*Original Paper*

# An innovative SMS intervention to improve adherence to stimulants in children with ADHD: Preliminary findings

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## Abstract

**Background:** Although large datasets document that stimulants decrease the risk for many adverse ADHD-associated outcomes, compliance with stimulants remains poor.

**Aims:** This study examined the effectiveness of a novel ADHD-centric text messaging-based intervention aimed to improve adherence to stimulant medications in children with ADHD.

**Methods:** Subjects were 87 children aged 6–12, who were prescribed a stimulant medication for ADHD treatment. Prescribers gave permission to contact their patients for participation in the study. Subjects were primarily from the primary care setting with a subsample of psychiatrically referred subjects for comparison. Age- and sex-matched comparators were identified (3:1) from the same pool of prescriber-approved subjects that did not participate. Timely prescription refills (within 37 days) were determined from prescription dates documented in patients' electronic medical record.

**Results:** Eighty-five percent of SMS intervention patients refilled their prescriptions in a timely manner compared with 62% of patients receiving treatment as usual (OR=3.46, 95% CI: 1.82, 6.58; $p < 0.001$). The number needed to treat statistic was computed as five, meaning for every five patients who receive the SMS intervention, we can keep one adherent to their stimulant treatment.

**Conclusions:** These preliminary findings support the potential utility of a readily accessible technology to improve the poor rate of adherence to stimulant treatment in children with ADHD. To the best of our knowledge, this study is the first digital health intervention aimed at improving adherence to stimulant medication for children with ADHD. These results support the need for further examination of this technology through more definitive randomized clinical trials.

**Keywords**
Pediatric ADHD, stimulant medication, medication adherence, SMS

## Introduction

Attention-deficit/hyperactivity disorder (ADHD) is a neurobehavioral disorder (Faraone et al., 2003) estimated to afflict up to 11% of children in the USA (Visser et al., 2014). Numerous studies have documented that ADHD is associated with negative academic and educational outcomes (Biederman et al., 2008), high rates of psychiatric comorbid disorders (Biederman et al., 2006b), smoking and substance use disorders (Biederman et al., 2006b), high risk of accidents and injuries (Jerome et al., 2006), TBI (Adeyemo et al., 2014; Max et al., 2004; McKinlay et al., 2009), and PTSD (Biederman, 2004; Kessler et al., 2006; Spencer et al., 2016). Because of its significant morbidity and disability (Goldman et al., 1998; Wilens et al., 2004), ADHD is recognized by the Center for Disease Control (CDC) as a major public health concern (Centers for Disease Control and Prevention (CDC), 1994).

Although stimulants are safe and effective in treating ADHD (Biederman et al., 2006a; Canadian ADHD Resource Alliance, 2008; Faraone and Buitelaar, 2010; Faraone and Glatt, 2010; Kendall et al., 2008; Kooij et al., 2010; Medori et al., 2008; Spencer et al., 2007, 2013) and help mitigate many of the complications (Barbaresi et al., 2007; Faraone et al., 2007), non-adherence to stimulant treatment in ADHD is very high (Adler and Nierenberg, 2010; Gajria et al., 2014; Olfson et al., 2007; Safren et al., 2007). For example, Sanchez et al. (2005) reported that, after 6 months, rates of non-adherence reached 81%. Similar findings had been reported by the National Institute of Mental Health Multimodal Treatment of Attention Deficit Hyperactivity Disorder (MTA) study (Pappadopulos et al., 2009), which found that less than 10% of children participating in this landmark study were adherent to their treatment at the 16-year follow-up (Swanson et al., 2017).

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As shown by Perwien (2006), non-adherence was 84% in children with ADHD after only 2 months of treatment, suggesting that that non-adherence is not only high but that it can be observed shortly after initiation of stimulant treatment. This latter finding is particularly noteworthy since short-term compliance with treatment is considered to reflect the patient's engagement in treatment. As shown in the literature, patients who engage in treatment have better clinical outcomes than those who do not (American Hospital Association, 2013).

