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Drug Holidays From ADHD Medication: International Experience Over the Past Four Decades

Kinda Ibrahim[1] and Parastou Donyai[1]

Abstract

Objective: ADHD is managed by stimulants that are effective but can cause growth retardation. Prescribers should ideally monitor children and trial a "drug holiday" to enable catch-up growth. Our aim was to map the experience of drug holidays from ADHD medication in children and adolescents. **Method:** A comprehensive search of the literature identified 22 studies published during the period 1972 to 2013. **Results:** Drug holidays are prevalent in 25% to 70% of families and are more likely to be exercised during school holidays. They test whether medication is still needed and are also considered for managing medication side effects and drug tolerance. The impact of drug holidays was reported in terms of side effects and ADHD symptoms. There was evidence of a positive impact on child growth with longer breaks from medication, and shorter breaks could reduce insomnia and improve appetite. **Conclusion:** Drug holidays from ADHD medication could be a useful tool with multiple purposes: assessment, management, prevention, and negotiation. *(J. of Att. Dis. XXXX; XX(X) XX-XX)*

Keywords

ADHD, drug holiday, medication, children, adolescents

Introduction

ADHD is characterized by hyperactivity/impulsivity and inattention, and is one of the most common psychiatric childhood conditions, affecting 3% to 6% of school-age children in the United Kingdom (National Institute of Health and Care Excellence [NICE], 2013). The condition is associated with many potential medical, emotional, behavioral, social, and academic consequences (NICE, 2006). Usually the treatment of ADHD is multi-disciplinary involving medical, behavioral, and educational interventions. The short-term effectiveness of stimulant medication such as methylphenidate and amphetamines in controlling the core symptoms of ADHD and enhancing cognitive function and academic performance among children and adolescents with ADHD are well documented (DuPaul, 2006; Hechtman et al., 2004; Pietrzak, Mollica, Maruff, & Snyder, 2006; Wilson, Cox, Merkel, Moore, & Coghill, 2006). However, the long-term effects (either positive or negative) of using stimulant medication among young patients with ADHD are not yet well documented. In addition, the short-term adverse events associated with stimulants can be very harsh for patients and their families. Research has shown a possible relationship between using stimulants and reduced growth of children with ADHD. Two review studies have linked stimulant use with decreases in height and weight especially during the first years of treatment (Poulton, 2005; Rapport & Moffitt, 2002). However, one other study that monitored the weight and height of 89 ADHD children over 3 years reported a low but not significant reduction in weight gain and no effects on the ultimate growth. The author of this study suggested that despite the possible negative effects of stimulants on growth, the benefits of medical treatment outweighed the growth-related side effects (Zachor, Roberts, Bart, Isaacs, & Merrick, 2004). However, clinicians are asked to monitor closely and regularly the height and weight of children who are treated with stimulants usually every 6 months to minimize the side effects and avoid undesirable events, and to take any necessary arrangement where needed (NICE, 2013; Taylor et al., 2004). One of the recommended arrangements if child growth is affected is to plan a break from medication as referred to as a "drug holiday" (van de Loo-Neus, Rommelse, & Buitelaar, 2011). NICE states,

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> If growth is significantly affected by drug treatment (that is, the child or young person has not met the height expected for their age), the option of a planned break in treatment over school holidays should be considered to allow "catch-up" growth to occur. (2013, pp. 36-37)

A drug holiday refers to "the deliberate interruption of pharmacotherapy for a defined period of time and for a specific clinical purpose" (Howland, 2009, p. 1). NICE guidelines in the United Kingdom and guidance by the American Academy of Child and Adolescent Psychiatry (AACAP) in the United States recommend intentional breaks from medicine-taking (drug holidays) to test the continuing need for therapy in children and adolescents with ADHD (AACAP, 2007; NICE, 2013). AACAP guidance recommends "patients should be assessed periodically to determine whether there is continued need for treatment or symptoms have remitted. Treatment of ADHD should continue as long as symptoms remain present and cause impairment" (AACAP, 2007, p. 913). This guideline states that clinicians should discuss the continuing need for medication with patients and their parents if the patient with ADHD has been free of symptoms for at least 1 year. Signs of remissions that could warrant consideration of planned drug holidays include the following: patient has been stable on the same dose for a prolonged period of time, ability to concentrate during previous drug holidays, and lack of deterioration when medication is missed. School holidays are good opportunities to withdraw the medication; however, parents should purposefully assign cognitively demanding tasks (reading a book, practicing mathematical problems) to test that remission has occurred. If symptoms of ADHD recur and affect child functioning at school and home, then doctors are advised to return the child to medication. The evidence that backs up advice relating to drug holidays is sometimes related to the Multimodal Treatment Study of ADHD (MTA), which showed that medication effectiveness can subside after 2 to 3 years of treatment (MTA Cooperative Group, 2004). European clinical guidelines for hyperkinetic disorder state, "If there are indications of growth retardation, drug holidays (e.g. during the summer vacation) are recommended" (Taylor et al., 2004, p. 16). In addition, in the United States the Institute of Clinical Systems Improvement (ICSI) recommends that linear growth impairment might be managed by limiting stimulant to high-priority needs, for example by trying weekend or vacation "drug holidays" (ICSI, 2012). Yet the European guidelines on managing the adverse effects of medication for ADHD are not in favor of applying drug holidays (Graham et al., 2011). These guidelines suggest taking into account the "the risk–benefit balance of drug holidays." Moreover, they report that to date, and despite their theoretical benefits, the evidence that drug holidays can help control side effects is very limited (Graham et al., 2011).

The NICE guidelines do not routinely recommend drug holidays but instead they emphasize finding a best pattern of use, which can include periods without drug treatment. However, it is not often clear whether drug holidays are systematically considered and introduced in children and adolescents with ADHD and what their real impact is, which provides the rationale for the current article. The attitudes toward and the outcomes of interrupting ADHD medication taking among children and adolescents could have an impact on the practice of drug holidays. Given that no reviews have been published that address the recorded experience of "drug holidays" from ADHD medication, the purpose of this review is to map the practice and impact of periodical breaks from medication among children and adolescents with ADHD. The specific aims of this review are to outline the prevalence of ADHD drug holidays among children and adolescents, explore the reasons for ADHD drug holidays, and extrapolate the impact of ADHD drug holidays in this patient group.

Method

Information Sources and Searches

A comprehensive search of the published literature was conducted to identify all studies that had examined the uptake of or attitudes toward "drug holidays" from ADHD mediation in children and adolescents. From January to March 2013 (with a supplementary search in January 2014), Medline and PsycINFO academic databases were searched for articles published between 1970 and 2013 on this subject. The aim of this review was to map the experience of ADHD drug holidays since the introduction of medication for this condition; therefore, the search period extended back four decades. In addition to the academic databases listed above, the search engine Google Scholar was used in an attempt to capture studies published online, which were not at first identified by the more traditional means. The reference lists of all important articles were also scanned to check for other relevant studies that may have been missed via database searching.

