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Methylphenidate delivery mechanisms for the treatment of children with attention deficit hyperactivity disorder: Heterogeneity in parent preferences

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Objectives: Extended-release therapies avoid the need for children with attention-deficit/hyperactivity disorder (ADHD) to take medication at school. Recently a transdermal delivery system has been developed which can allow symptom control all day long but with greater dosing flexibility. This study explored the parents' preferences regarding oral and transdermal therapy.
Methods: A nonsystematic and qualitative literature review and in-depth interviews with parents and physicians helped identify salient treatment attributes for a discrete choice experiment. Treatment attributes included mode of administration (tablet or transdermal), speed of onset (30–90 min); duration (lasts until 3–9 pm) and ability to tailor the drug to different needs (no flexibility, limited flexibility, easy to adjust to different days). A convenience sample of parents of children treated for ADHD ($n = 200$) were recruited using a recruitment agency. Data were analyzed using generalized estimating equations (GEE).

Results: Parents' preferred once-a-day oral therapy (odds ratio [OR] = 1.76 [95 percent confidence interval {CI}, 1.43 – 2.18]); rapid speed of onset (OR = 1.22 [95 percent CI, 1.07 – 1.39]), and symptom control until 9 pm (OR = 3.79 [95 percent CI, 2.98 – 4.82]). Analyses identified that 30 percent of parents preferred transdermal treatment and this subgroup preferred treatments with a fast onset of action.
Conclusions: This survey demonstrates that parents of ADHD children have different preferences for the ADHD treatments prescribed for their children. A distinct subgroup of parents prefer the transdermal therapy. These parents were less likely to be working and so monitoring compliance and doing after school activities may have been easier.

Keywords: Attention-deficit hyperactivity disorder, Patient preference, Transdermal administration

Attention-deficit/hyperactivity disorder (ADHD) is a prevalent child and adolescent condition which often persists into adulthood (1;17). It is characterized by developmentally inappropriate and pervasive expressions of inattention, overactivity, and impulsiveness. This can lead to academic impairment and social dysfunction; and an increased risk of underachievement, delinquency/criminality, substance abuse and social and relationship failure in the adult years (see Taylor and Sonuga-Barke, for a review) (25). The healthcare and social costs (both direct and indirect) of ADHD are substantial and growing (3;4).

Psycho-active medications have been used for many years to control the core symptoms of ADHD (1;7) and are included in treatment guidelines (European Network for Hyperkinetic Disorders, Taylor et al. (24); National Institute for Health and Clinical Excellence [NICE] (15;17) and the Scottish Intercollegiate Guideline Network (9); American Academy of Pediatrics (1). Historically, stimulants have been limited to immediate-release (IR) preparations that require midday dosing which potentially reduces adherence and therefore effectiveness, especially during the school day (22). The classification of stimulant therapies for ADHD as class 2 schedule drugs in the United Kingdom also creates additional problems because the treatment needs to be kept in a locked cupboard (26). Treatment guidelines from NHS bodies recognize the potential impact of problems with storage, administration of lunchtime doses, and problems caused by drug therapy wearing off (6;18). Poor adherence may result from the fact that taking medication at school is stigmatizing and so actively avoided (6;10;13). To address this shortcoming, there has been a range of different extended release (ER) stimulant therapies developed which are designed to be taken once a day in the morning. There is some evidence that ER formulations increase adherence and persistence by reducing the need for multiple daily dosing (11).

ER formulations offer advantages in dosing frequency which may increase adherence (6;10;11). Despite this some parents may prefer more flexibility of dosing—in particular in terms of duration of action. Such flexibility could make it easier to tailor the treatment to both the needs of the individual child and/or to meet the demands of a particular day or setting. For instance, for some children, stimulants have transient or persistent side effects such as insomnia and appetite loss (2). In this group of children, one might want a shorter duration of action so that tolerability in the evening is improved. The need for symptom control for longer and shorter periods during the day may vary also from day to day. IR stimulant treatments offer greater flexibility to parents. However, in choosing between different formulations, a lack of flexibility may be acceptable to parents to achieve long periods of symptom control without the inconvenience of multiple dosing.