Our team recently examined the rates and correlates of adherence to stimulant treatment in children with ADHD using data from electronic medical records (EMR) from a large healthcare organization (Biederman et al., 2019a). Of the 2200 pediatric patients identified in the EMR with stimulant prescriptions, only 46% refilled their prescriptions within a time frame to be considered consistently medicated, indicating that adherence to stimulant treatment for children with ADHD was poor. Although there were some small but statistically significant differences in the rates of medication adherence by age, sex, race, economic status, medication type (methylphenidate vs. amphetamines), and clinic source (psychiatry vs. non-psychiatry), a multivariable logistic regression model showed that only age, sex, and clinic source remained significantly associated with medication adherence after controlling for all other variables. Older children (adolescents) were at decreased odds of adhering to treatment, whereas boys and those children who got their prescriptions from a psychiatry clinic were at increased odds of being adherent to treatment. However, overall, this model yielded an AUC statistic of 0.57 indicating that these demographic and treatment characteristics were only slightly better than chance at predicting medication adherence (an AUC of 0.5 means the combined characteristics do not exceed chance in predicting the outcome).

Despite these very high and concerning rates of poor adherence to stimulants for ADHD (Adler and Nierenberg, 2010; Gajria et al., 2014; Olfson et al., 2007), there has been a paucity of research targeting this problem. Considering the high morbidity and disability associated with untreated ADHD, efforts aimed at improving adherence to stimulant treatment can have high clinical and public health relevance since increased adherence could improve the quality of life and functioning of millions of children diagnosed with ADHD.

There is an emerging literature on the successful use of digital health to improve adherence to treatment for various medical conditions. Among them, text messaging-based interventions have been particularly successful. For example text message reminders improved adherence to birth control pills (Mackenzie, 2008), smoking cessation interventions (Rodgers et al., 2005), safe sex practices among adolescents (Levine et al., 2008), sunscreen use (Armstrong et al., 2009), and medication regimens for HIV and pediatric liver transplants (Miloh et al., 2009; Safren et al., 2003).

We recently reported (Biederman et al., 2019b) that a novel ADHD-centric digital health intervention using text messages was highly effective in improving adherence to stimulants in adults with ADHD. Participants were adults aged 18–55, prescribed a stimulant medication for ADHD treatment. For comparators, we identified at a 5-to-1 ratio (age and sex matched) adult patients from the Partners HealthCare EMR who had been prescribed stimulant medications over a 1-year period. We determined whether patients had timely prescription refills, defined as refilled within 37 days, using prescriptions documented in their EMR. Our results showed that 68% of the SMS intervention group refilled their prescriptions in a timely manner. In contrast, only 34% of patients receiving treatment as usual refilled their prescriptions in a timely fashion (OR = 4.04, 95% CI: 2.49, 6.56; $p < 0.001$). These data indicate that a novel, ADHD-centric text messaging intervention significantly improved patient engagement to treatment with stimulants in adults with ADHD. However, whether this technology would have similar benefits in improving adherence in pediatric ADHD remains unknown.

The main aim of this study was to assess the effectiveness of a novel text messaging-based ADHD-centric intervention aimed at improving adherence to stimulant medications in pediatric ADHD in the primary care setting. We targeted the primary care setting based on our findings documenting that while adherence was poor in all settings, it was particularly poor in the primary care setting (Biederman et al., 2019a). For comparison purposes, we also included a subsample of psychiatrically referred subjects. We hypothesized that this ADHD-centric text messaging intervention would improve patient adherence to stimulant treatment in children with ADHD in the primary care setting. To the best of our knowledge, this study is the first digital health technology-based intervention aimed at improving adherence to stimulant medication for children with ADHD in any setting.

## Methods

### *Sample*

As shown in Figure 1, upon Institutional Review Board (IRB) approval of the protocol, a report was run using the Partners HealthCare EMR to identify 6- to 12-year old children who were taking stimulant medication for ADHD. This report generated a list consisting of the provider's name, child's name, medical record number, age, prescriber, date of encounter, diagnosis, medication prescribed, and sex of each child. The prescribers were then contacted by the principal investigator (PI) (JB) to request permission to contact the patients inviting them to participate in the SMS program. If the prescribers agreed, IRB-approved letters were sent to the patients with information on how to enroll in the SMS program. Letters were sent to patients between January 2018 and March 2019.