A variety of search terms was constructed for use within the databases, including attention deficit disorder (ADD) with hyperactivity (MeSH term), withholding treatment (MeSH term), medication adherence (MeSH term), patient compliance (MeSH term), drug holiday(s), treatment interruption, medication continuation, medication discontinuation, treatment continuation, treatment discontinuation, treatment cessation, medication cessation, treatment dropout, prescriptions, and prescribing. These terms were combined suitably according to the databases used. A number of

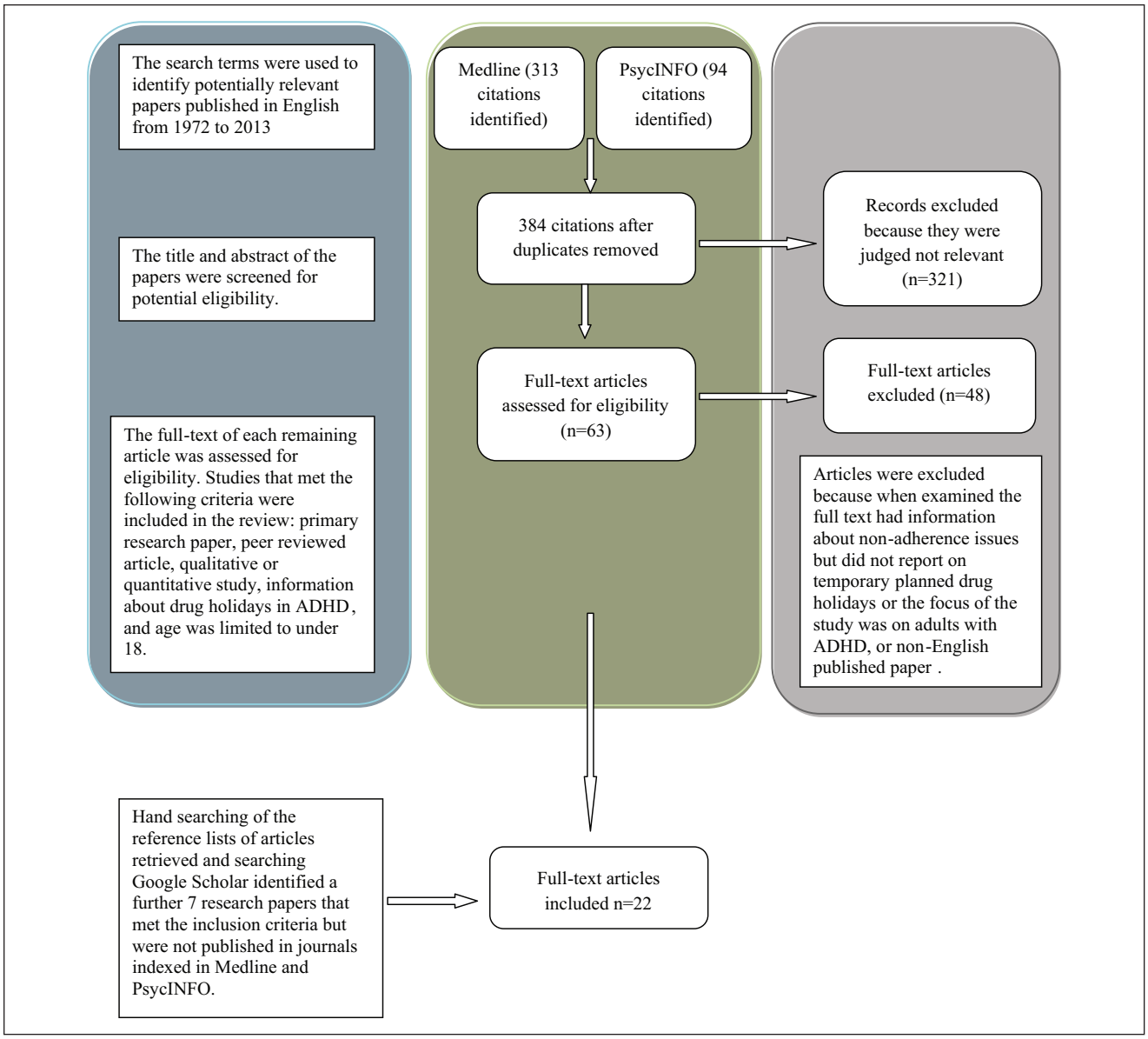

Figure 1. The literature search strategy and identification of publications included in this review.

additional terms potentially portraying drug holidays from ADHD medication were later identified through the articles retrieved and these were additionally inputted into the databases, but did not increase the yield of articles: trial off medication, trial without medication, break from medication, temporary medication cessation, medication vacation, structured treatment interruption, intentional non-adherence, and time on and off medication. The details of the search and retrieval strategy are outlined in Figure 1.

Study Selection

The title and abstracts of all articles initially identified (384) were scanned after duplicates (22) were removed. Studies of any design that had examined the reasons for, the prevalence of, or the impact of drug holidays from ADHD medication among children and adolescents patients published from 1972 to 2013 were included for initial review. A total of 63 articles were selected for full text assessment from which 15 were included in this review. Additional 7 articles were identified by searching reference lists of retrieved articles and Google Scholar search. So a total of 22 research articles were included eventually in this review. We chose to include articles with different epistemological bases because we wanted to gain in-depth information about the practice of "drug holidays" among children and adolescents with ADHD, which could include qualitative as well as quantitative data.

Inclusion and Exclusion Criteria

The following inclusion criteria were used to select articles for this review: primary research articles, qualitative or quantitative study, studies that reported information about drug holidays among patients aged between 6 and 18 years old, and English language publication. Articles were excluded if the focus was on treatment discontinuation per se or non-adherence rather than brief temporary medication cessation. Studies were also excluded if they were published in a language other than English and if the focus was on adults with ADHD rather than children and adolescents.

Data Abstraction, Appraisal, and Synthesis

The articles included in this review were analyzed in line with qualitative review methodology (Donyai, Herbert, Denicolo, & Alexander, 2011) to produce a number of themes that reflect published knowledge about ADHD drug holiday experience. A grid was created to record summaries of the articles for conceptualization and construction of the literature review. This initial tabulation presented information on study characteristics including the year of study, the study sample, country where research took place, research design, and a brief description of study aims (see Table 1). The full text of all included articles was reviewed and any information about drug holidays was extracted for further analysis. Data from articles included in the review and relating to the experience of "drug holiday" from ADHD medication were grouped into three categories: prevalence of ADHD drug holidays, outcomes of ADHD drug holidays, and reasons for ADHD drug holidays.

The quality of the studies was evaluated with criteria based on those established by Hawker, Payne, Kerr, Hardey, and Powell (2002). The critical appraisal tool consists of a nine-item checklist to evaluate the quality of both qualitative and quantitative studies. Accordingly, to assess the quality of the studies, for each article the title and abstract, introduction and aims, method and data, samplings, data analysis, ethics and bias, results, transferability and generalizability, and implications and usefulness were all individually rated as either good (g), fair (f), poor (p), or very poor (vp) before returning a total score for each of these rating categories relating to that article (see Table 2). The scoring system then allowed comparison of articles so that, for example, a study scoring "g = 7, f = 1, vp = 1" could be judged of *better* quality against one scoring "f = 4, p = 3, vp = 2." The quality of the included studies in this review varies widely. The aim of this review was to capture a wide and practical picture of the experience of drug holidays from ADHD medication. Therefore, all studies were included even those judged to be of low quality but interpreted carefully in the discussion. The majority of the studies contributed something new and added a novel perspective to the practice of drug holiday.

Results

Twenty-two studies met the criteria for inclusion in this review and were therefore selected for analysis. No systematic reviews were identified. The methodology that had been adopted in the articles included quantitative research (using, for example, surveys, clinical trials, and review of prescription rates) as well as qualitative research (using focus groups or interviews). Out of the 22 studies included, 17 research articles followed the nomothetic approach to knowledge construction using different quantitative methods, whereas only 5 studies followed the idiographic approach to knowledge construction using interviews and focus groups techniques. It is interesting to note that only 4 studies (Brinkman et al., 2009, 2012; Bussing & Gary, 2001; Hazell, McDowell, & Walton, 1996) in total actually referred to guideline recommendations about drug holidays, 3 of which were qualitative studies (Brinkman et al., 2009, 2012; Bussing & Gary, 2001).

