deterioration in fit [$\Delta\chi^2$ (3) = 205.135, $p$<.001], suggesting that the sex difference in average hyperactivity/impulsivity trajectory was statistically significant. Accordingly, the fit of the constrained model was poorer (CFI=0.95, TLI=0.94, RMSEA=0.11, SRMR=0.14).

Fit statistics for all hyperactivity/impulsivity GMMs tested are provided in Table S1 in Supplementary Materials. For males, considering the models with linear growth only, the LMR test favoured a 2-class model. However, considering the models with both linear and quadratic growth, a 3-class model was indicated. Of these two models, the 3-class model with quadratic growth had lower AIC, BIC and saBIC and was thus preferred overall. This model

is summarised in Table 3 and in Figure 2. The three classes could be characterised as 'low stable', 'high stable', and 'high increasing'.

For females, the linear growth model indicated by the LMR test was a 2-class model. The linear + quadratic growth model indicated by the LMR test was a 3-class model; however, given the tendency for the LMR test to over-extract (e.g. Nylund, Asparouhov & Muthén, 2007), we also considered a 2-class linear+ quadratic model given that the LMR test at this level was only marginally significant ($p$=.046). Of these three models, the 3-class model with both linear and quadratic growth had the lowest AIC, BIC and saBIC. For females, the 3-class model with both linear and quadratic growth was thus preferred on balance. This model is summarised in Table 2 and in Figure 2. The three classes could be characterised as 'low stable', 'high stable', and 'concave'. The prevalences indicate the proportion of individuals in the sample who were assigned to each class. The intercept, linear slope, and quadratic slope means are the means of the intercept, linear slope and quadratic slope factors. The covariances indicate the covariances between the intercept, linear slope and quadratic slope factors. Parameters are unstandardized and thus on the scale of the factor scores. All factor score means and variances are provided in Table S3 of Supplementary Materials.

**Inattention**

A multi-group latent growth curve model with linear and quadratic growth and no cross-group equality constraints fit well to the inattention scores ($\chi^2$ (42) = 169.24, $p$<.001; CFI=.99, TLI=.98, RMSEA=.06, SRMR=.03). The intercept and linear slope and quadratic slope factor means for males were: 0.09, -0.03, and 0.08. The corresponding factor means for females were: -0.18, -0.55, 0.40. These average gender trajectories are shown in Figure 1. Adding cross-group equality constraints on the intercept and linear and slope factor means

resulted in a significant deterioration in fit [$\Delta\chi^2$ (3) = 155.44, $p$ <.001], suggesting that the sex difference in average trajectory was significant. The fit of the constrained model was also poorer according to other fit indexes (CFI=0.97, TLI=0.96, RMSEA= 0.09, SRMR=0.11). Fit statistics for all inattention GMMs tested are provided in Table S2 of Supplementary Materials**.** For males, the LMR test favoured a 2-class model among the linear models and a 2-class model among the linear + quadratic growth models. For the linear and quadratic growth models, a 1-class model was also considered as the *p*-value at this level was only marginally non-significant. Of these three models, the 2-class model with both linear and quadratic growth had the smallest AIC and saBIC while the 2-class model with linear growth had the smallest BIC. On balance, we preferred the 2-class model with linear and quadratic growth because it was judged important to allow for the possibility of quadratic growth in the model, even if the evidence for its presence was equivocal according to the fit statistics. This model is summarised in Table 3 and in Figure 3. The two classes could be characterised as 'low stable' and 'high stable'.

For females, the LMR test favoured a 4-class linear model; however, it favoured a 3-class linear and quadratic model. Of these two models, the 3-class linear and quadratic growth model had the smaller AIC, BIC and saBIC values and was thus selected as the preferred model. This model is summarised in Table 3 and in Figure 3. The three classes could be characterised as 'high decreasing', 'moderate stable' and 'low stable'.

## Discussion

We evaluated whether males and females differed in their ADHD symptom trajectories across a period spanning age 7 to 15. We hypothesised that females would be more likely to show trajectory categories characterised by later onsets, while males would be more likely to show trajectory categories characterised by early onsets. This was partially

supported; however, there were also several other sex differences worthy of further investigation.