*Text messaging intervention group.* Subjects in the text messaging intervention group were children with ICD-10 or DSM-5 ADHD, 6–12 years of age, recruited from pediatric and psychiatric practices at the Massachusetts General Hospital (MGH). To be included, subjects had to (a) have an ICD-10 or DSM-5 diagnosis of ADHD; (b) be starting or currently on a stimulant medication; (c) be proficient in English; and (d) have a parent with a cellular phone with text messaging capabilities. We excluded potential subjects if they were unwilling or unable to comply with study procedures. No changes were made to the patients' clinical care other than the text messaging intervention. Concomitant medications were allowed. All participants receiving the text messaging intervention provided informed consent. All study procedures were reviewed and approved by the IRB at MGH.

*Comparison group.* For comparison purposes, we derived a sample of children from the same pool of contemporaneous patients receiving treatment with stimulants for whom the

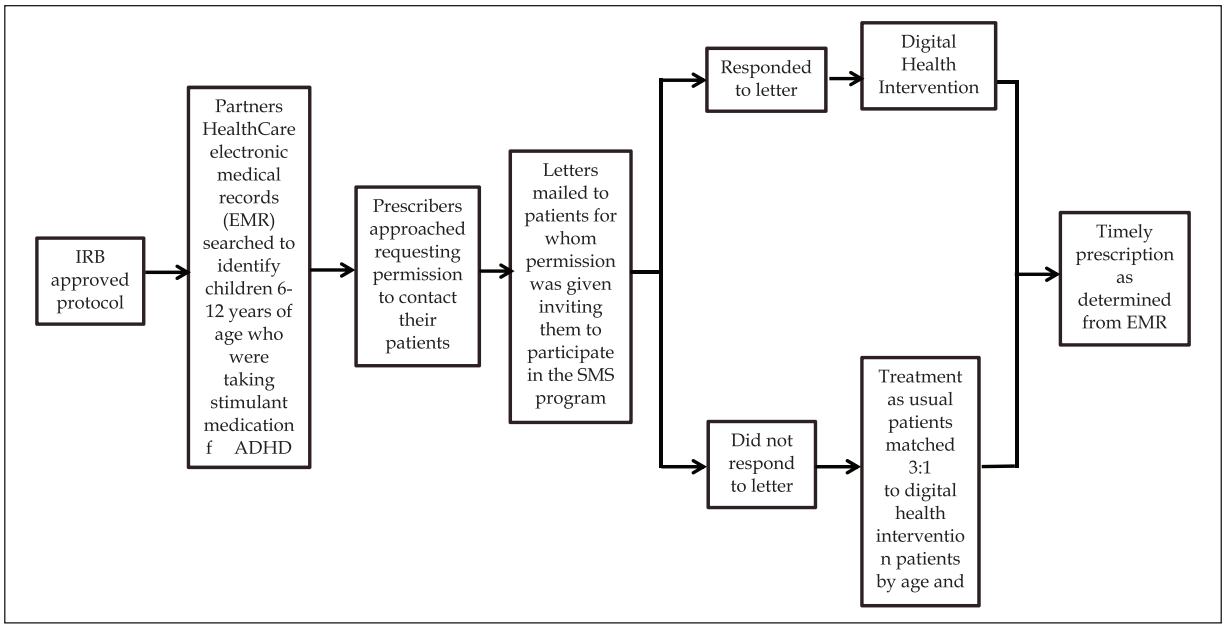


**Figure 1.** Study schema depicting order of events to obtain intervention and treatment as usual groups.

providers gave permission to contact but who never enrolled in the intervention. We matched these patients to our text messaging intervention subjects at a 3-to-1 ratio based on age and sex. Comparators received treatment as usual and no changes were made to their clinical care. Concomitant medications were allowed.

## *Text messages*

Text messages were delivered through a rules-based personalization engine built within the Partners firewall using an SMS platform that individually tailored text messages for medication adherence, treatment initiation, and digital patient support, provided by MEMOTEXT (MEMOTEXT Corp). Its algorithms used data provided by the parent to deliver appropriate educational content about ADHD and its treatment. For the text messaging intervention, decision-tree algorithms were built that used patient/user responses to determine next action based on evidence-informed logic in collaboration with the MGH team. User (parent) responses determined the most appropriate sequential message pathways. The messages were permission-based, thus the system only sent communications to those patients who gave permission to receive them. The platform is compliant with all security regulations and is HIPAA compliant.