The findings were grouped into three categories: prevalence of ADHD drug holidays, outcomes of ADHD drug holidays, and reasons for ADHD drug holidays.

Prevalence of ADHD "Drug Holidays"

The practice of drug holidays from ADHD medication among children and adolescents is a relatively common phenomenon according to the research identified. The majority of studies (13) included in this review provided information on the prevalence of drug holidays from ADHD medications by reporting either on uptake by parents or practice by doctors (see Table 3). Anything from 25% to almost 60% of families (with an average of 43%) surveyed in 6 of these studies appear to skip medication administration at some point during the treatment course especially at weekends and summer holidays (see Figure 2; Barnard-Brak, Schmidt, & Sulak, 2013; Dosreis et al., 2003; Faraone, Biederman, & Zimmerman, 2007; Hugtenburg et al., 2005; Snyman & Truter, 2012; Wilens et al., 2005). The main source of information about utilizing drug holidays in these studies was parents of children and adolescents with ADHD. This was confirmed by a study that examined prescription data among patients with ADHD who were on a medical treatment monthly for 4 years (Cascade, Kalali, Weisler, & Lenderts, 2008). This study revealed a seasonality pattern in prescribing methylphenidate among children and adolescents with ADHD, as the total volume of ADHD medication prescriptions decreases between May and July by almost 25%. This reflects a school-year-only dosing pattern adopted by some families who give their children the medication only during the school period and stop it during summer break.

A survey with 788 parents of children with ADHD showed that 70% of children stop taking their medication at some point; and only in 34% stopping the medication was

Table 1. Summary of All Studies Included in the Review in Reverse Chronological Order of Publication Year.

Author(s)	Year	Study design	Country	Study sample	Brief description of the study aim
Barnard-Brak, Schmidt, and Sulak	2013	Survey	The United States	259 parents of children with an average age of 10.61 years	Examine medication vacations among children with ADHD according to parent–child dyad
Snyman and Truter	2012	Survey	South Africa	51 parents of children with an average age of 10.27 years	Investigate the etiology, diagnosis, and treatment of children and adolescents with ADHD in South Africa
Brinkman et al.	2012	Focus groups	The United States	44 adolescents aged 13 to 18 years	Gain a detailed understanding of how adolescents with ADHD contribute to medication treatment decisions
Wong et al.	2009	Interviews	The United Kingdom	10 clinicians and 15 adolescents with ADHD aged between 15 and 21 years	Explore the process and outcome of medication cessation to understand how cessation can be appropriately managed
Brinkman et al.	2009	Focus groups	The United States	52 parents of children with ADHD aged between 6 and 17 years	Understand how parents make decisions about treatment for their child or adolescent with ADHD
Cascade, Kalali, Weisler, and Lenderts	2008	Prescriptions data	The United States	Patients with ADHD aged between 0 and 18 years	Investigate the trends in ADHD prescribing
Skilling, Robinson, and Fielding	2008	Survey	Scotland	17 child and adolescent psychiatry departments	Establish follow-up services available for children and adolescents with ADHD and adherence to guidelines
Faraone, Biederman, and Zimmerman	2007	Open-label study	The United States	407 children aged between 6 and 13 years	Analyze patient adherence to OROS methylphenidate during a 1-year open-label study
Spencer et al.	2006	Open-label study	The United States	170 children aged 6 to 13 years	Investigate whether prolonged therapy with long-acting stimulant affects growth in children with ADHD
Pliszka, Matthews, Braslow, and Watson	2006	Naturalistic study	The United States	179 children with average age of 9 years	Determine whether methylphenidate and mixed salts amphetamine have different effects on growth
Wilens et al.	2005	Open-label study	The United States	229 children aged between 6 and 13 years	Assess the effectiveness and tolerability of stimulants when used for prolonged periods in children with ADHD
Rafalovich	2005	Interviews	The United States	26 clinicians	Investigate clinicians' perceptions about the diagnosis and treatment of ADHD
Hugtenburg et al.	2005	Pharmacy dispensing data	The Netherlands	28 parents of children with ADHD aged between 4 and 14 years	Gets insight into the compliance with medication in children using methylphenidate
Martins et al.	2004	Double-blind controlled withdrawal study	Brazil	40 children aged between 6 and 14 years	Assess whether weekend drug holidays during methylphenidate administration would change drug efficacy and tolerability in children with ADHD
Stockl, Hughes, Jarrar, Secnik, and Perwien	2003	Survey	The United States	365 clinicians	Examine physicians' perceptions of using medication to treat ADHD in children and adolescents
Dosreis et al.	2003	Survey	The United States	254 parents of children with ADHD aged between 4 and 19 years	Assess parental attitudes and satisfaction with stimulant treatment
Salmon and Kemp	2002	Survey	The United Kingdom	100 clinicians	Identify the difference between CAMHS and pediatric approaches to the assessment and management of ADHD
Bussing and Gary	2001	Focus groups	The United States	25 families of children with an average age of 9.5 years	Examine parental evaluation of treatment approaches to ADHD and their attitudes regarding medication
Hazell, McDowell, and Walton	1996	Survey	The United Kingdom	788 parents of children with ADHD aged younger than 19 years	Examine the local procedures for assessment of ADHD and its management with stimulants
Klein, Landa, Mattes, and Klein	1988	Controlled withdrawal study	The United States	58 children aged between 6 and 12 years	Examine the effects of methylphenidate withdrawal on the growth of hyperactive children
Satterfield, Cantwell, Schell, and Blaschke	1979	Prospective study	The United States	72 children aged between 6 and 12 years	Examine the growth of hyperactive children treated with methylphenidate
Safer, Allen, and Barr	1972	Controlled withdrawal study	The United States	20 children with an average age of 10 years	Examine the long-term effects of stimulant drugs on indexes of growth in hyperactive children

Note. OROS = osmotic-controlled release oral delivery system; CAMHS = Child and Adolescent Mental Health Services.

Table 2. The Quality Assessment of Studies Included in This Review.

Study	1. Title and abstract	2. Introduction and aims	3. Method and data	4. Sampling	5. Data analysis	6. Ethics and bias	7. Results	8. Transferability and generalizability	9. Implications and usefulness	Total score
Cascade, Kalali, Weisler, and Lenderts (2008)	f	p	p	vp	vp	vp	f	p	f	f = 4 p = 3 vp = 2
Hugtenburg et al. (2005)	g	f	f	p	f	vp	g	p	p	g = 2 f = 2 p = 4 vp = 1
Satterfield, Cantwell, Schell, and Blaschke (1979)	p	vp	g	f	f	vp	g	f	f	g = 2 f = 4 p = 1 vp = 2
Pliszka, Matthews, Braslow, and Watson (2006)	g	g	g	g	g	vp	g	f	g	g = 7 f = 1 vp = 1
Bussing and Gary (2001)	f	g	g	g	f	g	g	p	g	g = 6 f = 2 p = 1
Spencer et al. (2006)	g	g	g	g	g	vp	g	f	p	g = 6 f = 1 p = 1 vp = 1
Stockl, Hughes, Jarrar, Secnik, and Perwien (2003)	g	f	g	g	g	vp	g	f	vp	g = 5 f = 2 vp = 2
Brinkman et al. (2012)	g	p	g	g	f	g	g	f	f	g = 5 f = 3 p = 1
Brinkman et al. (2009)	g	p	g	g	f	f	G	f	f	g = 4 f = 4 p = 1
Salmon and Kemp (2002)	p	g	f	g	f	vp	F	f	f	g = 2 f = 5 p = 1 vp = 1
Skilling, Robinson, and Fielding (2008)	f	f	f	f	p	vp	F	f	p	f = 6 p = 2 vp = 1
Klein, Landa, Mattes, and Klein (1988)	f	f	f	g	f	vp	F	f	vp	g = 1 f = 6 vp = 2
Dosreis et al. (2003)	f	f	g	g	g	f	G	f	g	g = 5 f = 4
Barnard-Brak, Schmidt, and Sulak (2013)	g	g	f	g	g	vp	F	f	p	g = 4 f = 3 p = 1 vp = 1
Wong et al. (2009)	g	g	g	g	g	g	G	g	g	g = 9
Faraone, Biederman, and Zimmerman (2007)	g	g	g	g	g	vp	G	p	vp	g = 6 p = 1 vp = 2
Hazell, McDowell, and Walton (1996)	g	f	f	g	p	vp	G	f	vp	g = 3 f = 3 p = 1 vp = 2