As previous studies have shown differential trajectories for hyperactivity/impulsivity and inattention symptoms, we analysed these domains separately (e.g. Arnold et al., 2014). Using a growth mixture modelling approach, for hyperactivity/impulsivity, the best fitting growth mixture model was, for both males and females, a 3-class model that included both linear and quadratic growth. In both cases the largest class (63% of males, 81% of females) could be described as 'unaffected' and was characterised by low levels that decreased steadily from childhood into late adolescence. Both males and females also showed a class that could be characterised as 'high stable' where ADHD symptoms began and remained high for the duration of the age 7 to 15 period. The high stable category had a higher prevalence for males (24%) than females (9%). The third trajectory category was gender-specific. Thirteen per cent of males belonged to a category that was labelled 'High increasing' but could also speculatively be labelled 'high/adolescence triggered'. The 'adolescence triggered' is a reference to the fact that there was an acceleration in the rate of symptom increases with a possible inflection point between ages 11 and 13. We thus speculate that for individuals in this group, the onset of adolescence triggered an escalation in hyperactivity/impulsivity symptoms. For females, the third hyperactivity/impulsivity category also showed evidence of an upturn in symptoms beginning around the onset of adolescence. This group could be speculatively characterised as 'adolescence-triggered'. It showed a mild elevation of symptoms in childhood followed by a minimum around early adolescence and then a rapid increase thereafter.

For inattention, the number of classes in the best fitting growth mixture models differed for males and females. For males, the best fitting model included two classes. The largest class (61% of males) was labelled 'low stable', reflecting the fact that level of

inattention in this group remained low across ages 7 to 15. The other class, which accounted for 39% of the sample was labelled 'high stable', reflecting the fact that symptom levels were persistently elevated across ages 7 to 15. For females, the largest inattention class was also a 'low stable' class characterised by persistently low levels of symptoms and accounting for 59% of females in the sample. The next largest class was a 'moderate' class characterised by moderate and slightly declining symptom levels over ages 7 to 15, accounting for 31% of females. Finally, females showed a third 'high decreasing' class characterised by initially high but declining symptom levels across ages 7 to 15. By age 15, levels in this trajectory class; however, remained higher than those in the 'moderate stable' and 'low stable' classes.

Perhaps the most striking sex difference was that between trajectories that involved symptom elevations at some phase of development. For females, hyperactivity/impulsivity symptom elevations seemed to begin only around early adolescence. For males, however, symptoms elevations were already evident at age 7, although an increase was also apparent around adolescence.

One major theory of sex differences in childhood-onset symptoms such as ADHD refers to a distinction between 'organisational' hormonal effects and 'activational' hormonal effects. The 'organisational-activational' hypothesis suggests that males are more sensitive to prenatal and early postnatal exposures such as stress because of the influence of 'organisational' androgens. On the other hand, females are assumed to be more vulnerable to psychopathology with onset around puberty, due to an increase in 'activational' hormones such as oestradiol around this time (Martel, 2013). The hypothesis is supported by evidence that suggest that prenatal insults increase the risk of ADHD for males but not females (see e.g. Glover & Hill, 2012). Typically, based on evolutionary arguments and to explain observed sex differences, these vulnerabilities have been mapped to externalising disorders for males and internalising disorders for females. Our results would; however, suggest that a

need for an expanded focus, beyond a mapping of externalising versus internalising vulnerabilities to males versus females respectively.

First, our results suggest that the female puberty-related vulnerability to psychopathology usually associated with internalising problems extends to hyperactivity/impulsivity. This is based on our observation that for females who showed evidence of elevated symptoms, this began just following the beginning of adolescence. It thus seems to add to the evidence from previous studies that suggested that females with ADHD are more likely to have a later onset (e.g. Agnew-Blais et al., 2015). It also shows a parallel to conduct problems, in which females are more likely to show an adolescent-onset than males (e.g. reviewed by Fairchild et al., 2013). In this context, and given the lack of an adolescent-onset group for inattention our results may reflect a generalised puberty-related vulnerability to externalising behaviour.

