# ADHD-hyperactive/impulsive subtype in adults

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## Abstract

This is the first study to evaluate ADHD-hyperactive/impulsive subtype in a large clinical sample of adults with ADHD. The Quality of Life, Effectiveness, Safety and Tolerability (QuEST) study included 725 adults who received clinician diagnoses of any ADHD subtype. Cross-sectional baseline data from 691 patients diagnosed with the hyperactive/impulsive (HI), inattentive (IA) and combined subtypes were used to compare the groups on the clinician administered ADHD-RS, clinical features and health-related quality of life. A consistent pattern of differences was found between the ADHD-I and combined subtypes, with the combined subtype being more likely to be diagnosed in childhood, more severe symptom severity and lower HRQL. Twenty-three patients out of the total sample of 691 patients (3%) received a clinician diagnosis of ADHD - hyperactive/impulsive subtype. Review of the ratings on the ADHD-RS-IV demonstrated, however, that this group had ratings of inattention comparable to the inattentive group. There were no significant differences found between the ADHD-HI and the other subtypes in symptom severity, functioning or quality of life. The hyperactive/impulsive subtype group identified by clinicians in this study was not significantly different from the rest of the sample. By contrast, significant differences were found between the inattentive and combined types. This suggests that in adults, hyperactivity declines and inattention remains significant, making the hyperactive/impulsive subtype as defined by childhood criteria a very rare condition and raising questions as to the validity of the HI subtype in adults.

## Introduction

The DSM-IV diagnosis of ADHD in adults and children describes three different subtypes: those who have six or more symptoms of inattention and hyperactive/impulsive symptoms are considered combined subtype (ADHD-C), while those who only meet this criteria for attention are considered inattentive subtype (ADHD-I), and those who only meet this criteria for hyperactive/impulsive symptoms are considered hyperactive/impulsive subtype (ADHD-HI). These subtypes were first launched with the DSM-IV field trials based on empirical evidence that each subtype was associated with impairment.[1,2]

Since 1994 there has been empirical evaluation of the validity of these three subtypes.[3] This research has all been carried out in children, and most of it has focused on the inattentive and combined types since the hyperactive/impulsive subtype is quite rare except in pre-school populations where environmental requirements for attention are not yet demanding.[4] Family studies show that the three subtypes do not breed true.[5] There is no evidence of differences in psychiatric comorbidity, executive function, academic performance or psychological testing for ADHD-I and ADHD-C.[6,7] In the only such study of ADHD-HI, there was a relative absence of academic impairment, which led the authors to question whether this subtype actually exists as a unique clinical disorder.[8-10] Even more interesting, in a study using teachers as informants, ADHD-HI was not identified at all.[11] Neuro - psychological testing on the ADHD-HI subtype suggests that the profile of patients with ADHD-HI and no attention problems is distinct from the other two subtypes.[12]

In those studies where subtype data in children were obtained, the prevalence ADHD-HI varied from as low as 2% to as high as 14%, with most epidemiological studies describing a prevalence between 6% and 8% of the total ADHD population.[9,13-16] This means that ADHD-HI is rare even in latency aged children. There are no studies to date which specifically examine the hyperactive/impulsive subtype in the adult population, since while already rare in childhood, the decrease in hyperactivity in general in ADHD with age[17,18] makes this subtype extremely rare in adults.[19]

ADHD-HI diagnosis is more common in preschoolers than in older age groups[20] and multisite, well powered, pre-school studies of ADHD

are relatively recent.[21] However, even in a latent class analysis of the pre-school population, the ADHD-HI model did not fit the data.[22] Lastly, ADHD-HI is not a stable diagnosis, either from pre-school to elementary school,[15] or from latency to adolescence,[23] with only 11% of patients (one out of 9 patients in a total sample of 138) diagnosed at baseline still meeting the diagnostic subtype category five years later.[24] In summary, current research suggests that ADHD-HI is rare, developmentally unstable, with no evidence of being a specific disorder, and often accompanied by subthreshold attention deficits suggestive of

ADHD-C. Hyperactivity in adults may also manifest as overwork, pressured speech, pressured driving, stimulus seeking behavior and fidgeting (picking, knee jerking. etc.), rather than gross motor activity.[18] The attenuation of the frequency of hyperactive/impulsive symptoms may represent a real improvement in hyperactivity, but it is also possible that the attenuation of hyperactive symptoms with age also reflects the items being developmentally inappropriate. Adults show a diminished frequency of impulsive behaviors over time,[25] although how this relates to actual impairment is unknown since relatively infrequent but salient impulsive actions (a car accident, drug abuse, quitting a job, having an affair) in adults can have enduring and devastating effects. The objective of this study is to examine the prevalence, reliability and clinical correlates of the hyperactive/impulsive subtype in a large sample of adults participating in a community based clinical trial.