(continued)

Table 2. (continued)

Study	1. Title and abstract	2. Introduction and aims	3. Method and data	4. Sampling	5. Data analysis	6. Ethics and bias	7. Results	8. Transferability and generalizability	9. Implications and usefulness	Total score
Snyman and Truter (2012)	g	f	f	p	p	f	F	p	p	g = 1 f = 4 p = 4
Wilens et al. (2005)	g	g	g	g	f	vp	G	f	g	g = 6 f = 2 vp = 1
Martins et al. (2004)	g	g	g	f	g	f	G	f	g	g = 6 f = 3
Safer, Allen, and Barr (1972)	f	f	g	f	g	vp	G	p	f	g = 3 f = 4 p = 1 vp = 1

Note. 1. Abstract and title: Did they provide a clear description of the study? 2. Introduction and aims: Was there a good background and clear statement of the aims of the research? 3. Method and data: Is the method appropriate and clearly explained? 4. Sampling: Was the sampling strategy appropriate to address the aims? 5. Data analysis: Was the description of the data analysis sufficiently rigorous? 6. Ethics and bias: Have ethical issues been addressed, and what has necessary ethical approval gained? Has the relationship between research and participants been adequately considered? 7. Results: Is there a clear statement of the findings? 8. Transferability or generalizability: Are the findings of this study transferable (generalizable) to a wider population? 9. Implications and usefulness: How important are these findings to policy and practice? Criteria: g = good; f = fair, p = poor; vp = very poor.

planned in order to test the real need for medication but the length of the break was not mentioned (Hazell et al., 1996). The length of and the reasons for drug holidays in the remaining cases (36%) and whether the break from medication was planned or unplanned were not reported in that published study.

Two open-label studies that evaluated the effects of osmotic-controlled release oral delivery system (OROS) methylphenidate among a combined total of 636 children with ADHD documented that about (32%-40%) of patients took drug holidays for a duration longer than a week during the study period (Faraone et al., 2007; Wilens et al., 2005). All patients in a third open-label study also had "some" degree of a drug holiday during the study course, with almost 29% of children taking drug holidays ≥30 days during 21 months of the study (Spencer et al., 2006).

The use of different definitions of "drug holiday" among the studies included in this review (see Table 4) could account for the differences in the reported drug holiday rates from ADHD medication. In some studies, not taking the medication temporarily at weekends and/or during school holidays is defined as a planned drug holiday, whereas other studies had proposed more specific definitions and considered any break from medication for at least 7 consecutive days as a planned drug holiday. Other studies did not differentiate between planned and unplanned drug holidays and considered any break from medication administration for more than 24 hr to be a drug holiday and this was linked with the largest prevalence rate of 70%. Furthermore, another possible reason for the differences in the prevalence of drug holidays reported could be the data collection method. Examining prescribing records revealed a lower prevalence rate of drug holidays than questioning parents of children with ADHD. This could be explained by the fact that many parents will initiate drug holidays themselves without doctor involvement or even without reporting to their doctors. Therefore examining medical records would not be enough to capture real experiences.

Doctors' attitudes toward and consideration of regular planned drug holidays were shown to vary culturally. A survey in the United States in 2003 with 365 prescribers of ADHD medication indicated that only 30% of doctors agree or strongly agree that drug holidays should be incorporated in the medical regimen of children with ADHD (Stockl, Hughes, Jarrar, Secnik, & Perwien, 2003). Whereas in the same decade, in the United Kingdom and Scotland, around 60% of surveyed pediatricians and child and adolescents psychiatrists said that they consider a trial without the medication on an annual basis (Salmon & Kemp, 2002; Skilling, Robinson, & Fielding, 2008). These differences could be due to culturally different views and beliefs of doctors about ADHD medications which might in turn impact on their attitudes toward drug holidays. The local guidelines and recommendations about the management of ADHD could also affect doctors' practice of drug holidays. However, currently this is not the case because nowadays both British and U.S. guidelines recommend that doctors consider periodical breaks from ADHD medication among their patients. The percentages reported in these surveys reveal only doctors' views about drug holidays but not their actual practice. Doctors might discuss having a break from medication with families but this does not guarantee parental agreement to interrupt the treatment.

Table 3. Summary of the Included Studies That Report the Prevalence of Drug Holidays From ADHD Medication.

Study	Study method	Medication	The main findings
Barnard-Brak, Schmidt, and Sulak (2013)	Survey	—	Almost 58.6% of parents of children with ADHD reported utilizing drug holiday
Snyman and Truter (2012)	Survey	Methylphenidate and atomoxetine	Almost 53% of patients took drug holidays at weekends, while approximately 59% went on drug holidays during school holidays. About 24% went off the medication sometimes during weekends and drug holidays
Skilling, Robinson, and Fielding (2008)	Survey	—	About 57% of the designated ADHD follow-up teams offer an annual drug holiday as standard while it is only considered by 40% of services where there is no ADHD follow-up team
Cascade, Kalali, Weisler, and Lenderts (2008)	Examining prescribing records	Methylphenidate	There is seasonality in prescribing methylphenidate as evidence by the finding that the total monthly prescription volume decreased from 22% to 29% between May and July for patients aged younger than 18 years
Faraone, Biederman, and Zimmerman (2007)	Open-label study	Methylphenidate OROS	A total of 130 patients (31.9%) took drug holidays. In almost a quarter of these children, the break was ≥30 consecutive days, whereas the duration of break in the remaining children was from 7 to 29 consecutive days. Older children, minority ethnic groups, and those with less severe symptoms are more likely to take medication breaks and to have lower adherence to therapy
Spencer et al. (2006)	Open-label study	Methylphenidate OROS	All children have some degree of drug holiday at some point. Almost 29% of children who participated in the study took drug holiday ≥30 days during 21 months of the study And 71% reported to have a drug holiday less than 30 days
Wilens et al. (2005)	Long-term open-label study	Methylphenidate OROS	About 40% of children had a drug holiday more than 7 days. Almost 22% of them had a break for 7 to 29 days and the rest had it for a longer time
Hugtenburg et al. (2005)	Examining pharmacy records	Methylphenidate IR	Almost 30% do not use methylphenidate at weekends, and 25% do not use medication during holidays (2 weeks or shorter). Slightly more than 30% do not use medications during summer holidays
Dosreis et al. (2003)	Survey	Methylphenidate ER and IR	About 42% of parents give their children the medication only during school days and 30% reported that they do not use medication at school time and some non-school days
Stockl, Hughes, Jarrar, Secnik, and Perwien (2003)	Survey	Stimulants and non-stimulants	Only 30% of doctors agree or strongly agree that drug holidays from ADHD medication should be incorporated
Salmon and Kemp (2002)	Survey	—	Almost 60% of the surveyed participants were reported to consider trial without the medication on an annual basis
Hazell, McDowell, and Walton (1996)	Survey	Stimulants	Almost 70% of children who had been receiving medication for a year will stop it at some time, but only in 34% stopping the medication was planned in order to determine whether the medication is still needed

Note. Dashes indicate that the medication type was not reported in the study. OROS = osmotic-controlled release oral delivery system; IR = immediate release formulation; ER = extended release formulation.