An alternative methylphenidate formulation, which is administered transdermally has been approved by the Food and Drug Administration in the United States (Daytrana®, Noven Therapeutics, LLC). Daytrana is only approved for the treatment of ADHD in the United States. The MTS provides symptom control during the day (12). Because the patch can be easily removed, it offers the prospect of greater flexibility of dosing. This may make it easier to meet the day-to-day needs of the patients' lifestyle and routine (e.g., helping to avoid problems with insomnia or appetite loss). This flexibility of dosing may be attractive to some patients and their families, but alternatively parents may prefer to know that once the child has taken their medication, the duration of action cannot be altered. Parents may be concerned about adherence with the patch but there is no systematic evidence that adherence is a problem. For ADHD treatment, NICE have stated that it is very important to consider the preferences of the child with ADHD and their caregiver in making treatment choices (17). NICE (16) have stated that patients should have a greater role in decision making regarding their treatment which may help to promote adherence. It also should be noted that other treatments with different characteristics are also available. In the United Kingdom, only MPH, dexamfetamine, and the nonstimulant atomoxetine are indicated for the treatment of pediatric and adolescent ADHD (4). In the United States and Canada, mixed amphetamine salts is approved for the treatment of pediatric, adolescent, and adult ADHD (www.fda.gov/drugs).

The present study was designed to explore parents' views regarding the ideal attributes of ADHD medication in relation to the therapeutic potential and/or perceived benefits of three different MPH formulations; a flexible MTS;

once-a-day ER MPH formulation and three times a day IR MPH for the treatment of ADHD. The study used a discrete choice experiment (DCE) approach to determine participants' treatment preferences (5;14;21). Applied to the evaluation of medicines, it allows us to explore the value of different aspects of a treatment including symptom control, mode of administration, occurrence of side effects, and other treatment attributes. The method can also be used to identify the characteristics of people who prefer certain attributes of a medication.

METHODS

Materials

The DCE survey was designed to present hypothetical treatments which varied in terms of attributes of therapy. Literature searches were conducted in Medline to identify any literature regarding the impact of ADHD on health-related quality of life (HRQL) and preferences to find evidence to support the selection of attributes and levels in the DCE. Search terms included "quality of life" OR "patient reported outcome" OR "preference" among other terms and "ADHD" OR "inattention" OR "hyperactivity" OR "impulsivity" which produced 261 hits. The search was designed to identify patient preference surveys that had previously been undertaken in ADHD. The search excluded publications not in English; published before 1998, animal studies, case studies, letters, editorials and commentaries; and included reviews, comparative studies, and clinical trials. No critical appraisal was undertaken. No relevant hits were identified at the time of the search (Mühlbacher et al., was published subsequently) (14).

The selection of attributes and their associated levels was guided by findings from in-depth interviews with seventeen parents and eleven of their children with ADHD. These interviews explored HRQL in ADHD and parents' views regarding ADHD treatment. From this work, four treatment attributes were taken forward. It was decided to keep the number of attributes to a minimum to keep the task as simple as possible and to also avoid an overly burdensome survey. The attributes included *mode of administration* (tablet once a day, tablet three times a day, or MTS), *speed of onset of effect* (30, 60, or 90 min after administration), *duration of effect* (lasts until 3 PM, 6 PM, 9 PM), and *ability to tailor the drug to different day-to-day needs* (no flexibility, limited flexibility, easy to adjust to different days). The selected attributes and proposed levels were discussed with a clinician and an ADHD research scientist both with substantial experience in the diagnosis and treatment of ADHD to explore their clinical relevance. The attributes were combined into choice sets using a published orthogonal array which had been folded over to produce an efficient design (www.research.att.com/~njas/oadir/). The survey included eighteen choices of two hypothetical treatments each and participants (parents of children or adolescents with ADHD) were asked to indicate whether they preferred theoretical treatment A or theoretical treatment B (Supplementary Table 1, which can be viewed online at www.journals.cambridge.org/thc2011014; Supplementary Figure 1, which can be viewed online at www.journals.cambridge.org/thc2011014). A second question in each choice asked participants whether they preferred the chosen treatment over their child's current treatment. Separate questions asked the participants to identify their child's current treatment in terms of the levels of each attribute. The survey also included some demographic, disease and treatment related questions (Appendix 1). A detailed description of each attribute was also provided so that participants could better understand the purpose of the survey.

