ADHD and Elimination Diets:
A Systematic Review of the Literature

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Abstract

The relationship between ADHD and diet has been a topic of interest for several decades. Early studies used a standardized approach to determine the effects of artificial food additives, primarily specific food colours, on ADHD-related behaviours. More recently, an individualized, approach has been increasingly used that examines the effects of specific culprit foods on individuals. This review first examines studies using a systematic historical approach. A meta-analysis is then applied that examines the differences in effect sizes when differences in individualized versus standardized diet approaches are employed. In addition, effect sizes are examined by the characteristics of the study samples, the type of outcome measure used and whether or not a positive response to a diet trial was used as a criterion for participation in the challenge portion of the studies. Results are also compared to previous meta-analyses that have examined the relationship between diet, food additives and ADHD.

Keywords: ADHD; hyperkinesis; elimination diet; restricted diet; Feingold; oligoantigenic

To my loving family…thanks for supporting me
and reminding me of what is important in life

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List of Acronyms

A-CRS	Abbreviated Conners Rating Scale
ADD	Attention Deficit Disorder
ADD-H	Attention Deficit Disorder with hyperactivity
ADHD	Attention Deficit-Hyperactivity Disorder
CRS	Conners Rating Scale
DSM	Diagnostic and Statistical Manual
FDA	Food and Drug Administration
IgG	Immunoglobulin G
IgE	Immunoglobulin E
KP	Kaiser-Permanente

Glossary

Artificial Food Colour	An artificial chemical substance that adds colour to food. It is differentiated from natural food colours that are derived from natural sources.
Artificial Food Flavour	A chemical substance added to foods to enhance taste and smell. It is differentiated from natural food flavours that are derived from natural sources.
Food Additives	An umbrella term that includes all substances added to foods such as colours, flavours and preservatives. Food additives can be derived from natural or artificial sources.
Food Preservative	A chemical or natural substance that is added to foods to prevent decomposition and extend shelf life.
IgE	An antibody that stimulates the release of histamine and is associated with common immediate physiological allergic reactions to substances.
IgG	An antibody that causes more delayed and long term reactions such as reduced mental clarity and energy levels and digestive symptoms. IgG antibodies are now thought to be associated with some drug side effects, exposure to chemicals and many food reactions.
salicylate	A chemical substance that protects plants from pests and disease and is naturally present in some foods.
urticaria	Hives

1. Introduction

The link between dietary factors and Attention Deficit/Hyperactivity Disorder (ADHD) has garnered a lot of research interest over the years, with some studies reporting a positive association (Benton, 2007; Conners, Goyette, Southwick, Lees & Andrulonis,1976; Cook & Woodhill, 1976; Feingold, 1975a;1975b; Goyette, Conners, Petti & Curtis, 1978; Levy et al., 1978; Pelsser et al., 2009; Pelsser et al., 2011; Rapp, 1978; Salzman, 1976; Swanson & Kinsbourne, 1980a; 1980b) and other studies finding no significant association (Conners, 1980a;1980b; Harley, Matthews & Eichman, 1978a; Harley et al., 1978b; Kavale & Forness, 1983; Levy & Hobbes, 1978; Mattes & Gittelman, 1981; Weiss et al., 1980). Interest in the topic has persisted as researchers continue to investigate if there is a relationship of significance that may have importance for interventions that support children and adults with ADHD. Various aspects of diet thought to moderate ADHD related behaviours have been studied such as specific reactions to sugar (Kruesi et al., 1987; Wender & Solanto, 1991); salicylates, preservatives, and food colourings (Conners et al., 1976; Feingold, 1975a; 1975b; Harley et al., 1978b; Swanson & Kinsbourne, 1980); and more broad allergic reactions to an array of foods (Boris & Mandel, 1994; Egger, Carter, Soothill & Wilson, 1985; Kaplan, McNichol, Conte, & Moghadam, 1989; Pelsser et al., 2009; Pelsser et al., 2011; Rapp, 1978; Schmidt et al., 1997). In addition, there is a stream of research that examines the effects of specific nutrients such as polyunsaturated fatty acids (Johnson, Ostlund, Fransson, Kadesjö, & Gillberg, 2009; Richardson & Montgomery, 2005; Sinn & Bryan, 2007), zinc and/or iron (Oner et al., 2010) on ADHD symptomology. More recently, an epidemiological study in the general population found increased prevalence rates of ADHD were associated with what has been described as a “western dietary pattern”, or one that is high in processed food, saturated fat, sugar and salt (Howard et al., 2011). Considering the multifactorial nature of the etiology of ADHD (Doyle et al., 2005), it is not surprising that one dietary cause or contributing factor has not been identified. Rather, it is possible that different dietary factors, or combinations of dietary factors, are significant

for different people with ADHD. It is this line of thinking that has fueled research in the area of restrictive diets combined with food challenges as a way of determining individual triggers of ADHD symptoms. Generally, baseline behaviour measures are obtained prior to being placed on an open elimination diet and are followed by post diet measures to determine changes in behaviour. After the effects of diet have been minimized by the restricted diet, participants are given double blind placebo controlled food challenges to explore whether specific foods or food additives function as triggers for ADHD symptoms.

Although the research design has been fairly consistent between studies with open trial diets followed by double blind placebo controlled challenges, there are specific variables that may impact the results, such as the type of diet used, specific sample characteristics, and the outcome measures used. Whether or not the elimination diet was standardized for every participant or whether it was tailored to each individual is of particular interest, as this particular study characteristic has not been examined to date and thus adds to the body of literature in this area. The purpose of this analysis, therefore, is to systematically review the research that examines the relationship between elimination diets and their effects on the symptom of ADHD and to conduct a meta-analysis that examines how specific moderating variables impact the mean effect sizes.

1.1. ADHD Diagnostic Criteria

In North America, ADHD is diagnosed by a physician according to a set of diagnostic criteria defined in the Diagnostic and Statistical Manual of Mental Disorders, which is currently in its fourth edition with a fifth version forthcoming. The concept of ADHD has evolved over the years. In 1968, the Diagnostic and Statistical Manual II (DSM-II) identified a condition referred to as the Hyperkinetic Reaction of Childhood, often referred to as hyperkinesis. This condition was thought to arise from children's reactions to his or her environment, and it was believed that they outgrew this condition in adolescence (Lange, Reichl, Lange, Tucha & Tucha, 2010; McGough & McCracken, 2006). Work began on the DSM-III in 1974 and culminated with its publication in 1980 and included the term Attention Deficit Disorder (ADD), with and without hyperactivity.

However, the revised DSM-III (DSM-III-R) in 1987 removed the version of ADD without hyperactivity, and changed the name of the disorder to ADHD (American Psychiatric Association, 2012b; Lange et al., 2010).

In the DSM IV, published in 1994, and in the current DSM IV-TR, published in 2000, ADHD is included in the broad category of neurodevelopmental disorders. A diagnosis of ADHD must include the presence of criteria in the areas of either inattention or hyperactivity and impulsivity, or a combination of all three, that are present in two or more settings for a period of more than 6 months, were present prior to the age of 7, interfere with functioning in academic, social or occupational domains, and they must not be accounted for by Pervasive Developmental Disorders (PDD), schizophrenia or other psychotic disorders, and other mental illnesses. Further, there are three possible types of ADHD: combined type, predominantly inattentive, and predominantly hyperactive (American Psychiatric Association, 2012a). If a person does meet the full criteria for ADHD, but has significant impairment in the areas of inattention or hyperactivity and impulsivity, they can be classified as ADHD, not elsewhere classified (American Psychiatric Association, 2012a).

A fifth edition of the DSM is currently being developed with a proposed release date of May, 2013 (American Psychiatric Association, 2012a). While the general areas of inattention and hyperactivity/impulsivity remain unchanged, there are some key proposed differences. Specifically, the criteria of the age of onset for the presence of symptoms is being changed from 7 to 12; a fourth presentation of restrictive inattentive, that is distinct from predominantly inattentive presentation, has been added; PDD has been removed from the exclusion criteria; and there is an increased emphasis on the need for information from at least two sources (American Psychiatric Association, 2012a).