Attitudes Toward and Reasons for ADHD "Drug Holidays"

Drug holidays from ADHD medication can be initiated either by doctors or by parents and their children. A brief description of the five qualitative studies included in this review is shown in Table 5. The analysis of the results and the quotes identified in these studies was grouped together into different themes that reflect the reasons for considering drug holidays.

Is the medication still needed? There is ongoing dialogue about the necessity of keeping children on the medication. Therefore, some clinicians seem to consider drug holidays from ADHD medication on an annual basis as standard practice to test the continuous need for medication. As one mother states in an article,

> We have done this about every year, along with the paediatrician. But he wants it to be consistent, normal time. Not over Easter

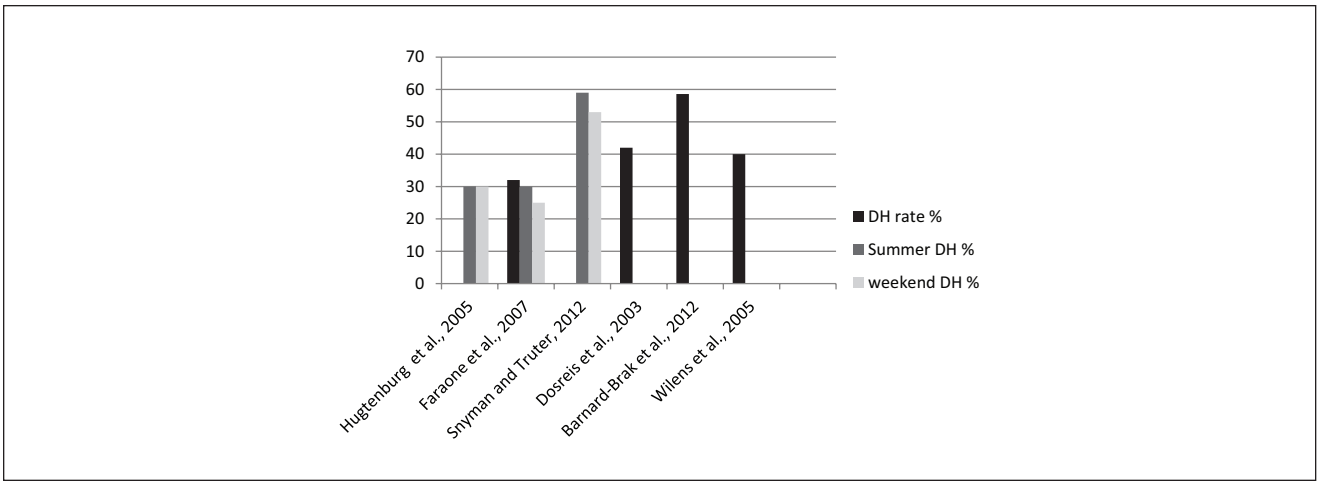

Figure 2. The different rates of "drug holidays" reported by parents of children with ADHD in the published literature identified as part of this review.
Note. DH = drug holidays.

Table 4. The Different Definitions of Drug Holiday Across Some of the Studies That Reported the Prevalence of Drug Holidays.

Study	Definition of a "drug holiday"	Drug holiday prevalence
Snyman and Truter (2012)	A drug holiday means having no or less medication at weekends or school holidays	53% at weekend, 59% at school holiday, and 24% sometimes at weekends and school holidays
Hugtenburg et al. (2005)	A drug holiday means having no medication at weekends and school holidays (such as holidays less than 2 weeks or summer holidays)	30% at weekends, 30% at summer holidays, 25% at school holidays less than 2 weeks, and 25% to 30% use less medication at weekends and school holidays
Faraone, Biederman, and Zimmerman (2007)	A drug holiday means missing the medication on ≥7 consecutive days	32% stopped the medication for more than 7 consecutive days
Wilens et al. (2005)	A drug holiday means missing the medication on ≥7 consecutive days	40% stopped the medication for more than 7 consecutive days
Barnard-Brak, Schmidt, and Sulak (2013)	A drug holiday is defined as any period of 24 hr or more without the administration of medication	58.6% took drug holidays
Dosreis et al. (2003)	A drug holiday means having no medication at weekends and school holidays	42% of parents reported undertaking drug holidays over school holidays
Hazell, McDowell, and Walton (1996)	A drug holiday refers to missing the medication any time	70% of parents report missing the medication at some point during the treatment course

> break. Give it maybe a month or two off the medication to see how it works. We have done it several times, and we have always went back on the medicine. (Brinkman et al., 2009, p. 585)

Parents also appear to use time on and off the medication to see the effect for themselves and check the continuous benefits of medication. Some parents may face a continuous debate about whether to continue to medicate their children driven by concerns about the adverse effects of ADHD medication, which might make them question whether their goals can be achieved without the medication. These trials without the medication enable parents to clarify whether they have to continue to medicate their children or not (Brinkman et al., 2009). Some parents have been convinced after a trial without the medication that their children need to keep taking the medication, finding, for example, that their child cannot function well at school without medication:

> We'd try to take her off and the teacher would write back, "What's going on? Behaviour is different, attention is different." We tried to see if the other stuff had kicked in . . . to see if the organizational stuff had kicked in. (Brinkman et al., 2009, p. 585)

Table 5. Summary of the Qualitative Studies Included in the Review.

Study	Method of data collection	Sample description	The main findings
Brinkman et al. (2012)	Focus group	44 adolescents aged 13 to 18 years	Many adolescents contrast trials on and off the medication to test the continued efficacy of medication. Some experimented over the summer holidays so they did not have to jeopardize their schoolwork
Brinkman et al. (2009)	Focus group	52 parents of children with ADHD aged between 6 and 17 years	Parents contrast time on and off the medication, which helped them inform decisions about whether to persist with medication. Medication was discontinued as a trial to see if the child still benefits from the medication
Wong et al. (2009)	Interviews	10 clinicians + 15 patients aged between 15 and 21 years	Drug holidays at weekends and school holidays are most suggested by clinicians or parents. Clinicians prefer drug holidays to take place outside term time to reduce any potential problems occurring at school. Drug holidays could exhibit in a form of intentional non-adherence such as smashing, hiding, or disposing the medication. These breaks are initiated by patients themselves as a result of dislike taking the medication due to their side effects
Rafalovich (2005)	Interviews	26 physicians (GPs, pediatricians, psychiatrists, and clinical psychologists)	The majority of clinicians recommend drug holidays when the demands at school are not present. Concerns about the medication adverse effects and the development of drug tolerance make doctors consider planned drug holidays
Bussing and Gary (2001)	Focus group	25 parents of children with an average age of 9.5 years	Many parents reported school-time medication use whereby stimulants are only administrated during school days and withheld at home and in summer

Note. GPs = general practitioners.