The survey was first piloted with five parents of children with ADHD who completed a cognitive debriefing interview regarding the survey to identify if people understood the task, whether any aspects of the choices were considered inappropriate or unrealistic and to identify any errors in interpretation. Participants in the pilot test were queried regarding several aspects of the survey; the clarity of the instructions and the questions, and the face validity of the choices. They indicated that other parents would understand the survey and that the length of the survey was appropriate, therefore, no modifications to the survey were made. (A copy of the survey is available from the lead author on request.)

Subsequently, a second pilot study with thirty parents of children with ADHD was conducted to determine if there were any issues with the interpretation of attributes and levels. The pilot study participants met the same study entry criteria as the participants in the main study and received the same compensation. These participants all completed the survey online and the data were analyzed. No problems (such as missing data, people ticking both responses, or coefficient weights indicating illogical preferences) were identified from this pilot and so the data were included in the main study analyses.

Main Study Procedures

Participants. A recruitment company contacted 1,200 families from a patient panel. Each had previously indicated that a member of their family had a confirmed diagnosis of ADHD. Potential participants completed a screener to determine if they were residents in the United Kingdom and currently caring for a child or adolescent (<18 years) with a diagnosis of ADHD. Eligible participants then accessed the online survey. Data collection continued until a sample of 200 participants had completed the survey. Participant recruitment and data collection were conducted according the professional standards of the UK Market Research Society and European Society for Opinion and Market Research (9). All participants were required to provide informed consent before beginning the survey and received £10 for completing it.

Statistical Analysis

Using a Generalized Estimating Equations (GEE) model (8), we estimated a regression with a binomial distribution and a logit link. To obtain the likelihood that a particular treatment would be chosen over another treatment, the following back-transformation was applied:

$$\frac{\exp(\beta 0 + \beta 1X1 + \cdots \beta nXn)}{(1 + \exp(\beta 0 + \beta 1X1 + \cdots \beta nXn)}$$

where β refers to the parameter estimates from the regression and X refers to the attributes.

The GEE model specification also accounted for the repeated nature of the data; the participants' eighteen responses were bundled as a cluster in the analysis.

The second part of the analyses built on the parents' stated preference for ADHD drug characteristics to better understand the preferences of parents who prefer drug delivery through a transdermal patch or by means of tablets. Univariate analyses (Chi-squared test or Mantel-Hanzel test result, or *t*-test for continuous variables) were undertaken to test whether these parents differed from the other parents who preferred tablets. Some variables such as employment status with eight categories were recoded as a simple dichotomous variable (working versus not working). Regression analyses also investigated whether parents who preferred the patch also consistently had a preference for patch treatments in a DCE setting or whether they were trading this attribute against some other treatment characteristics. To obtain the odds ratio (OR) for choosing a treatment with an attribute versus a treatment with the reference attribute the exponent of the parameter estimate was calculated.

RESULTS

Baseline Characteristics of Parents and Children

The study sample ($n = 200$) included a high proportion of mothers (73 percent), who were primarily white Caucasian (96 percent) (Table 1). From parent reports, it was evident that of the children with ADHD who form the basis of their responses, 83 percent were male, had a mean age of 11 years, and mean age of diagnosis and treatment initiation was 7 and 7.6 years, respectively.