All participants' parents received a customized ADHD-centric text message program that included reminders to adhere to the individualized medication regimen, to contact their clinician for a prescription refill, followed by reminders to pick up medication from the pharmacy. We also included educational reminders about ADHD and its treatment and useful tips on how to organize tasks, time management, and follow through. Patients' parents received text messages once a day Sunday through Friday (see Supplemental Table 1 for a sample of the messages delivered). No text messages were delivered on Saturdays. Parents could choose the time of day they wanted to receive the text message: 6–9 a.m., 9 a.m.–3 p.m., 3–7 p.m., or 7–11 p.m. Each text message included instructions to stop future messages if a participant wished to do so. Subjects who elected to stop receiving text messages were considered withdrawn from the study.

## *Defining the index date*

For patients receiving text messages, we considered their index date the date that the patient started receiving text messages. For patients receiving treatment as usual, we considered their index date the date that the patient was sent the enrollment letter.

## *Defining medication adherence*

We determined whether patients had timely prescription refills using prescriptions documented in their EMR. We defined a priori a patient as being adherent with their stimulant treatment (medication adherence) if a stimulant prescription was issued within 37 days of the start date of the text messages for those receiving the text messaging intervention, or within 37 days of the date the enrollment letter was sent for those receiving treatment as usual. Since patients received stimulant prescriptions for a 30-day supply, we decided to give a 7-day window beyond the 30 days to allow some margin of error for any minor delays or problems refilling exactly when the medication ran out (hence 37 days).

## *Variable derivation*

We used patients' zip codes to identify the median incomes for the towns in which they lived using the United States Census Bureau's 2015 American Community Survey 5-Year Estimates (U.S. Census Bureau) to estimate social class. We categorized index prescriptions as prescribed from a psychiatry or non-psychiatry clinic based on the clinic reported in the EMR.

**Table 1.** Demographic characteristics of patients who received the text messaging intervention and age- and sex-matched primary care provider-approved patients who did not participate in the intervention and received treatment as usual.

| | Text messaging intervention patients *N*=87 | Treatment as usual patients *N*=246 | Test statistic | *P*-value |
|---|---|---|---|---|
| | Mean ± SD | Mean ± SD | | |
| Age (years) | 9.2 ± 2.0 | 9.1 ± 1.9 | $t_{331}=0.18$ | 0.86 |
| Median income (dollars) | 86,249 ± 26,185 | 83,061 ± 27,982 | $t_{331}=0.93$ | 0.35 |
| | *N* (%) | *N* (%) | | |
| Male | 65 (75) | 180 (73) | $\chi^2=0.08$ | 0.78 |
| Prescribing clinic | | | $\chi^2=2.19$ | 0.14 |
| Psychiatry clinic | 14 (16) | 25 (10) | | |
| Non-psychiatry clinic | 73 (84) | 221 (90) | | |

Note: SD = standard deviation.

### *Statistical analysis*

As outlined in Figure 1, we derived our comparator group from the same pool of patients approved by their prescriber to be contacted but who did not enroll in the text messaging intervention. We matched this group to the text messaging intervention group at a 3-to-1 ratio by age and sex. We analyzed differences in demographic characteristics using *t*-tests for continuous data and Pearson's chi-square test for categorical data. We then used logistic regression models to compare the rate of medication adherence in the text messaging and treatment as usual groups. We included the intervention group (text messaging vs. treatment as usual), prescribing clinic source (psychiatry vs. non-psychiatry), and the interaction between the two variables in the model to see whether the prescribing clinic source moderated the association between intervention group and stimulant medication adherence. If the interaction term was not significant, we collapsed across prescribing sources; if it was significant, we examined the outcome within the strata of the prescribing source. We then used the adherence rates to calculate the number needed to treat (NNT) statistic to determine how many patients would need to be treated in order to keep one adherent to treatment. All tests were two-tailed and performed at the 0.05 alpha level using Stata (Version 15.1) (StataCorp, 2017). We report odds ratios (OR) and 95% confidence intervals (CI) from the models.