1.2. Behaviour Rating Scales

A diagnosis of ADHD involves the collection of information about the child in question from different sources in different environments such as from parents and teachers in home and school settings. To facilitate this process, screening tools such as

behaviour rating scales have been developed that align with the DSM diagnostic criteria for ADHD. Since the diagnostic criteria for ADHD have changed over the years with different versions of the DSM, so too have the behaviour rating scales, with current versions aligning with the DSM IV-TR diagnostic criteria (Pearson, 2012).

An example of a screening tool frequently used is a normed behaviour rating scale first developed by Dr. Keith Conners in 1968 (Conners, 1969). Subsequent editions of this scale, referred to as the Conners Rating Scales (CRS), and a revised version (CRS-R) evolved over the years into the current version, the Conners 3, released in 2008 (Pearson, 2012). In all versions, there are parent and teacher rating scales with items relevant to home and school environments that align with the particular DSM criteria of the time. For example, the original version developed in 1968 would have been developed for the DSM II criteria of the Hyperkinetic Reaction of Childhood, whereas the current Conners-3 aligns with the DSM-IV-TR criteria for ADHD in the areas of inattention, hyperactivity and impulsivity. The Conners-3 also includes self-reports for children and adolescents to report on their own behaviours (Pearson, 2012).

An abbreviated version of the CRS (A-CRS) was also developed that consists of 10 items drawn from the larger version of the tool with ratings ranging from 0 (not at all) to 4 (very much). The tool consists of items pertaining to restlessness and overactivity, inattention, impulsivity and mood imbalances. The individual ratings for each item are then added up for a total possible score that ranges from 0 to 30, with scores above 15 frequently used as an indicator of the presence of ADHD for screening purposes (Zentall & Barrack, 1977).

1.3. The Feingold (Kaiser-Permanente) Diet

As early as 1922, anecdotal evidence from case studies suggested that successful management of nervousness and aggressive behaviour could occur with the removal of specific foods, identified as possibly problematic by cutaneous tests, from the diet (Shannon, 1922). Feingold (1975a; 1975b) reported on the responsiveness of 194 case studies from five dietary programs and suggested that ingestion of salicylates, artificial dyes and preservatives was associated with increased hyperactivity in children

and adults. His work in this area began with studies of adults with aspirin sensitivity and evolved over time to research with children with hyperactivity and learning disabilities. Aspirin is the trade name for a chemical compound known as acetylsalicylic acid. Acetylsalicylic acid has a low molecular weight which allows for easy absorption into the bloodstream. Many foods contain a naturally occurring salicylate radical close in molecular structure to aspirin (Feingold, 1975). Food additives and colours are also low molecular structures and can therefore cause similar reactions in the body as drugs with similar molecular structures (Feingold, 1975a). The yellow colour, tartrazine or yellow # 5, was of particular interest to researchers, as many people with aspirin sensitivity also reacted to tartrazine (Feingold, 1975a). Based on the hypothesis that synthetic chemicals disrupt brain and nervous system function in a small group of children with a genetic predisposition, Feingold and his colleagues (Feingold. 1975a, 1975b) developed a restricted diet called the Kaiser-Permanente diet (KP) that removed all artificial colours, flavours, some preservatives and all foods containing naturally occurring salicylates. He claimed that the behaviour of 50% of children with hyperactivity and learning disabilities improved with the restricted diet, and he advocated for the clear labelling of additives in food (Feingold, 1975b). Further, he reported that age was an important factor in these clinical cases, with younger children aged 3-5 years experiencing a more rapid and complete improvement, and adolescents experiencing a slower and lesser degree of improvement (Feingold, 1975b). In addition, claims were made that when children were taking a course of stimulant medication while on the diet, ADHD behaviour could be aggravated, and discontinuation of the drug had no detrimental effect on the benefits of the diet (Feingold, 1975b). By 1976, the number of children in the five programs had increased to 360 with a favourable response rate of 30% to 50%, depending on the age of the child and the presence of neurological damage (Feingold, 1976).

Feingold's (1975a, 1975b, 1976) case reports and claims about the benefits of the diet received a lot of attention, and consequently, several open trial diet studies were conducted that included parent ratings of behaviour and anecdotal clinical observations to document improvements in hyperkinetic behaviour. Findings from these open trials also reported an improvement in hyperactivity when children followed the Feingold (KP) diet (Brenner, 1977; Cook & Woodhill, 1976; Palmer, Rapaport, & Quinn, 1975;

Salzman, 1976; Stein, 1976). In 1975, a National Advisory Committee on Hyperkinesis and Food Additives (NACHFA) was established to examine the validity of the evidence collected to date. In an initial report, the NACHFA determined that support for Feingold's claims was limited to anecdotal evidence, and the committee recommended that controlled clinical trials be undertaken to determine if there were any scientific bases supporting Feingold's claims (The National Advisory Committee on Hyperkinesis and Food Additives, 1975).

Over the next several years, Feingold's hypothesis was tested in studies that used either a controlled or crossover design, many of which also included double blind challenges of specific substances. In addition, reliable measures of learning and behaviour were used in an attempt to address the need for types of evidence other than anecdotal reports (Conners, 1980; Conners et al., 1976; Goyette et al., 1978; Harley et al., 1978a; Harley et al., 1978b; Levy et al., 1978; Levy & Hobbes, 1978; Mattes & Gittelman, 1981; Mattes & Gittelman-Klein, 1978; Rapp, 1978; Rose, 1978; Spring, Vermeersch, Blunden & Sterling, 1981; Swanson & Kinsbourne, 1980a; 1980b; Weiss et al., 1980; Williams et al., 1978). In 1976, Conners, Goyette, Southwick et al. conducted the first double blind crossover study with 15 hyperkinetic children that assessed the efficacy of the Feingold (KP) diet as compared to a control diet on teacher and parent measures of hyperactive behaviour. Results of behaviour ratings indicated that both teachers and parents rated hyperactive behaviour improved on the Feingold diet as compared to pretreatment baseline measures, but only the teachers found significant differences between the control diet and Feingold (KP) diet. However, a treatment order effect was found, where children who started on the control diet first and then switched to the Feingold (KP) diet had more positive ratings.

Generally, the majority of subsequent studies included experiments that followed a format where an open diet trial of the Feingold (KP) diet was implemented for a period of time, followed by a placebo controlled crossover challenge where children were given a cookie or capsule with either a placebo or a challenge substance: usually a specific food colouring or combination of food colouring. Outcomes were measured by behaviour rating scales completed by parents, teachers, or clinicians, as well as some direct measures of attention.

In 1978, Goyette et al. conducted a study that incorporated two double blind challenge experiments. In each experiment, the challenge substance was a chocolate cookie containing 13 mg, or half the estimated daily average of all the approved food colours at that time. Therefore, children ate two cookies for a total of 26 mg of all the approved food colours per day, and placebo cookies. Participants in the first experiment were 16 hyperkinetic children who were previously shown to be responsive to the Feingold (KP) diet by parents (57% reduction in behaviour problems) and teachers (34% reduction in behaviour problems). Differences between challenge and placebo conditions on ratings on the Conners Rating Scale (CRS) were not statistically detectable. However, within three hours of ingestion of the challenge cookie, challenge-control differences on a measure of visual motor tracking were significant. This led the authors to conduct a second challenge experiment with eight children where parental ratings of hyperkinetic-related behaviours were collected within three hours of ingestion of the challenge or placebo. Results of this trial showed a significant challenge effect ($p < .025$), with more problem behaviours reported when the children were ingesting the challenge substance as compared to the placebo.