Moreover, adolescents assume increased responsibility for managing their health and especially medication taking as they grow up and mature. Adolescents with ADHD, driven by their curiosity or rebellious nature, seem to interrupt the medication themselves (Brinkman et al., 2012). Trials without the medication seem to help adolescents with ADHD to see how they would manage without the medication. Thus, some adolescents get the confidence to attempt a more prolonged period of cessation (Wong et al., 2009) or in reverse they become convinced that they really need the medication: "when I went off, I wanted to see if I could be just ok without (medicine), my golf game went to hell" (Brinkman et al., 2012, p. 15). The experience of drug holidays among adolescents with ADHD was argued to be either a continuation of the medication usage patterns adopted by their parents which involved having regular breaks from medication or teenagers' curiosity or desire to rebel against their parents and doctors.

Managing medication adverse effects. Taking ADHD medications is associated with side effects such as sleep problems, appetite suppression, and growth retardation (van de Loo-Neus et al., 2011). Experiencing some medication side effects lead some doctors to consider drug holiday, which is seen a way of relieving the body from the unpleasant adverse effects:

> I will recommend a break from the meds if there is a consistent lack of caloric intake. That is one of the common side effects, lack of appetite. With the younger ones we have to really watch them. We give them a break so they can eat normally and get their caloric count on par with others their age. (Rafalovich, 2005, p. 316)

Parents' concerns about the medication side effects also result in some withholding medication at home and during the holidays (Bussing & Gary, 2001). Moreover, drug holidays can come about as a result of intentional non-adherence, which involves the child in smashing, hiding, or disposing the medication. These breaks are initiated by patients themselves as a result of dislike of taking the medication due to experiencing undesirable side effects (Wong et al., 2009).

Management of drug tolerance. Drug tolerance, described as a condition in which the effectiveness of medication is maintained only through increasingly larger doses, is another reason that was reported by some doctors for considering drug holidays from ADHD medication:

> When tolerance is built up the drugs are far less effective and that often means an increase in the dosage. It is better to allow the child to take a break from the medication and let the body readjust rather than to change the dose. (Rafalovich, 2005, p. 317)

Outcomes of ADHD "Drug Holidays"

The effects of having temporary breaks from ADHD medication were examined in seven research articles as outlined in Table 6.

Effects of drug holiday on child growth. Five studies included in this review examined the effects of drug holidays on child weight and height and yielded different results. Three studies reported a degree of advantages of summer drug holidays on child growth (Klein, Landa, Mattes, & Klein, 1988; Safer, Allen, & Barr, 1972; Satterfield, Cantwell, Schell, & Blaschke, 1979). Child's height and weight were measured and compared between two groups: those who continued with medication during the summer holiday(s) and those who stopped it. Safer et al. (1972) reported that children who showed delays in height and weight when treated with methylphenidate or dexamphetamine during the school year experience accelerated growth rate when medication is stopped during the summer. Children (on dexamphetamine) who discontinued the medication during the summer experienced twofold increase in weight gain and height velocity compared with those who continued on the medication (Safer et al., 1972). The weight and height velocity were, respectively, 68% and 15% more than expected among children (on methylphenidate) who stopped taking their medication during the 3 months summer. The other two studies examined the effects of two consecutive summer holiday drug holidays on child growth (Klein et al., 1988). The first study reported that after two summers of drug holidays from stimulant medication, significant positive effects were reported on height but not on weight. Children who were removed from medication during the two summer holidays were significantly taller than those who remained on it. The second study showed contradictory results where significant positive effects for discontinuing the medication during two summer holidays were reported on children weight but not on their height (Satterfield et al., 1979). The differences in reported findings could be interpreted due to different factors such as individual differences, the study design, the medication dosage, and the initial baseline of child height and weight. Moreover, it could be interpreted that the effects of stimulant medication on height are not secondary to the weight reduction. The length on treatment could also be a factor. None of the studies examined the possible link between how long children with ADHD were taking their medication and the impact of drug holidays on their growth. For example, some studies had enrolled drug-naïve children who had never used ADHD medication before, whereas others included children who had already started taking medication before entering the study.

Another two studies reported no significant impact of having breaks from medication on child growth (Pliszka, Matthews, Braslow, & Watson, 2006; Spencer et al., 2006). Patients were allowed to have breaks from medication themselves and all patients in the two studies were reported to have taken some degree of drug holiday. One study considered any gap between visits and refills as a drug holiday and reported that all patients have some degree of drug holiday at some point and that the length of drug holidays had no impact on child growth (Pliszka et al., 2006). The other study showed that almost 30% of patients took drug holidays lasting more than 30 days and 70% had less than 30 days without the medication, and no significant differences in child height and weight were reported between these two groups of patients (Spencer et al., 2006). Medication withdrawal in both studies was not controlled but left optional to families that participated in the study. Child growth was compared between groups of patients who had different degrees of drug holidays without using a control group (e.g., "no drug holiday" group). So the results of these two studies should be interpreted carefully because they may not accurately capture the impact of drug holidays on child growth. Differences in study design (controlled or uncontrolled), length, and whether or not breaks from medication were consecutive could all account for differences in findings in relation to child growth.

Effects of drug holiday on ADHD symptoms and medication side effects. In addition to the four previous studies that examined the effects of drug holidays on child growth, two studies reported the impact of drug holidays on medication side effects and symptoms of ADHD (Martins et al., 2004; Snyman & Truter, 2012). A double-blind controlled study with 40 children with ADHD compared the symptoms and medication side-effect profiles between two groups of children: those who took drug holidays at weekends and those who did not for 4 consecutive weeks. Rating scales to evaluate ADHD symptoms and medication side effects were completed by teachers and parents. Weekend drug holiday was reported to reduce insomnia and appetite suppression without increasing the symptoms of ADHD (Martins et al., 2004). Another study has shown that half of surveyed parents of children with ADHD (about 25 out of 50 parents), who had been on medication for an average of 16.7 months, stop giving their children the medication at weekends and/

Table 6. Summary of the Studies That Examined the Impact of Drug Holidays on Medication Side Effects and/or ADHD Symptoms.

Study	Design	Measures used	Study sample	Medication	Drug holiday length	The main findings
Klein, Landa, Mattes, and Klein (1988)	Randomized controlled withdrawal study	Standard height and weight measures	58 children aged 6 to 12 years	Methylphenidate	Two consecutive summer vacations (3 months each)	Summer drug holiday from methylphenidate showed no significant effect on children height after the first summer, but after two summers, children receiving continuous methylphenidate were 1.5 cm shorter than those on drug holiday. Weight did not differ significantly between on and off groups after the second summer
Spencer et al. (2006)	Open-label study for 21 months	Weight z scores, height z score, and BMI z score	178 children aged 6 to 13 years	Methylphenidate OROS	30 days or more within 21 months	Almost 29% of children who participated in the study took drug holiday ≥30 days during 21 months of the study. And 71% reported to have more than 30 days without the medication. Drug holiday did not reduce any impact of stimulants on growth
Satterfield, Cantwell, Schell, and Blaschke (1979)	Prospective study	Standard height and weight measures	72 children aged between 6 and 12 years	Methylphenidate	Two consecutive summer vacations (3 months each)	Children who did not take the medication during the two summer holidays had smaller height and weight deficits during the second year of treatment. This trend was statistically significant for weight but not for height
Safer, Allen, and Barr (1972)	Withdrawal study	Standard height and weight measures	20 children with an average age of 10 years	Methylphenidate or dexamphetamine	3 months/one summer	65% of children took drug holiday during summer. Those children gain more weight and height than the other group who continue with medication particularly those on dexamphetamine and higher doses of methylphenidate
Martins et al. (2004)	Double-blind study	Conners' Abbreviated Rating Scale + Barkley Side Effects Rating Scale	40 children with ADHD aged between 6 and 14years	Methylphenidate	4 consecutive weekends	Weekend holiday from methylphenidate administration reduces the side effects of insomnia and appetite suppression without a significant increase in symptoms either in weekends or in the first school day after them
Pliszka, Matthews, Braslow, and Watson (2006)	Linear regression method	Height z score	179 Children with ADHD with an average age of 9 years	Methylphenidate	Not specified	All patients had some degree of drug holiday either planned or unplanned. Patients showed to miss their medication for almost 32% of their time. This study has not found any effect of drug holiday on children growth
Snyman and Truter (2012)	Survey	Parents reports	51 parents of children with ADHD	Methylphenidate/ atomoxetine	Weekends and school holidays	Children are more active, less able to concentrate, more aggressive, more destructive during drug holidays. The impact of drug holidays on appetite is moderate as almost 9% reported that the appetite comes back