Our results would also suggest that early adolescence is a second critical period of vulnerability for boys who already show high levels of hyperactivity/impulsivity. This is based on the observation that for those who had high levels already and were on an increasing trajectory, there was an acceleration around the beginning of adolescence. This has not generally been observed in previous growth mixture studies of ADHD in either clinical or community-ascertained samples (e.g. Arnold et al., 2014; Döpfner et al., 2014; Robbers et al., 2011), although one trajectory group did show somewhat of a peak in a study in the community samples by Pingault et al. (2011) , van Lier et al. (2007) and Malone et al. (2010). There are several possibilities for this disceprancy between our and previous studies, possibly because many previous studies only fit linear growth parameters, including previous studies in the current sample (Murray, Eisner et al., 2017), whereas detection of a point of inflection or maximum around puberty requires at least quadratic growth to be modelled. Second, the majority of past studies have not separately analysed males and females. Combining males

and females may tmask important developmental trends in each sex where males and females show different developmental trajectories.

There are important clinical implications of both observations. First, the tendency for females to have a later onset of symptoms suggests that current diagnostic criteria that require onset before age 12 would exclude many females who could benefit from intervention (APA, 2013). As males tended to show an earlier onset, a smaller proportion would be excluded from diagnosis on this basis and thus females would be disadvantaged on average. It should thus be investigated whether removing the 'onset before age 12' stipulation in diagnostic criteria would help more girls who would benefit from intervention to be identified.

Second, our results suggest that while perceptions of ADHD as a childhood disorder are changing, more attention may need to be focussed on the period around the beginning of adolescence in terms of detection of symptoms. Greater awareness could be raised amongst potential referrers that this is a potential period of vulnerability for symptom onset or escalation. Still many diagnostic indicators for hyperactivity/impulsivity refer to childhood-specific behaviours and settings and revision of criteria to include indicators developmentally appropriate across the lifespan will be beneficial for identifying and monitoring ADHD symptoms at whatever stage in life they occur. A similar argument could be made for identifying ADHD in females. As ADHD is often conceptualised as a male-typical disorder, it may be more difficult to identify ADHD in females because test development and diagnostic conceptualisations have been implicitly male-biased. Researching more 'female' manifestations of hyperactivity/impulsivity and listing them alongside those currently listed in diagnostic criteria could help guard against female under-identification. It may be, for example, that females are more likely to report internal feelings of restlessness rather than overt hyperactive/impulsive behaviours, especially if symptoms do not reach impairing levels until puberty. Similarly, assessing females for emotion regulation problems may yield greater

sensitivity than assessing behavioural regulation difficulties. Ensuring that ADHD is considered in girls presenting with more female-typical problems such as anxiety, would also help to minimise diagnostic over-shadowing and mis-diagnosis. Further research in this area is, however, required to understand the potentially different manifestations of ADHD in males and females.

It is, however, not possible to discern from our results what the cause of the adolescence-associated increases in symptoms are for either sex. While it may be due to the hormonal changes occurring in puberty, it could also be a function of increased social stresses and academic pressures that coincide with puberty onset. Future research mapping timings of symptom increases to psychosocial and hormonal changes will be important for disentangling these possibilities.

Inattention symptoms arguably did not show as dramatic a sex difference as hyperactivity/impulsivity. Although males and females differed in optimal numbers of classes, the actual trajectories suggests that in both sexes, inattention symptoms differ in level across categories but are generally quite consistent across development, except for one trajectory class identified in females. The trajectory class in question was characterised by high initial levels and modest curvilinear declines over development. Thus, inattention did not show any peak or accelerated increase associated with adolescence. These trajectories fit with the general picture that inattention remains relatively stable across development (e.g., Döpfner et al., 2015; Hart et al., 1995); however, the observation of slight declines for females is, to our knowledge not something that is commonly reported in the literature. Possibly, this is again because most previous studies have not directly compared males and females on developmental trajectories. The reason for this possible female-specific decline is not clear. It may be that females are better at finding compensatory strategies over time or that they benefit more from strengthening of cognitive abilities that comes with maturity.