Harley et al. (1978a; 1978b) conducted two experimental trials. The first trial randomly assigned boys who met their inclusion criteria to either the Feingold (KP) diet or a control diet. Both parents and teachers completed the CRS weekly during the study. The authors reported that an analysis of variance of the mean CRS scores for both mother and father ratings showed a significant diet effect, with hyperactive behaviour improving on the Feingold diet. However, teacher ratings showed no significant diet effect. At the end of each diet period, neuropsychological measures assessing motor control, working memory, basic academic skills; nonverbal intelligence and attention were obtained. In addition, attention and activity data during free play and structured activities were collected by observers in classroom and laboratory settings. Most results failed to reach significance. The exception was a measure of motor control where, on average, the boys who were on the experimental diet outperformed their peers in the control groups ($p<.05$). Similar to findings from Conners' (1976) study, the authors reported a significant diet order effect with more positive effects being shown when the control diet was followed by the Feingold (KP) diet. However, when data from the small number of preschool children included in the study was analyzed separately,

results were inconclusive prompting the authors to suggest the need for further studies of preschool children.

In the second phase of the study, Harley et al. (1978b) included nine children from the previous study in a double blind placebo controlled challenge trial where cookies and candy bars with 13 mg of a blend of food colours were used as the challenge substance twice per day, for a total of 26 mg of food colour ingested per day. Dependent variables consisted of parent and teacher ratings of hyperactive behaviour collected twice per week using the CRS, classroom observations by trained observers collected twice per week, and the same neuropsychological tests used in the first phase of the study conducted four times within the 13 week time period. The parent and teacher ratings of behaviour did not show a significant challenge effect, nor did any of the neuropsychological tests or the classroom observations.

Levy et al. (1978) examined the effects of the Feingold diet on hyperactive behaviour followed by a double blind crossover placebo controlled trial using 5 cookies per day, each with 1 mg of the food colour, tartrazine, as the challenge substance. No significant differences between the challenge and placebo trials were noted on any of the CRS rating scales (parent, teacher, clinician) or on the ten neuropsychological tests administered throughout the fourteen week study. However, the authors, in following the observations of Goyette et al. (1978) who hypothesized the effects were too short in duration to be identified in the length of time between challenge and observation, conducted a further analysis of a subgroup of 13 children with observations occurring within 24 hours of the challenge/placebo trial. In this sub-group analysis, the CRS ratings of mothers were compared between the challenge and placebo trials and a significant challenge effect was determined ($p<.025$). The authors concluded that the results lent support to the findings of Goyette et al. (1978) but suggested a need for replication in further studies.

Also in 1978, Levy and Hobbes attempted to replicate the procedures of the Goyette et al. (1978) study with eight subjects using a placebo controlled crossover challenge experiment. However, the challenge substance used in this study differed substantially from that used by Goyette et al. (1978). Levy and Hobbes (1978) used 4 challenge cookies with 1 mg of tartrazine each, for a total of 4 mg of food colouring per

day, whereas Goyette et al. (1978) used cookies that contained a blend of food colours that equated to approximately 26 mg of food colour per day. The results indicated that differences in mothers' ratings of hyperactive behaviour on the CRS scale between challenge and placebo trials did not reach statistical significance.

Williams et al. (1978) conducted a double blind placebo controlled crossover challenge with 26 children who had been clinically diagnosed with ADHD to assess the effects of the Feingold diet on ADHD symptoms as compared to stimulant medication. The medication used was the type and dosage previously prescribed to each child, and the challenge cookies contained nine food colours equating to approximately 13 mg of total food colouring per cookie. A 2 (challenge, control cookie) X 2 (stimulant medication, placebo) factorial design was used. Both the CRS and the Abbreviated Conners Rating Scale (A-CRS) were completed by parents and teachers two times per week and at the beginning and end of the study. Findings showed that the effects of the diet on children's hyperactive behaviour were statistically significant as rated by teachers, but not parents, when children took the placebo drug and not detectable when the child was administered stimulant medication

Conners (1980) conducted three separate double blind placebo controlled crossover challenge trials, all using challenge cookies with all the approved food colours for a total of 26 mg/day. The first experiment included 16 children who were on the Feingold (KP) diet for three weeks prior to the challenge trial. Parents and teachers completed the CRS as a measure of child behaviour three times per week and at the end of the trial phases. The zero-input tracking analyzer (ZITA) was also used to measure visual motor tracking ability and was administered at the end of the phases of the experiment both before and after eating both a challenge and placebo cookie. The CRS ratings for both parents and teachers showed improvements in behaviour from baseline to the end of both the placebo and challenge phases, but the reported differences between placebo and challenge trials were not statistically significant. Differences in visual motor tracking ability between baseline and one hour after the ingestion of the challenge or placebo cookie were significant for three out of 26 children in the study, prompting the author to conduct a further experiment where outcomes were measured closer to the time the challenge or placebo cookie was eaten.

The second experiment (Conners, 1980) was conducted with 13 children using the same procedures as the first, with the exception of the timing of data collection. In this case, parents completed the CRS within three hours of the child eating the challenge or placebo cookie and the teacher completed the form during the first period of the day. The results of parent ratings of behaviour reached significance ($p<.025$). However, the author reported that teacher data was insufficient to complete an analysis. The results of the parent ratings of behaviour prompted the author to conduct a third study to replicate the findings.

A third trial was conducted by Conners (1980) with 30 children and parent ratings of behaviour using the CRS collected in the same manner as the second trial above. In this study, differences between the active and placebo trials were not statistically detectable, however the author noted that the baseline parent ratings of behaviour on the CRS of this group were much lower than those of the previous two trials. In addition, the author reported that new estimates of average daily intakes of food colour using FDA data was now 75 mg or more which was considerably higher than the previous estimate of 26 mg/day that was used in this study (Conners, 1980). The author recommended that a dose-response study using double blind conditions be conducted.

In 1980, Swanson and Kinsbourne conducted a double blind crossover trial with 20 children clinically diagnosed as hyperactive and 20 control children. A food dye blend in large doses (100 mg and 150 mg) was used as the challenge substance. Paired-associate learning tests were administered in which children were shown pictures of animals paired with numbers and then required to look at a picture and respond with the appropriate number. The number of errors made by the child prior to reaching a criterion where they successfully responded to a list of animals was the outcome measure of sustained attention. The task was administered .5 hour prior to the challenge, and .5, 1.5 and 3.5 hours after the challenge. In addition, the CRS was completed twice daily by both the teacher and test administrator as a measure of hyperactive behaviour. Findings showed differences in behaviour ratings between challenge and placebo trials were not statistically detectable. However, results of a four factor analysis of variance (ANOVA) showed that the interaction between the condition (challenge, control) and time of testing (.5 hour before, .5, 1.5, 3.5 hours after ingestion) on performance on the paired associate learning task was significant [$F(3,108) = 2.73$, $p < .05$]. Further inspection of

challenge-placebo differences on the paired associate learning task showed decreases in attention span became evident at .5 hours after ingestion, peaked at 1.5 hours and lasted 3.5 hours suggesting that any effect of food colour on attention span might be time sensitive.

Weiss et al. (1980) examined the responses of 22 children to a double blind challenge using a drink with a blend of seven food colours (35.26 mg total) and a placebo. Parental observations of target behaviours (such as short attention span, over-activity, whining, breaks things, and runs away) were conducted within 3.5 hours of consumption and another at a later unspecified time. Twenty out of 22 children showed no sensitivity to the challenge substance. The authors noted that the low dose of colouring used may mean that dosages greater than 35.26 mg of food colour may be necessary to detect the effects on behaviour.

In 1980, the National Advisory Committee on Hyperkinesis and Food Additives submitted a final report to the Nutrition Foundation with the conclusions from an analysis of the controlled clinical trials that had been conducted since their initial report in 1975. Included in the narrative analysis were the findings from Harley et al. (1978), Conners et al. (1976), Swanson et al. (1980), Weiss et al. (1980), Mattes & Gittelman-Klein (1978), Williams et al. (1978), and Levy et al. (1978). In addition, they included reviews of in vitro and animal studies that probed the effect of food additives on behaviour. The conclusions and recommendations stated that the challenges in implementing the Feingold (KP) diet superseded any documented benefit of the diet, and there was no need for changes to policy. Further, the committee concluded that Feingold's recommendation to create a policy requiring special labelling of additives in foods was not warranted given the lack of empirical evidence in support of the recommendation (The National Advisory Committee on Hyperkinesis and Food Additives, 1980).