## Materials and Methods

### Participants

This study is based on data collected in the Quality of Life, Effectiveness, Safety and Tolerability (QuEST) study, a phase IIIb open label study on the safety and effectiveness of mixed amphetamine salts extended release (MAS XR) extending for up to 30 weeks. This sample included 725 adults recruited from 84 different community based treatment sites in Canada and the United States. Details of the study have already been published.[26] Patients were excluded if they had a severe psychiatric or medical disorder for which stimulants were contraindicated, which would interfere with the protocol or which required treatment in its own right, as well as if there was evidence of substance use or abuse currently or within the last six months. After complete description of the study to the subjects, written informed consent was obtained. Demographic and presenting information on the sample is shown in Table 1. From the initial sample of 725 adults, participants with missing data on any variable used in this study were excluded from analysis, as were 5 participants diagnosed with the Not Otherwise Specified subtype, leaving a final sample of 691 adults.

### Procedures

The data from the trial were provided by Shire Pharmaceuticals for this study, with unrestricted access and no funding. Data relevant for this paper were gathered during baseline visits of the trial, prior to any medical intervention and following washout from any prior medications. The study was approved at each institutional review board and carried out according to the Declaration of Helsinki and Good Clinical Practice guidelines.

### Measures

ADHD symptoms were assessed using the Attention Deficit Hyperactivity Disorder Rating Scale for DSM-IV (ADHD-RS-IV),[27] an 18-item clinician administered semi-structured questionnaire. Items correspond to the symptoms of ADHD as stated in the DSM-IV-TR diagnostic criteria. Items are scored from 0 (symptom absent) to 3 (severe), with subscales for inattention and hyperactivity/impulsivity. Given that the study was carried out in many community based sites, the ADHD-RS-IV was supplemented by additional training at the start up meeting and by printed documentation of the kinds of prompts that clinicians might find useful in eliciting expression of evidence of symptom in an adult. Although the ADHD-RS-IV was used to inform the clinician diagnosis, the clinician was free to make an ADHD subtype diagnosis based on longitudinal, observational, and collateral information. Assessment of excluded comorbid Axis I diagnoses used the Semi-structured Interview for DSM (SCID).[28] Axis II disorders were not assessed. Assessment of severity of attention and hyperactive/impulsive symptoms was made by computing the total subscale scores on the ADHD-RS-IV.

A variety of secondary measures were used to determine whether the clinical correlates of the ADHD-HI subtype differed substantially from the other subtypes. Severity of illness was measured using the Clinical Global Impression – Severity scale.[29] Generic Health Related Quality of Life (HRQL) was measured with the gold standard for medical illness, the Short Form Health Survey Questionnaire, version 2 (SF-36).[30] Only the mental composite was used in the analyses, as physical conditions such as pain, mobility and physical limitations are not typically associated with ADHD. ADHD specific HRQL was assessed with the ADHD Impact Module for Adults (AIM-A).[31] This is a self-rated measure comprising Living with ADHD, Performance and Daily Functioning, General Well-being, Relationships and Communication, Bothersomeness/Concern and Daily Interference. Both the AIM-A and the SF-36 measures are scored from 1 to 100 with higher scores representing better quality of life.

The relationship between these measures and symptoms of ADHD were described in a previous study[32] using the same database as the present study. The SF-36 and the AIM-A were found to be more strongly related to inattention rather than hyperactive/impulsive symptoms as measured by the ADHD-RS-IV, and changes over time in symptoms and HRQL appeared to be largely contemporaneous rather than showing a substantial lag between treatment effects on symptoms and improvements in HRQL. Changes in the inattention subscale over time also had a greater influence on changes in HRQL than did changes in the hyperactive/impulsive subscale.