This question, along with the others raised in this study will require further study on sex differences in ADHD; an area which has arguably received comparability little attention given the body of empirical evidence pointing to the likelihood of substantively and clinically important sex differences (e.g. Gershon & Gershon, 2002).

Finally, we did not find evidence for an attenuating gap in average ADHD symptoms in males and females across development. Underlying this general trend were multiple trajectories in both males and females moving in different directions across development. At the aggregate level; however, differences in sex differences across time generally cancelled out across trajectory groups. Taken together, our findings of no overall decline in sex differences in the context of sex differences in trajectory categories underline the importance of modelling the variability in developmental trajectories. Not modelling subgroups of trajectories has the potential to obscure important developmental differences between males and females and removes the possibility of identifying potentially meaningful developmental subtypes that could provide a useful basis for clinical subtypes. Future studies could also examine the predictors and outcomes of following these trajectories in terms of comorbidities, neurocognitive traits, and genetic and environmental risk factors. If the subtypes can be differentiated on these bases, this would provide further support for considering them as clinical subtypes that carry information about not only the course, but potentially the causes and outcomes of symptoms.

**Limitations**

In terms of limitations of the current study, we used a brief measure of ADHD symptoms and replication with a more comprehensive measure would be a valuable. The brevity of our measure meant that we could not reliably look at distinctions finer than inattention versus hyperactivity/impulsivity. It is possible that different symptoms within

these broad domains show differential sex differences in developmental trajectories. Future studies could examine, for example, impulsivity versus hyperactivity trajectories or look beyond symptoms to neurocognitive variables associated with ADHD. Similarly, we used a measure of ADHD symptoms that is not directly based on DSM criteria. There are both advantages and disadvantages to a non-DSM approach. First, as noted, it has been argued that DSM symptom indicators for hyperactivity/impulsivity are often not developmentally appropriate beyond childhood. Given that males show a relatively more hyperactive-impulsive profile than females, the use of DSM-based measures could obscure sex differences in developmental trajectories. However, the use of non-DSM measures also makes it more difficult to compare our results with other studies and to guarantee the applicability of results to 'clinically defined' ADHD.

Second, we could not conduct statistical comparisons of sets of developmental trajectories across groups. Instead, our comparisons were purely descriptive. In addition, entropy – a measure of the separability of trajectory classes - was relatively poor for our best fitting 'inattention' models. As such, any inferences regarding developmental trajectories in this dimension should be treated with some caution.

Finally, the present study used teacher reports, rather than direct observation. ADHD is a behavioural disorder and the expression and perception of behaviours that comprise its symptoms can be influenced by a number of factors. These include the function that the behaviour serves as well as individual, situational and cultural factors, such as the gender of the pupil and teacher (Lancelotta & Vaughan, 1989) or 'implicit theories' about the child rather than actual child behaviour (Jackson & King, 2004). Future research based on direct measurement of actual behaviour across different contexts may help address this issue.

Third, it will be important to replicate the current analyses in a clinical sample. For ADHD and other conditions that show meaningful variation both above and below clinical thresholds, clinical and community samples provide complementary and equally crucial evidence on questions such as sex differences and developmental trajectories. Community samples like the current sample are important for avoiding issues such as ascertainment bias or range restriction due to focusing on a narrow range of symptom variation. They provide a 'population-level' picture of ADHD symptom. Clinical samples, however, are important for ensuring the applicability of results to those with the highest levels of ADHD symptoms and have automatic face validity for clinical disorders.

Finally, we had little information on the teachers that provided the ratings. Information on traits relevant to rater biases (e.g. depression, neuroticism; De Los Reyes et al., 2008) could be collected and controlled for in future studies. This would help rule out the possibility that the increases in symptoms observed around adolescence were partly attributable to, for example, changes from teachers with low levels of negative rating bias to high levels. Similarly, information on classroom contexts could help evaluate whether the increases in symptoms corresponding to the teacher change was, for some, influenced by a switch to a classroom that was more evocative of hyperactivity/impulsivity (e.g. more idle time, more peers with disruptive behaviour). Similarly, replication using data from other informants including self-, peer- and parent- reports would be valuable given the known tendency for different informants to disagree on levels of ADHD symptoms (e.g. Hartman et al., 2007).