Despite the outcome of this review, some research in this area continued. Mattes and Gittelman (1981) attempted to address the issue of dosage by conducting a double blind crossover challenge with a blend of food colours incrementally increased to 75 mg/day in 11 children with hyperactivity referred by the Feingold Association. The cookies used for the challenge each contained 13 mg of all approved food colours. The trial started with one cookie on the first day, and then a cookie was added each day

thereafter to a maximum of 6 cookies. On the days when multiple cookies were administered to the children, they were provided three times per day: two cookies in the morning, two at lunch, and two in the evening, thus spacing out the dosage over time. The majority of outcome measures (CRS, hyperactivity scale, psychiatric evaluation, Children's Diagnostic Scale) were completed at the end of each week. In addition, a distractibility test was administered 1.5 hours after the ingestion of two cookies (26mg of colour), and the short version of the CRS was completed by teachers and parents on the third and fifth day of each trial. The authors reported that the effects of the food colours relative to the placebo control were not statistically detectable on any of the measures. However, it is important to note the outcome data were collected outside of the .5 to 3.5 hour after ingestion of the cookie window that previous research (Swanson & Kinsbourne, 1980a; 1980b) suggested may be necessary to detect significant effects.

Spring et al. (1981) conducted a double blind placebo controlled crossover study with six children who were already on the Feingold (KP) diet. In this study, the challenge substances used were chocolate cookies with a blend of approved food colours in the amount of 13mg per cookie. Two cookies were eaten on challenge days, one before and one after school, for a total of 26 mg/day. Parental reports of hyperactive behaviour using the CRS were collected on challenge days. In addition, the parents were contacted by phone on the challenge days and asked to guess, based on their child's behaviour, if their child had eaten the cookie with food colouring or the placebo. Findings were reported as individual data. The parents and teacher of one of the six children (child E) reported ratings of hyperactivity that were greater after eating the challenge cookie relative to the control cookie. Hyperactivity ratings made by the parent, but not the teacher, of another child were also relatively higher in the challenge condition. The authors attempted to replicate the findings for the one child E, but were unable to do so.

In an effort to synthesize the findings on the influence of the Feingold (KP) diet on ADHD symptoms in children, a meta-analysis of 17 controlled studies was conducted by Kavale and Forness in 1983. The authors further divided the analysis of the results by experimental methodology: seven were diet crossover studies, and ten were challenge studies. The magnitude of effects sizes obtained is small. The diet crossover studies yielded an average effect size of .196 (95% confidence interval; .072, .320), and

the average effect size obtained from the challenge studies was determined to be .045 (95% confidence interval; -.046, .136). Further, while no statistically detectable correlation between effect size and sample size, hyperkinesis diagnosis, or duration of treatment was found, a weak correlation was reported between effect size and mean age of the children in the sample ($r = -.255$, $p<.01$). The negative direction of the correlation affirmed research findings that suggested diet interventions were more beneficial to younger children (Feingold, 1975b, Harley, 1978a). Overall, the findings showed that, on average, the Feingold (KP) diet had negligible effects on ADHD-related behaviours, leading the authors to conclude that the disruption to families that the Feingold (KP) diet posed and the delayed medical attention to treat hyperkinetic children was not warranted (Kavale & Forness, 1983).

Subsequent to the Kavale and Forness (1983) analysis and the 1980 final report of the National Advisory Committee on Hyperkinesis and Food Additives, comparatively few studies were conducted that examined the effects of food additives on ADHD symptoms (David, 1987; Gross et al., 1987; Pollock & Warner, 1990; Rowe, 1988; Rowe & Rowe, 1994; Sarantinos, Rowe, & Briggs, 1990; Thorley, 1984). Thorley (1984) conducted a study of 10 children with intellectual disabilities who were in a residential institutional setting, seven of whom showed signs of inattentive or hyperactive behaviour. The children were placed on an additive free diet and subsequently challenged with a cocoa drink with 91.8 mg of food colouring and a placebo. The CRS was completed by staff and two psychometric tests assessing nonverbal intelligence, and memory were conducted within 98 minutes of the challenge were used to determine effects of food colour on cognition and behaviour. Challenge-placebo differences on all tests failed to reach significance.

David (1987) conducted a double blind placebo controlled challenge trial with 24 children whose parents reported a behavioural response of their child to tartrazine or benzoic acid. A total of 300 mg of tartrazine was given once in two doses in a juice, and on a separate day, 300 mg of benzoic acid was given in the same manner. Unstructured observations of play behaviour were used to determine the effects of the additives. The author reported that there were no behavioural changes noted by either parents or the nursing staff when placebo and challenge substances were administered. From this, the author concluded that parent reports of reactions to additives are often unreliable.

Also in 1987, Gross et al. evaluated the Feingold (KP) diet in 39 children with learning disorders who were attending a private residential school. All the meals were prepared according to the Feingold (KP) diet for one week. In the following week, artificial food colouring and flavours were supplied in as much quantity as the children wanted. In both weeks, the meals were video recorded and analyzed, and the motor restlessness, disorganized behaviour, and misbehaviours of the children were rated by one of the authors and two teachers. Findings from their analysis showed no differences in behaviour between the two weeks, and that the children clearly did not like the Feingold (KP) diet.

Rowe (1988) conducted a double blind placebo controlled crossover challenge study with eight children who responded positively to the Feingold (KP) diet. The participants ingested 50 mg/day of tartrazine and carmoisine in capsules in separate two week periods. Parent observations of behaviour were recorded using a checklist created to include behaviours often reported by parents in relation to artificial food colours (over-activity, restlessness, impulsiveness, low frustration tolerance, aggression, short attention span, sleep disturbance). Reports from parents indicated that the behaviour of two children was different after taking the food dye challenges when compared to the placebo. The authors suggested that the equivocal results from previous studies may in part have been a result of using outcome measures that were not sensitive to the behaviours of irritability, sleeplessness, and restlessness.

Pollock and Warner (1989) studied 19 children who were reported to have responded positively to an additive free diet. The children underwent a double blind placebo controlled challenge using capsules containing 125 mg of a mixture of artificial food colours. Parents completed a daily questionnaire comprised of 10 behaviour questions taken from the A-CRS and 10 questions associated with physical symptoms such as eczema, wheezing, and hives. Results indicated a significant difference between the challenge and placebo conditions ($p<.01$) on measures of hyperactive behaviour. The mean daily ratings of physical symptoms, however, did not differ between active and placebo conditions.

Sarantinos et al. (1990) studied 14 children diagnosed with Attention Deficit Disorder (ADD) who had been on an artificial food colouring-free diet for 6 weeks prior to

undergoing a double blind placebo controlled repeated measures study. The children were divided into two groups: one received six challenges of 10 mg of tartrazine, and the other received three challenges of 10 mg of tartrazine and three challenges of 10 mg of sunset yellow. Changes in hyperactivity, restlessness, impulsivity, inattention, irritability and sleep behaviours were reported by parents using the A-CRS and a behavioural rating inventory developed by Rowe and Rowe in 1989. Results were significant between challenge and placebo conditions for two of the 14 children (repeated measures analysis of variance, $p<.05$) with behaviours such as irritability, sleeplessness, impulsivity, and restlessness worsening in the challenge condition. This led the authors to conclude that a diet free of artificial colours may be beneficial in a small number of children with ADD.