## Results

As shown in the Prisma Diagram (Figure S1), we enrolled 102 participants in the study. Of those, one was deemed ineligible due to not taking stimulant medication. Of the remaining 101 participants, eight never initiated the text messages and thus never started the trial. Of the 93 who initiated the text messages, five withdrew from the study within the first month and did not have adequate follow-up time to be included in the analysis. We excluded one more because the child did not have trackable prescriptions in the EMR. Thus, our final text messaging intervention group included 87 participants who had received text messages for at least 45 days (Figure S1). The treatment as usual comparator group comprised 261 age-, race-, and sex-matched patients. However, only 246 were available for analysis because 15 subjects did not have trackable prescriptions in the EMR.

As shown in Table 1, there were no significant differences in age, sex, social class, or type of clinic from which patients received their initial prescriptions between the subjects who received the text messaging intervention and the comparator patients who received treatment as usual.

Using the 37-day window to define stimulant medication adherence, we found no significant interaction between prescribing clinic and intervention group ($\chi^2=0.26$, $p=0.61$) (Table 2), indicating that the difference in the rate of medication adherence between the text messaging and treatment as usual groups did not significantly differ by prescribing clinic (psychiatry vs. non-psychiatry). Thus, we removed the interaction term and prescribing clinic term from the model. A highly significantly greater percentage of subjects receiving the text messaging intervention were adherent to stimulant treatment compared with comparator patients receiving treatment as usual (text messaging intervention: 85% vs. usual care: 62%; OR=3.46, 95% CI: 1.82, 6.58; $\chi^2=14.30$, $p<0.001$) (Table 2, Figure 2). Based on these findings, the NNT statistic was computed as five. That is, we can keep one in every five patients who receive the text messaging intervention adherent to their stimulant treatment.

## Discussion

We tested a novel ADHD-centric SMS-based intervention aimed at improving adherence to stimulant medication in children with ADHD. Results showed a highly significant increase in patient adherence to stimulant treatment when compared with children of the same age and sex receiving treatment as usual in the same healthcare system (85% vs. 62%, respectively; $p<0.001$). The NNT of five shows that these results are clinically meaningful.

These findings showing that our novel ADHD-centric, inexpensive, easy to use, text messaging intervention improved adherence to stimulants in children with ADHD are consistent with our previously reported findings in adults with ADHD (Biederman et al., 2019b), which also documented marked rates of improved adherence to stimulant medications using a similar digital health intervention. Such technology has never before been used to improve adherence to stimulants in pediatric ADHD.

An important strength of this study was the reliance on an objective metric of adherence based on the issuance of a timely

**Table 2.** Logistic regression models predicting stimulant medication adherence from A) the intervention group (text messaging vs. treatment as usual), prescribing clinic (psychiatry vs. non-psychiatry), and their interaction; and B) only the intervention group.

| A. Model with interaction term | OR (95% CI) | Test statistic | *P*-value |
|---|---|---|---|
| Intervention group (reference: treatment as usual) | 3.79 (1.84, 7.79) | $\chi^2=13.13$ | <0.001 |
| Prescription from psychiatry clinic (reference: non-psychiatry clinic) | 0.90 (0.39, 2.10) | $\chi^2=0.06$ | 0.81 |
| Intervention group × prescribing clinic | | $\chi^2=0.26$ | 0.61 |
| **B. Model without interaction term and prescribing clinic** | **OR (95% CI)** | **Test statistic** | ***P*-Value** |
| Intervention group (reference: treatment as usual) | 3.46 (1.82, 6.58) | $\chi^2=14.30$ | <0.001 |

Note: CI = confidence interval; OR = odds ratio.