Parents' reported preferred medication profile for their children is presented alongside the child's current medication profile (Table 2). The current medication profile is presented in terms of the attributes included in the choice questions. For mode of administration most parents (60 percent) stated that they preferred their child to take just one tablet a day, but 33 percent of parents stated a preference for a transdermal patch. Furthermore, 54 percent of parents preferred a treatment that was easy to tailor to meet their child's different day-to-day needs. Almost 40 percent stated that they wanted to minimize the amount of medication their child took. Just under half of parents (45 percent) preferred for the effects of the treatment to last into the evening.

Choice Data

Two GEE models were estimated on the aggregated data from all 200 parents. The first model estimated the preference for a treatment based on the four treatment attributes (Table 3). The second model allowed parameter estimates to vary between parents who stated their preference for the transdermal patch and parents who preferred tablets (Supplementary Table 2, which can be viewed online at www.journals.cambridge.org/thc2011014).

Results from the first model indicated that all treatment attributes were significant in predicting choices. The intercept represents the reference treatment consisting of one tablet a day, with speed of onset of 30 minutes, the treatment effect lasts until approximately 3 PM and the treatment offers no flexibility. In comparison, parents preferred in general one tablet a day to either the patch (OR = 0.57; 95 percent CI, 0.46 – 0.70) or three tablets a day (OR = 0.19; 95 percent CI, 0.15 – 0.25). Faster onset (30 min) of symptom control was preferred. Participants also preferred treatments which lasted until 9 PM (OR = 3.79; 95 percent CI, 2.98 – 4.82) or 6 PM (OR = 2.63; 95 percent CI, 2.22 – 3.12) rather than 3 PM. There is a difference or discordance between the stated importance of flexibility or tailoring (Table 3) and the strength of preference that emerged from the DCE data. The DCE data revealed that treatments that had dosing flexibility were less preferred to treatments with no flexibility (OR = 0.49; (95 percent CI, 0.41 – 0.56). This finding contradicts the parents' stated preference (Table 2) which indicated that just over half of them would prefer a treatment which was easy to tailor to the child's needs.

The second analysis contrasted the preferences of parents who had a stated preference for the patch (33.0 percent; Table 2) versus parents who preferred oral medication. For the purposes of these analyses the administration mode variable was dichotomized to either patch or any number of tablets. Univariate analyses identified some differences between the groups. Parents who preferred the patch also preferred longer acting treatments ($p = .005$); and treatments which are easy to adjust or tailor to the needs of different days ($p = .0492$). This group of parents also preferred treatments with a fast onset of action ($p = .0491$). Parents who preferred the patch were less likely to be working ($p = .0119$); and related to this, reported a lower average income ($p = .0352$). Lastly parents who preferred the patch were also more likely to have a daughter with ADHD ($p = .0025$).

A second choice model (Supplementary Table 2) includes the stated patch preference as a covariate, as well as interactions of this variable with the four treatment attributes. The model described the data well. Interaction terms were built into the model to explore the differences in preferences

Table 1. Demographics of Adult Participants and Their Child with ADHD

Demographics of adults	Parents ($N = 200$)
Age mean (SD)	38 (7.38) (Median 38; range 24–60)
Gender (% female)	73%
Ethnic group	
Asian or Asian British[a]	1.5%
Black or British Black	0.0%
Chinese or other	0.5%
Mixed race or other	1.5%
White	96.5%
Employment status	
Full time/part time	56.5%/ 18.0%
Student/seeking work/not working	8.5%
Stay at home	32.0%
Carer	2.5%
Prefer not to answer	0.5%
Education – leaving age	
Left school at 16	31.5%
Vocational/college qualifications	45.0%
University	22.5%
Prefer not to answer	1.0%
Demographics of children	($N = 200$)
Mean age (SD)	11 (3.32) (Median 12; range 5–17)
Gender (% male)	83.0%
Ethnic group	
Asian or Asian British	1.5%
Black or British Black	0.5%
Chinese or other	0.5%
Mixed race or other	3.5%
White	94.0%
History of ADHD	
Mean years of school (SD)	7.23 (3.12) (Median 8; range 0–13)
Mean age when diagnosed with ADHD (SD)	7.01 (2.42) (Median 7; range 2–15)
Mean age when 1st treated for ADHD (SD)	7.61 (2.5) (Median 7; range 2–15)