Note. BMI = body mass index; OROS = osmotic-controlled release oral delivery system.

or during school holidays. Those parents reported noticing some changes in child symptoms during drug holidays at weekends and/or during school holidays such as being more active, less able to concentrate, more aggressive, and more destructive (Snyman & Truter, 2012). At the same time, the effect of drug holidays on child appetite was reported to be low as only 9% reported that the appetite comes back when medication is stopped at school holidays and weekends. The findings of this study should be interpreted carefully because no control groups were used to compare the

symptoms of ADHD or side-effect profiles. The effects of drug holidays were obtained from questioning parents of children with ADHD without being objectively verified. Recall bias could also influence parents' answers and ratings.

Discussion

A total of 22 studies were examined in relation to the prevalence, the outcomes, and the reasons for ADHD drug holidays in children and adolescents. Prevalence data were reported using different methods including parental surveys, examination of medical records, and analysis of prescribing data, and indicated that drug holidays are prevalent in 25% to 70% of families and are more likely to be exercised at weekends or during summer holidays in general. But as well as being marred by different data collection methodologies, articles reporting prevalence data did not all report the length of the break, did not differentiate between planned and unplanned breaks from medication, and used different definitions of what constitutes a "drug holiday." Drug holidays were considered for different reasons, namely, to test if medication was still needed (especially with parents and adolescents), for managing persistent medication adverse effects (for both parents and doctors), and for managing drug tolerance (doctors only). Qualitatively, some children returned to medication after a drug holiday, whereas others did not and this was specifically true with adolescents. The impact of drug holidays from ADHD medication was reported in terms of child growth, other side effects, as well as impact on core ADHD symptoms. Although there were weaknesses in the conduct and reporting of some studies, there was evidence of a positive impact on child growth with longer breaks from medication during the summer holidays. In addition, shorter breaks from medication exercised at weekends had the potential to reduce sleep problems and improve appetite with questionable results about whether or not the symptoms of ADHD intensify.

The practice of planned drug holidays with ADHD medication is acknowledged by many researchers interested in measuring patients' adherence to medication, who actively take into account the experience of drug holidays in their research (Charach, Ickowicz, & Schachar, 2004; Thiruchelvam, Charach, & Schachar, 2001; Zhang, Du, & Zhuang, 2010). These adherence studies show that adherence rates to ADHD medications are higher when drug holidays are taken out of the equation. In the current review, all planned drug holidays were found to be undertaken when children are not at school, perhaps when the demands on the child are lower. Certainly, studies show that behavioral and attention problems among children and adolescents with ADHD are mostly located within a school context (Evans, 2001) and medication such as methylphenidate is shown to be very effective in improving children's performance and behavior at the school setting (DuPaul, 2006; Hechtman et al., 2004). Therefore, understandably, worries about disrupting children's academic performance and upsetting the balance of the school day could be the reason why drug holidays from ADHD medication are mainly practiced outside of school days, at weekends, during summer, or other breaks from schooling. A study reported a remarkable discontinuation of ADHD medication once young people reach the age of 16 years for different reasons such as adolescents' autonomy, feeling matured and not needing the medication anymore, and experience with unpleasant medication side effects (Marcus, Wan, Kemner, & Olfson, 2005). The majority of clinicians in the study had experience of disagreement between patients and their families on the issue of cessation. Drug holidays from ADHD medication appeared useful as a way of resolving conflicting ideas about the need for continued medication.

Taking a drug holiday is a strategy that has been used to manage side effects with a range of medication including antiretrovirals (anti-HIV medication), bisphosphonates (for osteoporosis), and antidepressants (Cohen, Colson, Sheble-Hall, McLaughlin, & Morse, 2007; Curtis, Westfall, Cheng, Delzell, & Saag, 2008; Rothschild, 1995). Similarly, in this review it was found that worries about potential adverse effects or the actual experience of side effects lead doctors, parents, and adolescents to consider drug holidays from ADHD medication. The impact of interrupting the medication on both the symptoms of ADHD as well as medication side effects appears to depend on the length of the drug holiday, whether the days of the break are consecutive or not and also which side effects are being measured. So, for example, a significant increase in child growth is reported with drug holidays taken during summer holidays, but not with inconsecutive shorter breaks from ADHD medication. However, there is some evidence that temporary withdrawal of medication at the weekend can reduce side effects relating to sleep and appetite without increasing the symptoms of ADHD. In the same vein, the benefits of taking drug holidays from antiretroviral drugs, such as reducing fatigue, vomiting, nausea, and even toxicity, are linked to the length of the drug holiday (eMC, 1999). In that situation, taking the medication for 5 days and stopping for 2 days every week was shown to be beneficial in reducing the toxicity of antiretrovirals, while keeping the HIV suppressed (Cohen et al., 2007).

Interestingly, the shorter breaks from medication with antiretrovirals appear to be the only safe option because when randomized clinical trials are conducted to assess the benefits of long-term drug holidays the result is a worsening of clinical outcomes in relation to immunological and virological status compared with continuous therapy (Strategies for Management of Antiretroviral Therapy Study Group [SMART], Lundgren, et al., 2008). So, while the longer

drug holidays with ADHD medication appear to be beneficial in terms of effect on child growth, none of the studies included in this review documented the impact on clinical symptoms, which might well be an important limitation of these studies. It is important to measure clinical symptoms because the perception of returning symptoms while on a drug holiday can potentially result in children being put back on ADHD medication without good reason. However, measuring the symptoms of ADHD is not without its own problems because there are no real clinical parameters to measure apart from using rating scales, which can be subjective. This is in contrast to many physical conditions where the impact of drug holidays on disease progression can be assessed objectively. So, for example, clinical parameters such as bone mass density (BMD) measurements are used to monitor the impact of bisphosphonate drug holidays, and viral load and CD4 cell count are used in HIV (Curtis et al., 2008; SMART, Emery, et al., 2008).