Differences among the subtypes in measures of functional impairment (lifetime number of traffic accidents, days of work or school missed in the last year, doctor's appointments related to accidents in the last year, lifetime number of jobs held) were assessed as direct questions.

### Design

Subtype groups were compared on the various measures of interest using $\chi^2$ or ANOVA analyses, as appropriate to the measure being analyzed, using SPSS 14.0. For categorical outcomes, standardized residuals were used to identify specific between group differences when the $\chi^2$ test was significant. For dimensional outcomes, Levine's test of equality of variances was used to screen for violations of the assumption of equal variances, which is a particular concern given the unequal sample sizes among the three groups, as unequal sample sizes exacerbate the impact of unequal group variances. Unequal variances were detected in only 2 cases: the ADHD-RS-IV HI subscale and the number of doctor's appointments related to accidents. In these cases, Brown-Forsythe and Welch statistics were calculated as alternatives

**Table 1. Presenting characteristics of the overall QuEST study sample and the three subtype groups.**

| | Total sample | Hyperactive impulsive | Combined | Inattentive | $\chi^2$ | P |
|---|---|---|---|---|---|---|
| Gender (female) | 51.5% | 52.2% | 51.7% | 51.3% | 0.01 | 0.99 |
| Race (Caucasian) | 89.4% | 95.7% | 88.9% | 89.6% | 1.05 | 0.59 |
| Martial status (married) | 49.9% | 34.8% | 46.8% | 55.6% | 7.23 | 0.03 |
| Childhood diagnosis | 18.4% | 26.1% | 22.2% | 12.5% | 11.03 | 0.004 |
| | | | | | F | p |
| Mean Age[a] | 37 (11.04) | 37 (10.48) | 36 (11.19) | 38 (10.72) | 4.41 | 0.012 |
| Group n | 691 | 23 | 389 | 279 | | |

SD in parentheses where appropriate. Percentages may not add up to 100% due to rounding. For F tests, df=(2.688). For $\chi^2$ tests, df=2.
[a]Age range was 18-69 years.

to ANOVA and Tamhane's T2 as an alternative to the Bonferroni, as these statistics do not assume equal variances between groups. Given the large discrepancies in sample size, Brown-Forsythe and Welch analyses were run for all variables analyzed with ANOVA in case subthreshold heterogeneity in variance was enough to bias the F statistic when Levine's test for homogeneity of variance was non-significant. However, apart from the two specific variables described above, this made no difference to the findings.

## Results

Of the 691 subjects included in the analyses, clinician diagnoses for subtype were: 279 ADHD-I (40.3%), 389 ADHD-C (56.2%), and 23 ADHD-HI (3.3%). The ADHD-I group was significantly more likely than the other groups to have been diagnosed as adults rather than children and was more likely to be married, as well as being significantly older, by 1 to 2 years than the ADHD-C group (Table 1). There were no subtype differences in race or gender.

Clinician rating of overall illness severity on the CGI-S showed ADHD-C (m=4.42, sd=0.93) to be more severe than ADHD-I (m=3.91, sd = 1.14; F(2,688)=19.66,P<0.001). Pairwise comparison of the ADHD-C and ADHD-I groups to the ADHD-HI group (m=4.17, sd=1.30) showed no significant differences.

Severity scores for attention and hyperactive/impulsive symptoms were compared across the three subtype groups. Inattention was more severe in ADHD-C (m=19.99, sd=5.13) than ADHD-I (m=18.50, sd=5.24; F(2,688)=6.73, P=0.001). Attention deficit in the clinician-diagnosed ADHD-HI group (m=18.74, sd=6.32) was not significantly different from the other subtypes. The Inattention mean for the ADHD-HI group was, in fact, slightly above the mean for the ADHD-I group, contrary to what would be expected given the ADHD-HI group's presumed lack of inattentive symptoms. Hyperactive impulsive symptom severity was significantly less in the ADHD-I group (m=9.99, sd=5.85) than in the ADHD-C group (m=15.92, sd=5.41; Welch F(2, 58.70)=87.82, P<0.001), as would be expected from the DSM-IV definitions, while a significant difference between the ADHD-HI group (m=13.83, sd=7.16) and the ADHD-I group using the Bonferroni test statistic disappeared when the unequal variances in these groups were compensated for by use of Tamhane's T2.