[a]Asian is used to refer to people whose origins can be traced to the South Asian subcontinent (e.g., India, Pakistan, Bangladesh, and Sri Lanka).

between both parent groups. For parents who stated they prefer tablets, the OR of choosing a treatment with a patch versus tablets was 0.33 (95 percent CI, 0.26 – 0.43), the OR for choosing a treatment which lasted until 9 PM versus 3 PM was 3.57 (95 percent CI, 2.63 – 4.85).

Among the parents who preferred the patch, the OR for choosing a treatment that lasts until 9 PM versus a treatment that lasts until 3 PM was 5.00 (95 percent CI, 2.24 – 11.14). Therefore, in comparison with parents preferring tablets, parents who preferred the patch also preferred longer lasting treatments (OR for choosing a treatment until 9 PM versus 3 PM for parents with patch versus parents preferring tablets = 5.00/3.57 = 1.40 [95 percent CI, 0.85 – 2.30]). Parents who stated that they preferred the patch were more likely to choose a treatment that was administered by a patch than by means of tablets (OR = 1.74 95 percent CI, 0.93 – 3.26). They were also less likely to choose treatments with a slower onset time (OR = 0.60, 95 percent CI, 0.39 – 0.92 and 0.45, 95 percent CI, 0.26 – 0.77) for 60 min and 90 min versus 30 min, respectively) than parents who preferred tablets. Treatment flexibility was not viewed very positively. Parents disliked very flexible treatments, and were effectively indifferent between treatments with no flexibility and those with limited flexibility.

The clear differences in parameter estimates for the subgroups defined by their stated patch preference supports the face validity of the results. People who stated they preferred a patch chose treatments that featured the patch.

DISCUSSION

Summary of Main Findings

This study surveyed parental preferences across several different characteristics of treatment for their children's ADHD.

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Table 2. Current and Preferred Profile of ADHD Medications

	Current treatment	Treatment parents would prefer
Administration		
1 Tablet per day (AM)	45.0%	59.5%
2 Tablets per day (AM)	9.0%	—[a]
2 Tablets per day (AM & PM)	21.5%	—
3 Tablets per day	12.0%	7.5%
Other	12.5%	—
Transdermal patch[b]	0%	33.0%
Estimated time for medication to take effect		
Less than 30 min	33.5%	36.5%
30–60 min	54.5%	46.0%
1–2 hr	9.0%	11.5%
More than 2 hours	3.0%	0.5%[c]
Ability to tailor treatment to different needs each day[d]		
Easily tailored	35.5%	53.5%
Difficult to tailor	20.0%	—
Cannot be tailored/same effect all day	18.0%	24%
No need for tailoring	26.5%	—
Prefer to minimise amount of medication taken	—	39.5%
Duration preferences		
Treatment effect until 3–4 PM	30.5%	17.5%
Treatment effect until 5–6 PM	16.5%	37.5%
Treatment effect until 7–9 PM	33.0%	45.0%
Other	20.0%	—

[a]Parents were not asked their preferences regarding some options.
[b]Transdermal patch is not marketed in the United Kingdom.
[c]A total of 5.5% of patients stated that they had no preference.
[d]Parents ticked each statement they agreed with and so values should not be summed.