**Conclusions**

There are sex differences in ADHD symptom trajectories that have potentially important implications for clinical practice. Specifically, to guard against under-identification

of females, later symptoms onsets should be considered in diagnostic criteria and hyperactivity/impulsivity diagnostic indicators should be made more suitable for adolescence and adulthood.

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## Tables

**Table 1: Item contents and wave-wise sample sizes**

| | Sample size | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| **Item** | **Age 7** | **Age 8** | **Age 9** | **Age 10** | **Age 11** | **Age 12** | **Age 13** | **Age 15** |
| <CHILD> is impulsive, acts without thinking. | 1343 | 1323 | 1292 | 1264 | 1060 | 976 | 1252 | 1287 |
| <CHILD> has difficulty awaiting turn in games or groups. | 1340 | 1319 | 1292 | 1265 | 1064 | 974 | 1255 | 1287 |
| <CHILD> can't sit still, is restless, or hyperactive. | 1347 | 1324 | 1293 | 1268 | 1062 | 977 | 1258 | 1288 |
| <CHILD> fidgets. | 1340 | 1319 | 1291 | 1265 | 1063 | 976 | 1258 | 1287 |
| <CHILD> cannot settle to anything for more than a few moments. | 1345 | 1322 | 1293 | 1268 | 1064 | 976 | 1257 | 1284 |
| <CHILD> is distractible, has trouble sticking to any activity. | 1343 | 1322 | 1293 | 1267 | 1063 | 977 | 1257 | 1286 |
| <CHILD> can't concentrate, can't pay attention for long. | 1343 | 1324 | 1294 | 1269 | 1061 | 977 | 1256 | 1285 |
| <CHILD> is inattentive. | 1332 | 1307 | 1292 | 1267 | 1063 | 973 | 1256 | 1286 |

**Table 2:**

**Hyperactivity/Impulsivity Growth Mixture Model Solutions for Males and Females**

| Class | Prevalence* | Intercept Mean | Linear Slope Mean | Quadratic Slope Mean | Intercept-Linear Slope Covariance | Intercept-Quadratic Slope Covariance | Linear Slope - Quadratic Slope Covariance |
|---|---|---|---|---|---|---|---|
| | **Males** | | | | | | |
| **High stable** | .24 | 0.529 | -0.327 | 0.233 | -0.354 | -0.185 | -1.438 |
| **High increasing** | .13 | 0.595 | -0.576 | 1.798 | -0.354 | -0.185 | -1.438 |
| **Low stable** | .63 | -0.012 | -0.425 | -0.309 | -0.354 | -0.185 | -1.438 |
| | **Females** | | | | | | |
| **Low stable** | .81 | -0.407 | -0.419 | -0.038 | -0.436 | 0.197 | -0.447 |
| **High stable** | .09 | 0.754 | 0.566 | -0.951 | -0.436 | 0.197 | -0.447 |
| **Concave** | .10 | 0.008 | -3.493 | 4.442 | -0.436 | 0.197 | -0.447 |

*Note.* *Based on estimated posterior probabilities.

**Table 3: Inattention Growth Mixture Model Solutions for Males and Females**

| Class | Prevalence* | Intercept Mean | Linear Slope Mean | Quadratic Slope Mean | Intercept-Linear Slope Covariance | Intercept-Quadratic Slope Covariance | Linear Slope - Quadratic Slope Covariance |
|---|---|---|---|---|---|---|---|
| | | | **Males** | | | | |
| High stable | .39 | 0.825 | 0.307 | -0.416 | -0.724 | 0.377 | -1.616 |
| Low stable | .61 | -0.370 | -0.244 | 0.391 | -0.724 | 0.377 | -1.616 |
| | | | **Females** | | | | |
| High decreasing | .10 | 1.555 | -2.183 | 1.059 | -0.176 | 0.098 | -1.450 |
| Low stable | .59 | -0.755 | 0.041 | 0.098 | -0.176 | 0.098 | -1.450 |
| Moderate stable | .31 | 0.329 | -1.115 | 0.729 | -0.176 | 0.098 | -1.450 |

*Note.* *Based on estimated posterior probabilities.