Rowe and Rowe (1994) conducted a six week open trial of a diet free of synthetic food colouring with 200 children referred for suspected hyperactivity of which 150 whose parents reported behavioural improvement on the diet. A double blind placebo controlled repeated measures study was conducted with 34 children identified as benefitting from the diet (reactors), and 20 who served as a control group (non-reactors). The challenge substance used were capsules of 6 different quantities of tartrazine (1, 2, 5, 10, 20, and 50 mg) administered at different times and a placebo. Behaviour was evaluated daily by parents using the Behavioural Rating Inventory developed by the authors in 1989, which is sensitive to sleeplessness, restlessness and irritability, as well as the A-CRS. Results indicated that the changes in behaviour between placebo and challenge substance were significant at all food colour levels for the group identified as reactors, as was the difference in behaviour between the reactor and non-reactor group beyond the 2 mg dosage level ($p<.05$). The placebo days showed no significant differences in both groups.

Schab and Trinh (2004), in a subsequent meta-analysis, synthesized the research findings of the effects of artificial food colouring on the behaviour of children with ADHD as reported by parents and teachers on behavioural rating scales. In contrast to Kavale and Forness (1983), these authors limited their meta-analysis to studies that examined only the effects of artificial food colouring on behaviour rating scales. In addition, they updated the analysis by including studies published since 1983 (David, 1987; Pollock & Warner, 1990; Rowe, 1988; Rowe & Rowe, 1994; Sarantinos et

al., 1990; Thorley, 1984), and earlier studies not included in the Kavale and Forness (1983) meta-analysis (Adams, 1981; Rose, 1977).

In their primary analysis, the authors synthesized information from 15 studies of children who either had a clinical diagnosis of hyperactivity; a CRS cut-off score of greater than 15; or were referred for an assessment of hyperactivity. The mean effect size obtained from comparing the challenge condition to control conditions from the primary analysis of all reported behaviour was 0.283 (95% CI, 0.079 to 0.488). The authors further examined parents', teachers' and clinicians' ratings separately. While the mean effect sizes obtained from clinicians' and teachers' ratings did not reach significance, the mean effect size (.441; 95% confidence interval, .161 to .721) from parents' ratings of behaviour was moderate. Further, in the primary analysis, the authors also examined studies that screened for diet responsiveness in an open trial or by reviewing parental reports as an inclusion criterion for the challenge trial. This method resulted in a mean effect size of .535 on behaviour rating measures (95% confidence interval, .149 to .920).

In their secondary analysis, Schab and Trinh (2004) synthesized 8 studies that either included a mix of hyperactive and non-hyperactive children in the sample, or were solely non-hyperactive. The mean effect size for these trials was .117 (95% confidence interval, -.113 to .347) and not statistically significant. However, when the trials that screened for diet responsiveness using open trials or parent reports (as an inclusion criterion for the challenge/placebo trial) were analyzed separately, the mean effect size obtained was .316 (95% confidence interval, .157 to .475).

From the results of their meta-analysis, Schab and Trinh (2004) concluded that the hypothesis that the ingestion of artificial food colours increased ratings of hyperactive behaviours in children diagnosed as hyperactive was supported. Further, they suggested that specific types of behaviours are influenced by artificial food colours, such as sleeplessness and irritability. These particular behaviours, they postulated, are more likely to be noticed by parents at home in unstructured environments than by teachers in structured classroom settings.

Subsequent to the Schab and Trinh (2004) meta-analysis two studies were conducted (Bateman et al., 2004; McCann et al., 2007) that have contributed to legislative changes pertaining to the identification of food additives in Europe. Bateman et al. (2004) conducted a study of the population of 2878 three year old children on the Isle of Wight in the U.K. who were screened for identification of hyperactivity (HA) and atopy (AT), defined as a positive allergic histamine response to allergens through a skin prick test. Two hundred seventy seven children were divided into four groups: HA/AT, Non-HA/AT, HA/Non-AT and Non-HA/Non-AT and underwent a double blind placebo controlled crossover challenge study using 20 mg of a mix of food colours and 45 mg of sodium benzoate mixed in fruit juice. Using an aggregated parental hyperactivity rating of the mean differences in scores during the placebo and challenge trials, an effect size of .51 was obtained. This increase in behaviour after exposure to artificial food colours and sodium benzoate lead the authors to propose that the removal of artificial food colouring and sodium benzoate from the diet may result in a reduction in children's hyperactive behaviour.

Another study of the effects of food additives on childhood behaviour in the general population was conducted in 2007 in the U.K. (McCann et al., 2007). This study replicated Bateman et al. (2004)'s study of three-year-olds and extended it by including two different mixtures of additives as well as a second group of 8 and 9 year olds. The research design used was a randomised double blind placebo-controlled crossover trial with two different mixtures of additives used for the challenge trials. Mixture A replicated that of the Bateman et al. (2004) study, and mixture B contained a different mix that was thought to mirror the daily consumption of food additives in the U.K. A global hyperactivity aggregate (GHA) comprised of ratings made by teachers, parents and classroom observations was used to measure behaviour outcomes for both age groups. In addition, the continuous performance test II (Conners, 1994) was used to measure the attention and response inhibition aspect of executive function for the 8 and 9 year olds. The effect sizes on the GHA obtained in this study were .32 (95% confidence interval, .05 to .60) for 3 year old children and .12 (95% confidence interval, .02 to .23) for 8/9 year olds, mix A and .17 (95% confidence interval, .07 to .28) for mix B. From these results, the authors concluded that food additives increase hyperactive behaviours in some children, and the effects are more pronounced in young children.

The results of the Bateman et al. (2004) and McCann et al. (2007) studies suggest that artificial food colouring and sodium benzoate are associated with some ADHD symptoms in the general population, and may be indicative of a general health concern. In 2008, an ad-hoc committee was formed by the European Food Safety Authority to review the McCann et al. (2007) results and other relevant available literature to provide scientific opinion on the effects of some food colours and sodium benzoate on children's behaviour (European Food Safety Authority, 2008). Results of this review state that while there is limited evidence to indicate a small effect of food colours and sodium benzoate on attention behaviours in some children, it is difficult to determine the effects in the general population. In addition, the mixture of food colours and benzoate used in the McCann et al. (2007) study makes the identification of individual problematic substances difficult, and the clinical significance of the observed effects on behaviour is also unclear.

Despite the inconclusive findings of the European Food Safety Authority (2008), The Food Standards Agency (FSA) has requested that manufacturers participate in a voluntary ban of the colours used in the McCann et al. (2007) study, and has suggested that avoidance of these colours may be useful for parents of children showing hyperactive behaviours. Manufacturer guidelines for the replacement of these colours have been published and made available by the FSA (Food Standards Agency, 2011). In addition, the European Union has enacted regulations that require the mandatory labelling of specific food colours "to include the additional information that those colours may have an adverse effect on activity and attention in children" (Commission Regulation (EU) No 238/2010 of 22 March 2010, amending Annex V to Regulation (EC) No 1333/2008 of the European Parliament and of the Council with regard to the labelling requirement for beverages with more than 1.2 % by volume of alcohol and containing certain food colours, p. 17).

In Canada, Health Canada is currently proposing to change food labelling requirements to better enable consumer choice in avoiding artificial food colours. Based on a review of studies in the field, such as the McCann et al. (2007) study, Health Canada felt that recent research is consistent with and builds on previous findings suggesting that the ingestion of certain artificial food additives can result in behavioural changes in some children (Health Canada, 2010). Therefore, Health Canada is

proposing to require all artificial food colours to be listed by either their common name or number instead of simply the generic term “colour”. While the exact mechanism for clear labelling has not been decided upon, it is clear that enabling consumer choice is a priority and best facilitated by clear labelling. It is interesting to note that Feingold first suggested the use of labels to clearly indentify food additives in 1975 (Feingold, 1975b), but given the lack of empirical evidence at that time, this suggestion was rejected by the National Advisory Committee on Hyperkinesis and Food Additives in 1980 (The National Advisory Committee on Hyperkinesis and Food Additives, 1980).