Table 3. Result of Generalized Estimating Equations Model*

Parameter		Estimate	SE	95% Confidence limits		*P*	Odds ratio	95% Confidence limits	
Intercept		0.597	0.106	0.390	0.805	<.0001			
Administration	Patch	−0.570	0.108	−0.782	−0.359	<.0001	0.566	0.458	0.699
(ref = 1 tablet)	Three tablets	−1.646	0.121	−1.884	−1.408	<.0001	0.193	0.152	0.245
Speed of onset	60 min	−0.200	0.064	−0.326	−0.073	0.0019	0.819	0.722	0.929
(ref = 30 min)	90 min	−0.735	0.077	−0.887	−0.584	<.0001	0.480	0.412	0.558
Duration of effect	6 pm	0.968	0.087	0.797	1.139	<.0001	2.633	2.220	3.122
(ref = Until 3pm)	9 pm	1.332	0.123	1.091	1.572	<.0001	3.789	2.976	4.817
Ability to tailor	Limited flexibility	−0.185	0.059	−0.301	−0.070	0.0017	0.831	0.740	0.933
(ref = No flexibility)	Very flexible	−0.709	0.088	−0.882	−0.536	<.0001	0.492	0.414	0.585

*The intercept represents a treatment which is one tablet a day, with speed of onset of 30 min, the treatment effect lasts until about 3 pm, and the treatment offers no flexibility.

Two hundred parents of children with ADHD from the United Kingdom completed the preference survey which included simple questions to identify what treatment characteristics they prefer for their children in addition to discrete choice-based questions which were designed to elicit preferences more formally. The socio-demographic profile of the sample was broadly similar to other similar studies (20). In the ADORE study of 1,573 children with ADHD (24), 86 percent were male (present study 83 percent), treatment initiated at 7.6 years (present study 7.61 years), but the UK participants were slightly younger (9.3 years, present study 11.0 years).

Parents first completed questions indicating what their preferred ADHD medication would be like. With regard to their child's ADHD treatment, parents generally preferred their child to take less medication either by switching to a once-a-day therapy or the patch. The ability to tailor a treatment to different day-to-day demands was seen as important for some parents, but this was not supported by subsequent multivariate analyses.

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The discrete choice component of the survey was designed to determine the importance of the treatment attributes when considered simultaneously. All four attributes (type of administration, onset of effect, duration of treatment, and flexibility) included in the DCE were significant predictors of parents' preferences. The results for the group overall indicate that people preferred a once-a-day medication, with a rapid onset of action, where the treatment benefit (or symptom control) lasted until the evening. The parents also indicated that having a treatment that was flexible was less important for them relative to the other attributes.

As well as reporting patterns of preference at the group level, the study was also able to parse the overall group of participants in terms of their treatment preference and related characteristics. This enabled the authors to study the heterogeneity in the factors likely to influence parents' treatment choices for the treatment of children with ADHD. At one level, the data show that, overall, parents prefer oral ER MPH and its treatment characteristics in relation to duration of action. However, within the overall sample, there was a subset of parents (approximately one third) who prefer the MTS (the patch). The specific and individual reasons for this stated preference have not been explored in any depth in the current study. This should perhaps be the focus of future work. However, our analyses have indicated that these parents have a significantly stronger preference for treatments that act rapidly compared with parents who prefer tablets. This group of parents was less likely to be working, and so it's possible that they had more time to engage in after school activities. However, they also had a lower income which may limit their ability to do such things. It's also possible that given that fewer were working they may have believed it was easier to monitor the proper adherence to the use of the patch.

The findings can be contrasted with data from Mühlbacher et al. (14) who used the discrete choice experiment methodology to understand treatment preferences in ADHD. This study examined duration of treatment effect (all day or half day), side effects (weight loss or none), dosage (variable or always the same), discretion (whether taking the drug is discrete or obvious), emotional state (mood swings), and social situation (none or some problems with friends, hobbies) in a survey of parents of ADHD children (88 percent) or adolescents with ADHD (6 percent) or older people with ADHD (6 percent). The study found that no problems with friends or hobbies; no mood swings and duration of effect all day were the most important attributes of treatment. Our study also identified a long duration of effect as important. Whether taking the drug is obvious or discrete was not highly valued by the participants, which has some relevance for the transdermal system. This finding from Mühlbacher et al. (14) does contradict some of the treatment guidelines in ADHD which highlight the stigma children feel from taking their medication (19). The other attributes did not overlap substantially which makes comparisons between the studies difficult. It is clear that people value many different aspects of treatments and it is not possible to capture all of that within a single DCE.