There were no significant differences between the three subtype groups in the number of jobs held, the number of motor vehicle accidents, the number of doctor's visits due to accidents or the number of days of work or school lost (Table 2). The ADHD-HI subgroup did not show significant differences from the other sub-

types on HRQL as measured by the SF-36 or on most AIM-A scales (Table 3). The ADHD-C group was worse on the SF-36 than the ADHD-I group. This pattern was replicated on all the AIM-A scales, including: Performance and Daily Life Functioning, Relationships/Communication, Bothersomeness and Interference in Daily. Both the Combined and ADHD-HI subtypes showed greater impairment than the ADHD-I subtype on the General Well-being scale, while no subtype differences were found on the Living with ADHD scale. While the small sample size of the ADHD-HI subtype reduced the power of pair-wise comparisons, it is notable that the means of the Combined and ADHD-HI subtypes were very close on most variables, and there was no measure for which the ADHD-HI group showed better functioning than the ADHD-I group.

## Discussion

This study found that were no significant differences between those patients diagnosed as ADHD-HI and the other subtypes in attention, demographic variables, functional impairment, generic quality of life, ADHD specific quality of life, or severity of illness. By contrast, there were significant differences in many of these variables between the ADHD-C and ADHD-IA subtypes. While 3% (23/691) of subjects were diagnosed by clinicians as having ADHD-HI subtype, there were no indications that they reported less severe inattentive symptoms than either of the more common subtypes. This is the first study of the characteristics of the Hyperactive-Impulsive subtype (ADHD-HI) in adults. Our method clearly differentiated the Combined and Inattentive subtypes. However, the same method found the patients identified by clinicians as Hyper-active-Impulsive subtype were more inattentive than the Inattentive type, and did not differ in quality of life, driving, work or school impairment. The ADHD-HI subtype was neither statistically nor clinically significantly different from the other two subtypes in adults with ADHD.

### Limitations

The sample excluded individuals with sig-

**Table 2. Comparison of the subtype groups on measures of functioning.**

| Measure | Hyperactive impulsive | Combined | Inattentive | F | P |
|---|---|---|---|---|---|
| Number of jobs | 10.00a (8.52) | 9.29a (9.13) | 8.45a (10.26) | 0.76 | 0.47 |
| Dr.'s visits for accidents | 5.96a (12.88) | 3.04a (4.96) | 2.49a (5.77) | 1.46[1] | 0.24 |
| Motor vehicle accidents | 3.09a (3.37) | 2.45a (2.56) | 2.14a (2.38) | 2.75 | 0.10 |
| Work or school days absent | 1.96a (4.64) | 3.59a (11.95) | 3.16a (17.22) | 1.93 | 0.82 |

SD in parentheses. For F tests, df = (2.688). For Welch test, df=(2.56.98) a, b: groups with different subscripts are significantly different, P≤0.05. [1]Welch, Brown-Forsythe and Tamhane's T2 tests used due to unequal variances. Welch F statistic is reported rather than ANOVA.

**Table 3. Comparison of the subtype groups on measures of health related quality of life.**

| Scale | Hyperactive impulsive | Combined | Inattentive | F | P |
|---|---|---|---|---|---|
| SF-36v2 | 33.07a,b | 36.25a | 39.38b | 6.44 | 0.002 |
| Mental composite | (14.89) | (12.58) | (12.49) | | |
| **AIM-A Scales** | | | | | |
| Living with ADHD | 51.46a (14.68) | 51.78a (11.84) | 51.91a (12.07) | 0.21 | 0.98 |
| General well-being | 39.72a (17.95) | 45.75a (15.97) | 49.45b (16.74) | 6.54 | 0.002 |
| Performance & daily functioning | 28.26a,b (19.46) | 28.84a (18.56) | 32.88b (20.14) | 3.74 | 0.02 |
| Relationships/communication | 59.24a,b (22.52) | 57.54a (20.30) | 62.94b (19.83) | 5.82 | 0.003 |
| Bothersomeness | 37.80a,b (21.43) | 35.21a (19.91) | 43.42b (21.73) | 12.76 | <0.001 |
| Interference with daily life | 38.74a,b (23.84) | 38.68a (21.19) | 47.35b (21.71) | 13.55 | <0.001 |

SD in parentheses. For F tests, df=(2.688). a,bgroups with different subscripts are significantly different, P<0.05.

nificant co-morbidity, substance use, or diagnoses that represent contraindications to use of stimulants, thus potentially representing a referral bias towards more mild illness. However, the exclusion of significant comorbid diagnoses would most likely increase the relative prevalence of patients with ADHD-HI and no attention problems in this sample, thus strengthening the results found.