More recently, Nigg, Lewis, Edinger and Falk (2012) conducted a meta-analysis that examined the effect of restricted diets and FDA approved food colours on ADHD symptoms as measured by parent, teacher and observer reports as well as psychometric tests of attention. The analysis of the FDA approved food colours included studies that followed the Feingold (KP) diet, or other diets that eliminated food colours, and then implemented a challenge trial with foods, drinks or capsules containing either one or a mixture of food colours. The parent ratings of behaviour yielded an average effect size of .18 (95% confidence interval, .08 to .24, p =.0007), whereas the teacher/observer ratings yielded an average effect size of .07 (95% confidence interval, -.03 to .18, p=.14). The average effect size obtained on the psychometric measures, however, was .27 (95% confidence interval, .07 to .47, p = .007).

In general, the meta-analyses conducted to date that have synthesized and analyzed findings from studies of artificial food colours and the Feingold (KP) diet have obtained mean effect sizes that are relatively small. One exception is the Schab and Trinh (2004) meta-analysis of studies in which study samples consisted of children with ADHD who were selected on the basis of parental or clinician positive response to diet intervention. In these cases, the effect sizes can be considered moderate by generally accepted guidelines (Cohen, 1988). However, the results of these analyses must be considered in light of several significant limitations of many of the individual studies that may have resulted in an underestimation of the effects of the Feingold Diet and additives on ADHD behaviours.

Table 1 summarizes the results of meta-analyses that have examined the effects of food additives on ADHD symptoms.

Table 1: Results of Meta-Analyses Analyzing the Relationship between Food Additives and ADHD

Study	Subject	Mean Effect Size
Kavale & Forness, 1983	**Feingold (KP) Diet/Food Additives**	
	Challenge studies	0.045 (95% CI, -.046 to .136)
	Crossover studies	0.196 (95% CI, .072 to .320)
Schab & Trinh, 2004	**Artificial Food Colours**	
	Hyperactive subjects	0.283 (95% CI, .079 to .488)
	Parents	0.441 (95% CI, .161 to .721)
	Teachers	0.081 (95% CI, -.073 to .235)
	Clinicians	0.107 (95% CI, -.128 to .343)
	Diet responsive	0.535 (95% CI, .149 to .920)
	Heterogeneous subjects	0.117 (95% CI, -.113 to .347)
Nigg et al., 2012	**Artificial Food Colours**	
	Parents	0.18 (95% CI, .08 to .29)
	Teacher/observer:	0.07 (95% CI, -.03 to .18)
	Attention tests	0.27 (95% CI, .07 to .47)

1.3.1. Limitations of Early Food Additive/Feingold (KP) Diet Research

The issue that dosages of the challenge substances used in many of the trials being too small to detect the effects of food additives has been raised over the years (Conners, 1980a; 1980b; Mattes & Gittelman, 1981; Rimland, 1983; Rowe & Rowe, 1994; Swanson & Kinsbourne, 1980), and identified as an area for further research in two of the meta-analyses (Nigg et al., 2012; Schab & Trinh, 2004). The reason for the varied dosages used in study trials seems to stem from a lack of precise information regarding how much food colouring children consume on average each day. Initially, when the need for controlled studies that incorporated double blind placebo controlled challenge trials was made apparent, the Nutrition Foundation produced chocolate cookies with 13 mg of all of the FDA approved colours to be used as the challenge substance in the trials (Conners 1980a; 1980b). Two cookies would provide 26 mg of food colours, which the Nutrition Foundation estimated to approximate the average daily

intake at that time (Conners 1980a; 1980b). Therefore, many of the early studies used these cookies in the challenge trials (Conners 1980a; 1980b; Goyette et al., 1978; Harley et al., 1978; Mattes & Gittelman, 1981; Spring et al., 1981; Williams et al., 1978). Others used even smaller amounts of a single food colour, most often tartrazine, in the amount of 1 mg per cookie (Levy et al., 1978; Levy & Hobbes, 1978; Rose, 1978). The daily intake was initially calculated using the total amount of all the approved food colouring consumed in the United States divided by the population to yield a per capita consumption amount of 27.29 mg/day (Wender, 1986). However, subsequent analyses suggested that children eat a larger number of foods with artificial colouring and the amounts used in the early challenge studies were too low to detect effects on behaviour for this population. This led to a re-estimation of daily intake of food colouring to be closer to 36 mg for children (Weiss et al., 1980; Wender, 1986). Yet another estimate of average daily consumption using the Federal Department of Agriculture (FDA) data that included miscellaneous foods eaten by children was 75 mg (Mattes & Gittelman, 1981; Conners, 1980a). However, the 90th percentile for children aged 1-5 was 121.3 mg/day, and 146 mg/day for children aged 6-12, with maximum levels of 315 mg/day (Conners 1980a; Mattes & Gittelman, 1981; Swanson & Kinsbourne, 1980). This resulted in later studies using substantially higher amounts of food colouring in the challenge trials than in previous studies (Boris & Mandel, 1994; David, 1987; Egger et al., 1985; Egger et al., 1992; Mattes & Gittleman, 1981; Pollock & Warner, 1990; Rowe & Rowe, 1994; Swanson & Kinsbourne, 1980; Thorley, 1984). Therefore the amount of food colouring used in challenge substances ranged from 1.2 mg/day (Rose, 1978) to 150 mg/day (Egger et al., 1985; Swanson & Kinsbourne, 1980a; 1980b), with one study using 300 mg/day (David, 1987).

In addition to the dosage of the challenge substance used in studies, another factor that has been discussed in the literature that may influence the outcomes used to measure changes in behaviour is associated with when the outcome measure is administered (Conners, 1980a, 1980b; Goyette et al., 1978; Swanson & Kinsbourne, 1980a; 1980b). That is, the lapse in time between the ingestion of the challenge or placebo substance and the administration of the outcome measure may mediate the effects of artificial food colouring on ADHD-related behaviours. In some studies, it was found that when outcomes were assessed within three hours of the challenge, an

increase in inattentive behaviours relative to the control baseline were found (Conners, 1980a, 1980b; Goyette et al., 1978; Swanson & Kinsbourne, 1980a; 1980b), whereas in other studies, any mediating effect due to when the outcome measures were taken was statistically not detectible (Conners, 1980a, 1980b; Mattes & Gittelman, 1981; Thorley, 1984). However, the dosage of the challenge substances also varied among these studies, suggesting that it may be a combination of dosage and outcome measurement timing that is important. The only study that has combined a large dose of challenge substance (100 to 150 mg) with a short time lapse (1.5 to 3.5 hours) between the ingestion of the challenge substance and the outcome measurement is that reported by Swanson and Kinsbourne (1980a, 1980b). As previously discussed, the results of this particular study suggest that performance on the paired associate learning task after the ingestion of the large amount of food colouring was depressed relative to performance after eating a placebo cookie at 1.5 hours, but that by 3.5 hours, these differences had abated.

Another factor for consideration when analyzing the results of previous studies is the variations in the type of substances used as the challenge material. The Feingold (KP) diet eliminates over 3000 additives from the diet along with foods containing naturally occurring salicylates (Feingold, 1975a), yet most studies used one or more food colours for all participants as the challenge substance as a means to test the efficacy of the diet. For example, some studies used one food colour, usually tartrazine (Levy et al., 1978; Levy & Hobbes, 1978; Rose, 1978; Rowe & Rowe, 1994), whereas others used a blend of several colours (Conners, 1980a; 1980b; Goyette et al., 1978; Harley et al., 1978; Mattes & Gittelman-Klein, 1978; Swanson & Kinsbourne, 1980; Thorley, 1984; Weiss et al., 1980; Williams et al., 1978), and some used a combination of food colours and preservatives (Bateman et al., 2004; McCann et al., 2007), or a singular preservative alone (Dengate & Ruben, 2002). In addition, chocolate or cocoa was used in many of the cookies and/or drinks in the challenge substances to mask the food dyes (Goyette et al., 1978; Harley et al., 1978; Levy et al., 1978; Williams et al., 1978; Mattes & Gittelman, 1981; Thorley, 1984), which was later found to cause reactions in 59% of study participants (Egger et al., 1985) and 64% of study participants (Carter et al., 1994). Similarly, wheat, a common ingredient in baked goods, was found to provoke symptoms in 49% (Egger et al., 1985) and 45 % (Carter et al., 1993) of

children tested. This is problematic in that both the challenge and placebo substances in these cases contained a potential culprit item for a large percentage of participants. The standardized methodology and challenge substances used in the studies assessing the efficacy of the Feingold (KP) diet can be considered problematic in that the relationship between food and ADHD behaviours appears to differ from person to person. A standardized approach would likely only trigger a relapse in symptoms in a proportion of the study sample, thereby underestimating the effect of the diet. Thus, a more efficacious approach that more accurately reflects the outcomes of an elimination diet would be one that is more individualized.