Clinical Implications

There is a wide range of different treatments for ADHD patients which offers greater flexibility to parents and clinicians. This is important because, as the NICE ADHD guidance makes clear, adherence (and so effectiveness) is likely to be greatest where patients are offered treatments which match their expectations or preferences (15;17). The study provides one of the first assessments of the issue of parental treatment preference with regard to their child's ADHD medication. Clearly, not all parents value the same features of their MPH treatment and these individual differences in preferences may be related to very practical aspects of the day-to-day lives of patients and their families. Crucially, the current study highlights some key differences between the dimensions of MPH characteristics deemed important to parents of ADHD children.

From a practical perspective, the study therefore encourages clinicians, in keeping with recent guidance, to adopt a more systematic approach to assessing treatment preferences of parents and caregivers when treating children. It also provides a step toward a potential methodology by which clinicians could engage parents and patients regarding their preferences for treatment options. While the current method is probably too time consuming and elaborate to be made part of normal clinical practice, it may be possible to develop a simplified version to help understand individual preferences during a consultation which could include children and their parents.

Limitations

The study was designed as a UK nationwide survey in an attempt to capture a broad scope of parents' preferences regarding their child's treatment. The use of an online survey worked well with these parents, who clearly have many demands on their time. There are limitations with this study that should be noted. It is necessary to restrict the number of attributes that are included in the survey. This means that we do not capture preferences for all aspects of ADHD therapy, but just for the four attributes that were chosen. Effectively, no side effects attribute was taken into account in this survey. Our survey only addresses some aspects of ADHD therapy, other important aspects could be examined in future studies. For example, we did not include treatments which are not stimulant based, nor do we include issues such as tolerability and side effects. The use of an online survey for collecting these data may have restricted the sample to people with online access, but this may be much less of an issue than it was just a few years ago.

It is worth noting also that the transdermal patch is not available in the United Kingdom; and, therefore, parents would not have any experience with it. We provided parents

with information about the patch and graphics demonstrating how it is worn. The study participants were still, however, making hypothetical judgments about how the transdermal patch might benefit their child. (However, the concept of treatments being delivered by means of a transdermal patch is quite well recognized.) Similarly, the concept of flexibility of dosing was also difficult to convey to some parents because with sustained release treatments it is simply not an option. The analyses suggest, however, that the measure of the flexibility preference may have been confounded by the fact that the patch is always flexible. Therefore, some hypothetical choice questions which combined "no flexibility" and "patch" (because of the constraints of the orthogonal design) in the same treatment profile may have been considered unrealistic or even not possible by study participants. This may have affected the results, making it difficult to have a clear understanding of the level of preference parents have for treatment flexibility. Lastly, it's also possible that the study was underpowered. The estimation of sample size in choice experiments is unclear (4). Our sample size was similar to other studies (e.g., Mühlbacher et al.) (14) but may not have been sufficient to fully explore the differences between sub-groups.

Methods to systematically assess treatment preference need to be developed and introduced as a matter of course in clinical practice. This will help clinicians to better match treatment options to caregivers and parents needs and preferences with regard to the treatment of those in their care.

SUPPLEMENTARY MATERIAL

Supplementary Table 1
Supplementary Table 2
Supplementary Figure 1
www.journals.cambridge.org/thc2011014

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CONFLICT OF INTEREST

Andrew Lloyd is employed by and has received payment for preparing this manuscript from Oxford Outcomes. Paul Hodgkins is an employee of Shire Pharmaceuticals and a stockholder. Rahul Sasané was an employee of Shire Pharmaceuticals. Sarah Dewilde is an independent consultant. Shona Falconer was an employee of Oxford Outcomes.

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