## Figure Captions

**Figure 1: Average ADHD symptom developmental trajectories**

**Figure 2: Hyperactivity/impulsivity developmental trajectories**

**Figure 3: Inattention developmental trajectories**

**Table S1: Fit statistics for growth mixture models for hyperactivity/impulsivity**

| Model | AIC | BIC | aBIC | Entropy | LMR | p-value |
|---|---|---|---|---|---|---|
| **Males** | | | | | | |
| 1 class linear and quadratic | 13750.71 | 13858.75 | 13785.71 | - | - | - |
| 1 class linear | 13753.35 | 13842.6 | 13782.26 | - | - | - |
| 2 class linear and quadratic | 13543.81 | 13670.63 | 13584.89 | 0.859 | 207.174 | 0.013 |
| 2 class linear | 13572.27 | 13675.61 | 13605.74 | 0.854 | 178.214 | 0 |
| 3 class linear and quadratic | 13469.21 | 13614.82 | 13516.38 | 0.833 | 79.621 | <.001 |
| 3 class linear | 13523.4 | 13640.83 | 13561.44 | 0.802 | 52.266 | 0.2074 |
| 4 class linear and quadratic | 13416.07 | 13580.46 | 13469.32 | 0.826 | 86.16 | 0.1319 |
| 4 class linear | 13466.75 | 13598.27 | 13509.35 | 0.811 | 59.681 | 0.01 |
| 5 class linear and quadratic | 13385.1 | 13568.28 | 13444.43 | 0.83 | 37.568 | 0.3468 |
| 5 class linear | 13448.3 | 13593.91 | 13495.46 | 0.829 | 23.293 | 0.1368 |
| 6 class linear and quadratic | 13359.46 | 13561.44 | 13424.89 | 0.823 | 32.424 | 0.1934 |
| 6 class linear | 13418.84 | 13578.54 | 13470.57 | 0.797 | 33.774 | 0.4092 |
| **Females** | | | | | | |
| 1 class linear and quadratic | 9862.723 | 9969.319 | 9896.285 | - | - | - |

| | | | | | | |
|---|---|---|---|---|---|---|
| 1 class linear | 9899.781 | 9987.839 | 9927.506 | - | - | - |
| 2 class linear and quadratic | 9572.506 | 9697.641 | 9611.905 | 0.937 | 287.387 | 0.0041 |
| 2 class linear | 9674.125 | 9776.087 | 9706.228 | 0.908 | 220.574 | 0.0021 |
| 3 class linear and quadratic | 9391.264 | 9534.937 | 9436.499 | 0.944 | 182.371 | 0.046 |
| 3 class linear | 9579.938 | 9695.804 | 9616.418 | 0.891 | 95.394 | 0.2199 |
| 4 class linear and quadratic | 9317.775 | 9479.987 | 9368.847 | 0.945 | 78.53 | 0.1555 |
| 4 class linear | 9520.444 | 9650.213 | 9561.301 | 0.892 | 62.361 | 0.279 |
| 5 class linear and quadratic | 9230.037 | 9410.788 | 9286.946 | 0.927 | 92.261 | 0.1162 |
| 5 class linear | 9464.902 | 9608.576 | 9510.137 | 0.883 | 63.41 | 0.1516 |
| 6 class linear and quadratic | 9182.711 | 9382.001 | 9245.457 | 0.93 | 69.074 | 0.3819 |
| 6 class linear | 9426.536 | 9584.114 | 9476.149 | 0.892 | 42.243 | 0.2753 |