1.4. Individualized Elimination Diets

In addition to the studies of the Feingold (KP) diet, there have been others that examine the effects of different types of diets that exclude a wide range of foods for a period of time and involve a process of identifying culprit foods by reintroducing them in a sequential order to determine effects that can be unique to individuals. These are also commonly referred to as elimination diets, but are more individualized in nature. One such type of elimination diet is referred to as the oligoantigenic or “few foods” diet and was first described by Egger et al (1983; 1985). Typically, this diet includes two meats such as lamb and chicken; two carbohydrates such as rice and potatoes; two fruits such as apple and banana; specific vegetables and calcium and vitamin supplements (Egger et al., 1985). The intention of the oligoantigenic diet is to eliminate all possible sources of food sensitivities or allergies and then reintroduce each food one at a time to determine if it is responsible for changes in behaviour or other allergy symptoms such as headaches, eczema, abdominal discomfort, bedwetting and urticaria. The identified culprit foods are then used as challenge substances in a double blind placebo controlled crossover experimental design. There have been relatively few studies that use this approach as compared to the Feingold (KP) diet/artificial food colours with only a handful of studies having been conducted in the past several decades. This is a substantially different approach than the Feingold (KP) diet that focuses on the removal of food additives and foods containing salicylates. The studies conducted consisted of challenge trials that tested whether specific food additives influence ADHD-related behavior and used the same challenge substance for each individual.

The first study incorporating an oligoantigenic diet was conducted by Egger et al. (1985). In this experiment, 76 children with varying degrees of hyperkinetic syndrome or overactivity were treated with a four week oligoantigenic diet. Overactive Behaviour of 62 children was reported by parents to have improved using the A-CRS, and hyperactive behaviour of 21 of the 62 (33%) was reported to have reached a normal range. In the second phase of the study, the diet responders were reintroduced to one food a week that had been previously removed from their diet. If the symptoms did not reoccur, then the food was kept in the diet, but if symptoms did reoccur, the food was withdrawn. A reintroduction of tartrazine was done with 150 mg/day in capsules for one week, and benzoic acid in the same amounts in a separate week. Using this process, 48 foods were identified as triggering behavioural symptoms in different combinations in different individuals. A striking finding was that 79% of children tested reacted to artificial food colours and preservatives, but none of them reacted to these alone, further emphasizing the complexity of the role of diet in children's behaviour. The third phase of the study involved 28 children and utilized a double blind placebo controlled crossover design in which an identified culprit food was reintroduced. Differences in ratings of overactivity between active and placebo trials were statistically significant when made by a paediatric neurologist ($p<.001$), parents ($p< .001$), and a psychologist ($p = .01$). However, differences in performance on neuropsychological tests conducted at the end of placebo and active periods failed to reach significance.

In 1993, Carter et al. conducted a similar study with 78 children referred for hyperactive behaviour. The children were placed on an oligoantigenic diet, also referred to as a "few foods" diet, for three to four weeks. Of the 78 who participated in the open trial diet, 59 showed improvements in hyperactive behaviour and underwent the reintroduction phase to determine culprit foods. Nineteen children completed the double blind placebo controlled challenge phase. Behaviour was measured at the entry to the challenge phase, and after each experimental period using the parent portion of the CRS, a global rating of severity of behaviour problems completed by a parent, psychologist observations of fidgetiness, restlessness and inattentiveness during laboratory testing and a paired associate learning test and the familiar figures test to estimate attention span. A significant effect of the challenge foods relative to the placebo was found in parent ratings ($p<.05$), psychologist observations ($p<.01$), and

matching familiar figures test ($p<.01$), but not the paired associate learning test. The authors concluded that parental observations of the effects of food on behaviour can be confirmed with double blind placebo controlled trials.

Schmidt et al. (1997) compared the effects of stimulant medication to the effects of the oligoantigenic diet using a double blind placebo controlled crossover design. Forty-nine inpatients, with ages ranging from six to twelve years old and referred for treatment of hyperactive/disruptive behaviour disorder, were treated with both an oligoantigenic diet and a control diet, each for nine days. Assessments of disruptive behaviour during play and testing situations were conducted by members of the research team and ratings of classroom hyperactive behaviour were completed by teachers in the clinic school using the A-CRS. All assessments were conducted at baseline, day 3 and day 8. After a three day washout period, a second baseline measurement was taken, and 37 children were put on the medication, methylphenidate in an open trial. Tests were administered on days 3 and 5, and testers were not blind to the medication provided to the children. Significant improvements in behaviour were found in both the testing (F (df 2;47) = 8.65; $p=.0006$) and play (F (df 2;47) = 10.49; $p=.0002$) situations for the oligoantigenic diet compared to baseline. A responder was considered to be those children who improved greater than 25% on behaviour rating scores used in the study in both the testing and play situations. Using this criterion, 12 of 49 (24%) children were considered responders. The Methylphenidate trial results obtained found 16 of the 36 (44%) of the children who completed the trial responded. However, the authors noted that, while the response rate was higher, the amount of change in behaviour was similar to that with the diet. In addition, 3 of 49 children responded to the diet only suggesting that dietary treatment may be an important option for some children.

Uhlig, Merkenschlager, Brandmaier, and Egger (1997) used EEG mapping to determine brain electrical activity during the consumption of provoking foods. Forty-five children diagnosed with attention deficit hyperkinetic syndrome were placed on an oligoantigenic diet for three weeks. Seventy-one percent (32 of 45) had scores on the A-CRS drop below the cut-off for clinical significance (i.e.15) and were considered responders to the diet and who then entered the reintroduction phase. Foods were reintroduced sequentially every five days to identify foods that provoked ADHD related

behavioural symptoms. Fifteen of the 32 children identified as responders then entered the crossover study of EEG mapping and the recordings were interpreted by two investigators, one of whom was blind to the treatment order. Topographic EEG mappings were performed during each of the days of the eating and avoiding provoking food challenge trials under four conditions: resting state, eyes closed; right fist closing with eyes closed; resting state, eyes fixed on an object; and resting state with eyes closed. Results showed a significant association between the ingestion of provoking foods and brain electrical activity. Further, A-CRS ratings of behaviour by two investigators obtained during the crossover trial were found to be higher during the period the children were eating provoking foods ($p = .009$). While the mechanism for the alteration of brain activity during the ingestion of provoking foods as compared to non-provoking foods is not clear, one idea put forth by the authors is that provoking foods may interrupt the interaction between the nervous system and the gut and thus alter brain activity.

Pelsser et al. (2009) conducted a randomised control trial using a few foods diet intervention group and a control group that maintained their original diet. The 24 participants were diagnosed according to DSM IV criteria with ADHD combined inattentive and hyperactivity-impulsive type or predominantly hyperactive-impulsive type and were randomly assigned to one of the two groups. Parents and teachers were not blinded to the interventions and completed the A-CRS (abbreviated as ACS in the study) and the ADHD Rating Scale (ARS) before and after the diet period for both groups. In addition, a structured psychiatric interview (SPI) was conducted before and after the diet periods. Results of parent ratings showed a significant few foods diet effect in the mean differences on both the A-CRS [17.6 (95% confidence interval, 12.5 to 22.6, $p < .001$)] and the ARS [9.4 (95% CI, 5.9 to 12.8, $p < .001$)] measures. Similarly, the teacher reports showed a few foods diet effect of 13.3 (95% confidence interval, 7.5 to 19.1, $p < .001$) on the A-CRS and 8.4 (95% CI, 4.8 to 11.9, $p < .001$) on the ARS measures. An analysis of the comorbid symptoms of Oppositional Defiant Disorder (ODD) as measured with the SPI, that is based on DSM-IV criteria for ODD, showed a mean difference between intervention and control groups of 2.4 (95% CI, .4 to 4.3, $p < .02$).