This study was limited in that it did not assess other variables which may have an impact on the functional impairment of ADHD symptoms, such as IQ. Variables such as educational attainment and adaptive skills are likely to covary with both ADHD symptoms and IQ. The inclusion of these variables in future studies would be useful to identify predictors of risk and resiliency in functional outcomes of ADHD. The ADHD-HI sample was so small that we may not have had sufficient power to detect subtle differences between this group and the others, which also lead to uneven sample sizes among the groups. However, there were no findings that differentiated the ADHD-HI group in the data even at the trend level or in absolute values, suggesting that our findings are not due to lack of power or statistical artifacts.

## Clinical implications

Previous research has demonstrated that it is attention and not disruptive behaviors that is most persistent in adults with ADHD.[33,34] The major risk factor for adult impairment in children with ADHD is problems with attention rather than the disruptive behaviors that are probably the most common reason for childhood referral.[33] The finding that we did not demonstrate evidence for an ADHD-HI subtype in adults further reinforces previous research demonstrating that while disruptive symptoms are the most noticeable aspect of ADHD in childhood and the most common reason for referral, persistence, functional impairment and burden of illness in adults is driven by deficits with attention combined with hyperactive/impulsive symptoms, but not by hyperactive/impulsive symptoms in the absence of attention. The results of this study do raise the question of why clinicians made the diagnosis of ADHD-HI in the first place, given that it was not validated by the very interview they had administered. Given that this was a community based study, we suspect clinicians made this diagnosis when impressed by the prominence or severity of hyperactive and impulsive symptoms, irrespective of attention difficulties which are less obvious. As hyperactive symptoms are typically more overt (e.g. fidgeting, interrupting others) than inattention and may, in some cases, be associated with marked impairment (e.g. disruption of social relationships and interpersonal conflict, risky behaviors, impulsively leaving jobs) the use of this subtype may reflect clinicians being particular-

ly struck by the salience or impact of hyperactive and impulsive symptoms in particular cases, while perhaps underestimating the impact of more subtle impairments in attention. This suggests that clinicians need to develop concrete points of reference or probe carefully for concrete manifestations of attention problems and their impact.

If ADHD-HI is so rare in adults, what happens to the pre-schoolers and children who are diagnosed as ADHD-HI in childhood? Children with ADHD-HI may be diagnosed with time as ADHD-C, as demands for attention increase developmentally and teacher ratings become available. Patients who are diagnosed as ADHD-C as children may be later diagnosed as ADHD-I, as problems with hyperactivity and impulsivity abate or become covert. Lastly, of course, there may be a population of pre-schoolers and children who are hyperactive and impulsive but are not referred in adulthood because these symptoms have either remitted or are no long impairing in adulthood. Several factors may contribute to clinicians failing to appreciate the presence and clinical significance of attention problems. First, in adults we do not obtain teacher reports. Second, many adults have found employment in which they can compensate for attention deficits by delegating tasks or are working in an area of interest where they hyperfocus rather than drifting off. Finally, attention and executive dysfunction are hard to observe in the office. A patient may look like he is listening carefully to all that is being said while he is thinking of something else. The opposite also often occurs. The patient appears to be thinking of many other things at once while in fact he has absorbed the full nature of the conversation. In this sample of 691 adults with ADHD there was no patient who met the DSM-IV cut off for having six out of nine hyperactive and impulsive symptoms and less than six out of nine inattention symptoms. This would indicate that the Hyperactive-Impulsive subtype in adults is either so rare that it represents a tiny minority of patients, or simply does not exist as a clinical condition in adults at all.

From our view, the presence of clinical distinct hyperactive subtype in ADHD in adults is at least questionable and so we would suggest a careful evaluation of the empirical data to increase reliability within the upcoming DSM-V criteria.

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