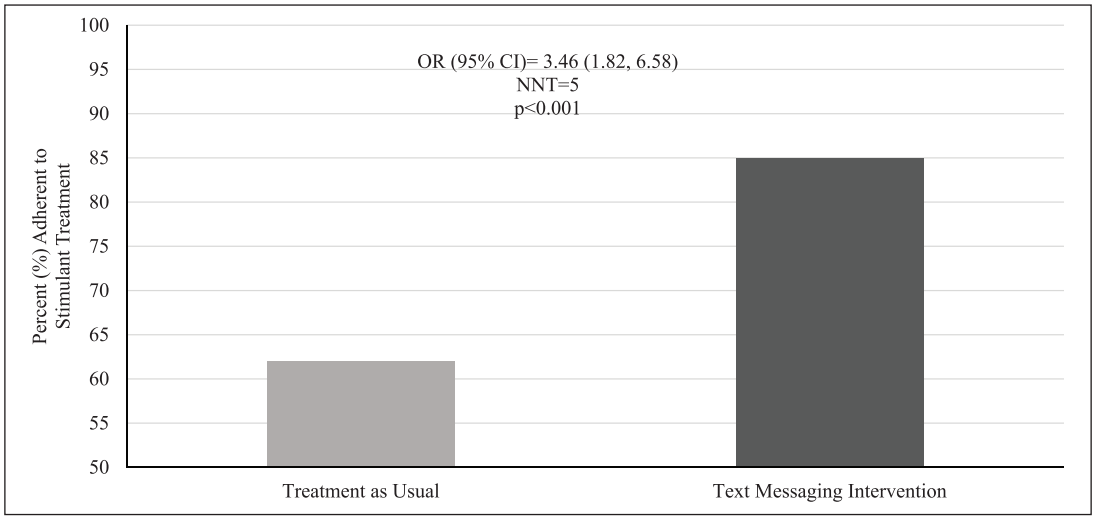


**Figure 2.** The rate of patient adherence to stimulant treatment in patients who received the text messaging intervention (*N*=87) and age- and sex-matched primary care provider-approved patients who did not participate in the intervention and received treatment as usual (*N*=246) using a 37-day window to define adherence.

prescription for a stimulant and an ecologically informative, demographically matched comparison sample of pediatric patients seen in the same healthcare organization. Another strength of our digital health intervention was the disease management approach in which the text messages included educational messages about ADHD and its treatment, and tips for improving daily life for children with ADHD and their families. Also innovative was the reliance on a passive, automated delivery of the secured messages allowing the messages to be consistently delivered to subjects without reliance on subjects remembering to log in to any website or application. Ease of application is especially important for individuals with ADHD, who often are prone to procrastinate or not follow through.

Although the precise reasons for the high effectiveness of our SMS intervention are not entirely clear, we can posit several explanations for its success. Our program not only addressed the unique complexity of renewing stimulants, but it also provided important evidence-based information on ADHD and its treatment. As discussed by Moldavsky and Sayal (2013), recent research documents that parents have significant misconceptions about ADHD, which may lead to stigmatizing experiences and result in non-adherence to treatment. A recent Institute of Medicine report stated that a key component of patient-centered care is ensuring that patients have the education and support they need to make decisions and participate in their own care (Berwick, 2009). Thus, the informed educational messages included in the SMS messages could offset misinformation and biases about ADHD in the media and on the Internet, which could improve adherence. More work is needed to further elucidate what components of this multipronged approach for disease management is key to its effectiveness.

When children do not take their stimulant medication regularly, treatment is less effective due to the short half-life of the medications. This circumstance can have a snowball effect, where the irregular medication administration minimizes the positive effects of the treatment causing parents to feel discouraged and discontinue treatment altogether. This idea is consistent with the finding by Gau et al. (2006) that 20% of parents attribute missed stimulant doses to the "medication having no effect."

Another factor that could lead to forgetfulness and poor adherence to medication treatment pertains to what is known as the knowledge deficit component of the treatment, defined as an insufficient understanding of the severity of ADHD and the critical importance of its treatment. The commonly fluctuating clinical picture in which the child is symptomatic in one setting (school) and not in another (watching TV or playing video games), may create the impression that the symptoms may be volitional and under the child's control and not a real morbid

neurobiological disorder. This view is frequently promulgated by the media, which tends to trivialize the severity of the disorder and its consequences, or exaggerate the putative dangers of stimulant treatments, such as its potential for addiction (Nissen, 2006). Parents may also believe that they may cause their children to become substance dependent by using controlled medicines such as stimulants (Swanson, 2003), despite contrary evidence from review of the literature on the topic (Wilens et al., 2003). Some uninformed parents may also be unaware that the stimulants are not effective once the time period for which they are prescribed has worn off. Thus, these parents may not see any benefits in the evening hours if the medication is administered early in the morning or during times when the treatment may be stopped, such as weekends and holidays. Some parents may have a limited understanding of the seriousness of the disorder, its potential for long-term detrimental consequences on their children, and the critical importance of treatment. Thus, these parents may "forget" to administer the treatment regularly to their child. More research is needed to further clarify the heterogeneous causes of low adherence to stimulant treatment in pediatric ADHD to construct the most appropriate measures to mitigate them.