The development of drug tolerance and the need for higher doses over time was reported in the literature as a reason for planned drug holidays from ADHD medication. The pharmacological treatment of Parkinson's disease (PD) with levodopa (L-DOPA) is also linked with the development of tolerance to the medication. Research suggests that taking a 7-day drug holiday from L-DOPA may re-sensitize dopaminergic receptors and lower the patient's L-DOPA requirements, or at least prevent the need for increasing L-DOPA dose in the near future (Corona, Rivera, Otero, & Stopp, 1995). Stimulants' ability to cause tolerance is controversial, but certainly, the need for increasing the dose over time has been reported in the literature. For example, the AACAP guidelines state, "most children will need dose adjustment upwards as treatment progresses" (AACAP, 2007). In addition, the MTA study reported that stimulants' effectiveness subsides over time (MTA Cooperative Group, 2004). However, these specific sources do not directly suggest the development of tolerance because dose escalation could be due to adherence problems, inadequate dosage, or wrong initial diagnosis.

However, other studies do suggest the idea of tolerance more explicitly. Some studies suggest that after oral administration of methylphenidate, while the high concentrations are maintained at the site of action in the brain, the effectiveness on controlling behavioral symptoms dissipate. This was suggested to be due to acute tolerance to medication, which might be a result of an adaption response at the synaptic level to the blockade of the dopamine transporter (DAT; Swanson et al., 1999). Other research has suggested that the need for higher doses of stimulants over time could be as a result of changes in pharmacokinetics as children develop, the natural worsening of the underlying illness with time, or could be due to changes in the environment of the child (Yanofski, 2011). The medication itself could also worsen ADHD because dependence and tolerance have caused "paradoxical decompensation" (Yanofski, 2011). Here, the chronic use of stimulants can result in adaptive physiological changes in the neurons of the central nervous systems, resulting in delayed therapeutic effects, the development of tolerance, and anecdotally the loss of therapeutic effects during long-term treatment (Yanofski, 2011). Safer and Allen (1989) reported that about 6% of children treated with methylphenidate for 3 to 10 years developed tolerance to the drug effect. They did not explain the reasons for developing tolerance but suggested it could be due to physiological mechanisms or possibly due to the development of other co-morbidities that might reduce the therapeutic response to stimulants over time (Safer & Allen, 1989). It has been hypothesized that drug holidays from medication could partially reverse the adaptive effects of chronic pharmacological stimulation and re-sensitize neurons when medication is restarted (Howland, 2009). One study suggests that children with ADHD may initially manage with a smaller dose when methylphenidate treatment is restarted after a drug holiday (Davis & Sabir, 2009).

Implications

Although most prescribed medications should be taken consistently to maintain their therapeutic effects, drug holidays in children with ADHD can sometimes serve a useful purpose. NICE guidelines do not recommend doctors to include drug holidays routinely in the therapeutic regimens of their children with ADHD but advise them to form an agreement with parents and their children about the best pattern of use. Apparently, from this review, a considerable percentage of families incorporate planned drug holidays in their patterns of medication use. The literature retrieved suggests that drug holidays from ADHD medication among children and adolescents are helpful rather than harmful. They could be a tool for confirming the benefits of medication, helping verify the need for medication, and checking coping without the medication. The qualitative data included in this review suggest that a trial without the medication could also be a tool for testing the feasibility of long-term medication discontinuation. However, drug holidays could be helpful in convincing adolescents or parents to continue taking medication while if the medication is no longer needed, then drug holidays could be useful in persuading parents that permanent cessation is a viable option. Quantitative data suggest that short breaks from medication could be a useful way of alleviating problems related to medication taking such as side effects and drug tolerance. The NICE guidance (NICE, 2013) presents experiences of some parents of children with ADHD in relation to using medication. As well as the published literature, these descriptions also suggest that children may develop a tolerance to ADHD medication with time. Therefore, we believe that doctors who deal with children with ADHD should consider planned drug holidays on non-school days

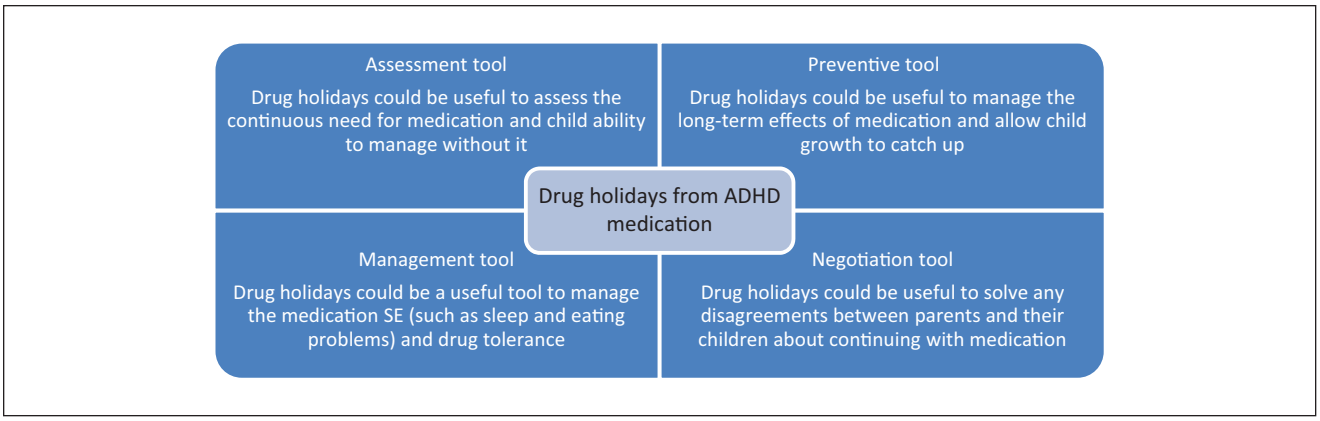

Figure 3. A model that explains the multi-application of drug holidays from ADHD medication.

with children who show a need to increase the dose of medication with time instead of increasing the dose continually. This could, on one hand, help to prevent developing tolerance to ADHD medication and, on the other hand, it could help avoid exposing children to side effects as a result of increasing the dose. Longer drug holidays such as those taken during the summer months could be helpful for preventing or managing medication adverse effects on child growth. Thus, a drug holiday from ADHD medication can be a multi-purpose tool for assessing the need for medication, preventing and managing problems related to medication, and negotiating medication continuation or discontinuation (see Figure 3). In this sense, planned drug holidays from ADHD medication could be helpful and should be advised and presented to some if not all families at some point in the treatment of the child as a positive approach.

Study Limitations

The results of this literature review are subject to some limitations. First, the experience of drug holidays was not the primary focus in most of the studies retrieved, which meant that these studies were not ideal for capturing the prevalence of or attitudes toward drug holidays. Second, the aim of this literature review was to encapsulate the whole documented experience of drug holidays from ADHD medication since the introduction of medication. Therefore, even low-quality studies were included in this review if they met the basic inclusion criteria. However, low-quality studies were interpreted carefully in the discussion and conclusion of this review.

Conclusion and Future Work

The pattern of use recorded in the literature indicated that planned drug holidays from ADHD medication among children and adolescents are very common phenomena that usually take place over the weekend or during school holidays. This comprehensive literature review explains the different implications of drug holidays from ADHD medication. Moving forward, a common definition for what constitutes a planned drug holiday from ADHD medication would help standardize future research. Clearly, distinguishing between planned and unplanned drug holidays is important for accurately reflecting the prevalence of drug holidays. Planned intentional drug holidays should refer to a break from medication for a specific purpose (managing medication side effect, checking the continuing need for medication, etc.) and can be initiated by doctors, parents, or older children. Measuring the impact of long breaks from medication on actual ADHD symptoms as well as medication side effect is necessary and could be achieved by controlled withdrawal studies. Moreover, research could also identify whether drug holidays should be considered for any child with ADHD or whether there are specific cases where drug holidays are more worthwhile and also the different factors that contribute to successful drug holiday trials.

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