**Table S2: Fit statistics for growth mixture models for inattention**

| Model | AIC | BIC | aBIC | Entropy | LMR | p-value |
|---|---|---|---|---|---|---|
| | | | **Males** | | | |
| 1 class linear and quadratic | 13104.46 | 13212.49 | 13139.45 | NA | - | - |
| 1 class linear | 13116.42 | 13205.66 | 13145.32 | NA | | -- |
| 2 class linear and quadratic | 13053.72 | 13180.54 | 13094.8 | 0.657 | 56.628 | 0.0497 |
| 2 class linear | 13065.28 | 13168.61 | 13098.75 | 0.656 | 54.429 | 0.0015 |
| 3 class linear and quadratic | 13038.93 | 13184.54 | 13086.1 | 0.632 | 21.966 | 0.5099 |
| 3 class linear | 13049 | 13166.42 | 13087.03 | 0.622 | 21.224 | 0.3122 |
| 4 class linear and quadratic | 13016.68 | 13181.08 | 13069.93 | 0.689 | 20.735 | 0.2467 |
| 4 class linear | 13028.37 | 13159.89 | 13070.97 | 0.697 | 25.363 | 0.0158 |
| 5 class linear and quadratic | 13011.27 | 13194.46 | 13070.61 | 0.728 | 12.924 | 0.3053 |

| | | | | | | |
|---|---|---|---|---|---|---|
| 5 class linear | 13024.02 | 13169.62 | 13071.18 | 0.674 | 9.865 | 0.7636 |
| 6 class linear and quadratic | 13002.79 | 13204.76 | 13068.21 | 0.735 | 17.525 | 0.249 |
| 6 class linear | 13016.54 | 13176.24 | 13068.27 | 0.706 | 12.837 | 0.0912 |
| **Females** | | | | | | |
| 1 class linear and quadratic | 11163.93 | 11270.53 | 11197.49 | NA | - | - |
| 1 class linear | 11205.64 | 11293.7 | 11233.36 | NA | - | - |
| 2 class linear and quadratic | 11068.13 | 11193.27 | 11107.53 | 0.759 | 100.031 | 0.0255 |
| 2 class linear | 11105.9 | 11207.86 | 11138 | 0.771 | 100.679 | 8.00E-04 |
| 3 class linear and quadratic | 11019.27 | 11162.94 | 11064.5 | 0.797 | 54.796 | 0.001 |
| 3 class linear | 11061.57 | 11177.44 | 11098.05 | 0.781 | 47.92 | 3.00E-04 |
| 4 class linear and quadratic | 10967.92 | 11130.13 | 11018.99 | 0.812 | 57.195 | 0.0739 |
| 4 class linear | 11043.7 | 11173.47 | 11084.56 | 0.784 | 42.466 | 0.0183 |

| | | | | | | |
|---|---|---|---|---|---|---|
| 5 class linear and quadratic | 10951.99 | 11132.74 | 11008.9 | 0.815 | 23.059 | 0.5669 |
| 5 class linear | 11020.3 | 11163.98 | 11065.54 | 0.784 | 27.988 | 0.5056 |
| 6 class linear and quadratic | 10915.77 | 11115.06 | 10978.51 | 0.816 | 42.618 | 0.1833 |
| 6 class linear | 10990.11 | 11147.69 | 11039.73 | 0.829 | 22.349 | 0.3308 |

**Table S3: Means and variances of factor scores used in analyses**

| | Hyperactivity/impulsivity | | Inattention | |
|---|---|---|---|---|
| **Wave** | **Mean** | **SD** | **Mean** | **SD** |
| Age 7 | 0.00 | 0.93 | 0.00 | 0.93 |
| Age 8 | -0.16 | 0.92 | -0.14 | 0.93 |
| Age 9 | -0.21 | 0.89 | -0.16 | 0.90 |
| Age 10 | -0.11 | 0.96 | -0.09 | 0.96 |
| Age 11 | -0.18 | 0.86 | -0.11 | 0.95 |
| Age 12 | -0.26 | 0.83 | -0.12 | 0.90 |
| Age 13 | -0.35 | 0.88 | -0.07 | 0.91 |
| Age 15 | -0.35 | 0.91 | -0.11 | 0.90 |