Our positive results using digital health technology to improve adherence to stimulants in pediatric ADHD are consistent with the successful use of text message reminders to improve both preventive practices and compliance with treatment for various chronic medical conditions including smoking cessation interventions (Rodgers et al., 2005), safe sex practices among adolescents (Levine et al., 2008), sunscreen use (Armstrong et al., 2009), and compliance with complex medication regimens for HIV (Safren et al., 2003). Text messaging is an attractive, relatively inexpensive and widely available technology. Mobile phones are ubiquitous—more than 2.7 billion people of all ethnic and social class strata own mobile phones worldwide. In the USA alone, users have increased from 34 million in 1995 to 290 million in 2010. However, this technology has never before been used to improve adherence to stimulants in ADHD in any age group.

Our results should be seen in the context of some methodological limitations. Because we did not have a placebo intervention, we cannot rule out possible non-specific effects. Since the study was not randomized, we cannot rule out potential confounding bias due to variables including ADHD severity, comorbidities, or concomitant medications. Future studies could benefit from a randomized double-blind design approach examining the effect of potential confounding variables. However, it is important to note that all subjects were derived from the same pool of contemporaneous patients receiving treatment with stimulants in the same healthcare organization, who were approved by their prescriber to be approached for participation in the digital health intervention (Figure 1).

It is also important to note that we did not control the treatment that was selected by the prescriber, and all subjects had the same chance to receive a variety of stimulants and doses and any other form of treatment (i.e., counseling). Such differences may not be large as the two groups did not differ in other characteristics such as median income, sex, or age. Future studies should evaluate the potential contributions of other sociodemographic variables to further assess the effectiveness of the text messaging intervention. We did not examine whether there were differences in the parent-selected timing of the text messaging delivery, thus we do not know whether timing of text messaging delivery affected the results. However, the time of delivery was tailored to parents' individual preferences. Furthermore, because this was the first stage of evaluating the intervention, we focused our analysis on patient adherence defined by a timely refill of the first prescription and thus we do not know the effects of the intervention over longer periods or in patients with chronic use of stimulants. More work is needed to evaluate the long-term benefits of this intervention and its benefits in patients receiving chronic stimulant treatment. Although our metric of adherence was the timely issuance of a prescription, we did not have data confirming the dispensing of the medication or whether patients took the medication. However, the issuance of a prescription is a reasonable proxy for adherence. Because our sample was derived from a single New England healthcare organization, whether our findings will generalize to other regions remains unknown.

Despite these considerations, our data indicate that a novel digital health intervention using text messaging significantly improved patient adherence to treatment with stimulants in pediatric ADHD. Results support the utility of this readily accessible, inexpensive, and widely available technology to improve adherence to stimulants in children with ADHD.

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In the past year, Dr Faraone received income, potential income, travel expenses for continuing education support and/or research support from Tris, Otsuka, Arbor, Ironshore, Shire, Akili Interactive Labs, Enzymotec, Sunovion, Supernus and Genomind. With his institution, he holds US patent US20130217707 A1 for the use of sodium-hydrogen exchange inhibitors in the treatment of ADHD. He also receives royalties from books published by Guilford Press: *Straight Talk about Your Child's Mental Health*, Oxford University Press: *Schizophrenia: The Facts*, and Elsevier: *ADHD: Non-Pharmacologic Interventions*. He is principal investigator of www.adhdinadults.com.

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has a US patent (#14/027,676) for a non-stimulant treatment for ADHD, and a patent pending (#61/233,686) on a method to prevent stimulant abuse. In 2018, Dr Biederman was a consultant for Akili and Shire. In 2017, Dr Biederman received research support from the Department of Defense and PamLab. He was a consultant for Aevi Genomics, Akili, Guidepoint, Ironshore, Medgenics, and Piper Jaffray. He was on the scientific advisory board for Alcobra and Shire. He received honoraria from the MGH Psychiatry Academy for tuition-funded CME courses. In 2016, Dr Biederman received honoraria from the MGH Psychiatry Academy for tuition-funded CME courses, and from Alcobra and APSARD. He was on the scientific advisory board for Arbor Pharmaceuticals. He was a consultant for Akili and Medgenics. He received research support from Merck and SPRITES.

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## Supplemental material

Supplemental material for this article is available online.

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