In a subsequent study Pelsser et al. (2011) conducted another randomised controlled trial that consisted of two phases: a five week open label restricted elimination

diet phase with 100 children and masked paediatrician assessments followed by a double blind crossover food challenge phase with 29 children. Instead of assessing IgE levels associated with typical allergies, Pelsser et al. (2011) used IgG blood levels associated with non-allergy sensitivities. Challenge substances were selected by IgG blood samples to determine substances that evoked high and low blood IgG levels when introduced sequentially. The mean difference between the diet and control group at the end of the diet phase was measured with the masked paediatrician ARS scores and showed the effect of diet was statistically significant (23.7; 95% CI, 18.6 to 28.8, $p < .0001$), as did changes induced by the challenge trial (20.8; 95% CI, 14.3 to 27.3, $p<.0001$). Similarly, the A-CRS scores rated by parents showed a mean difference after the challenge trial of 11.6 (95% CI, 7.7 to 15.4, $p<.0001$).

In addition to the oligoantigenic or “few foods” diet, there are other elimination diets that are distinct from the Feingold (KP) diet. For example, Kaplan et al. (1989) implemented what was referred to as the Alberta Children’s Hospital (ACH) diet. This process eliminated food dyes, artificial flavours, monosodium glutamate, chocolate and caffeine from the children’s diet and decreased the amount of simple sugars ingested. In some cases, other foods such as dairy products were also eliminated. In addition, a multivitamin was given to all children. In this study, twenty-four preschool boys identified as hyperactive and who had co-morbid sleep problems or other physical symptoms, such as stuffy nose or stomach ache, were included in a 10 week placebo controlled crossover diet study in which all food for both the ACH diet and the equivalent control diet was provided to the participating families. Parents were blind to treatment conditions and completed both the A-CRS and an Abbreviated Symptom Questionnaire (ASQ). In addition, parents added up to four items not accounted for in the behaviours scales that they observed and were particular to their child. Allergy symptoms were recorded three times per day, and daycare staff completed the ASQ daily. Results of parent ratings of behaviour showed a significant treatment effect between baseline, control and treatment conditions ($F; 2, 46 = 17.24$, $p<.0001$), but the daycare measures were low, which the authors partially attributed to high turnover in daycare staff. Overall, 42% of children demonstrated a 50% improvement in behaviour over control conditions, and 16 % demonstrated a marginal 12% improvement in behaviour over control conditions when administered the ACH diet.

Similarly, Boris and Mandel (1994) implemented a two week elimination diet that eliminated dairy products, wheat, corn, yeast, soy, citrus, egg, chocolate, peanuts, artificial colours and preservatives with 26 children diagnosed as having ADHD. While this diet eliminated artificial colours and preservatives, it did not eliminate salicylates found naturally in many fruits and vegetables as does the Feingold (KP) diet. It also was not as restrictive as the oligoantigenic diet that is very prescriptive in the few foods allowed. At the conclusion of the elimination diet, 19 of 26 children (73%) showed improvement in hyperactive behaviours as reported by parents on the A-CRS. Further, 18 of the 26 children (69%) were atopic. Open food challenges were then conducted every two days to identify individual culprit foods. Sixteen children then completed a double blind placebo controlled food challenge in which specific foods and placebos were randomly administered over a seven day period. Results showed a significant difference between challenge and placebo days (p=.003).

In 2007, Benton conducted a meta-analysis that examined the link between restricted diets and ADHD that was part of a larger review of the impact of diet on anti-social, violent and criminal behaviour. Here, the author synthesized four diets that were considered similar in that a wider range of foods were excluded (Boris & Mandel, 1994; Carter et al., 1993; Egger et al., 1985; Schmidt et al., 1997). The effect size of restricted diet interventions as compared to a control determined by this particular analysis was large at 0.87 (95% CI 0.38 to 1.37). However, the inclusion of only four studies can be considered too small to synthesize effectively and is a major limitation of this particular analysis (Borenstein, Hedges, Higgins, & Rothstein, 2009).

More recently, as part of a meta-analysis of studies that investigated restriction diets and synthetic food colours on ADHD behaviours, Nigg et al. (2012) examined the specific results of dietary restriction separately from the analysis of food colours. In this analysis, the authors identified six studies that examined restricted diets in either a crossover or placebo-controlled diet challenge experimental design (Conners et al., 1976; Egger et al., 1985; Harley et al., 1978; Kaplan et al., 1989; Pelsser et al., 2011; Schmidt et al., 1997). The data were analyzed using a fixed effects model, and the Pelsser (2011) study was removed as an outlier to reduce heterogeneity. The results of this synthesis was an effect size of g = 0.29 (SE=.12, 95% CI = .016-0.52; p=.014). Upon closer examination of the studies included in this analysis, it is apparent that the

term “restricted diet” is inclusive of all diets that are modified in some way. As such, of the five studies included, two used an oligoantigenic diet (Egger et al., 1985; Schmidt et al., 1997), two used the Feingold (KP) diet (Conners et al., 1976; Harley et al., 1978), and one used the Alberta Children’s Hospital diet (Kaplan et al., 1989), suggesting that the differences in diet type may account for some of the differences.

2. Research Questions

The primary purpose of this synthesis is to re-examine the studies that have investigated the influence of diet restrictions on ADHD behaviours with a specific view to examining the contribution of specific moderating variables. Based on the body of literature consisting of studies examining the efficacy of the Feingold (KP) diets as compared to studies of other types of elimination diets, it is clear that there may be significant differences in the influence of the two diet types on ADHD-related behaviours. There are substantial differences between the Feingold (KP) diet and the oligoantigenic diet that are commonly grouped together as "restricted diets" in the literature (Berkely, Scruggs & Matropieri, 2010; Forness, 2001; Nigg et al., 2012). The Feingold (KP) diet was developed by Feingold and eliminates food colours, preservatives and naturally occurring salicylates from the diet, whereas other elimination diets, such as the oligoantigenic diet, are much more restrictive in that they also eliminate a wide range of foods commonly known to provoke allergic responses in children in addition to food additives. This diet is also often referred to as the "few foods" diet, as allowed foods are specified instead of listing the restricted foods. In addition, a key aspect of studies of the other elimination diets is the inclusion of a reintroduction phase that identifies the specific reactive substances for each individual. Therefore, many of the studies that assessed the efficacy of the elimination diets used a challenge trial that incorporated individualized challenge substances. This contrasts with the challenge studies examining the Feingold (KP) diet that used the same, often singular, substance for each study participant. The first question in this analysis, therefore, will examine whether or not the magnitude of effect size is greater for individualized elimination diets as compared to those that are standardized.

Similar to the methods employed by Schab and Trinh (2004) and Nigg et al (2012), the second question addressed here pertains to the type of outcome measure used in studies. Specifically, the differences in the magnitude of effect sizes of measures of cognition compared to measures of behaviour will be examined. Most often

in studies examining the effects of diet on ADHD behaviours, neuropsychological measures of various aspects of executive function such as attention, working memory, and task switching as well as some measures of intelligence, achievement, and motor control have been administered in laboratory settings by clinicians at key times during the experiments. In contrast, the measures of behaviour consist of behaviour rating scales completed by parents at home and teachers in classroom settings, as well as clinician ratings of behaviour during testing situations and structured observations in classroom settings. Findings from previous meta-analyses show differences between the magnitude of effect size obtained when parents rate behaviour compared to the ratings made by teachers or others, with parent ratings of their children's behaviour yielding larger effect sizes (Nigg et al., 2012; Schab & Trinh, 2004). Therefore, the effect sizes determined by the behaviour ratings of parents, teachers and clinicians will be examined separately from the neuropsychological measures.

It has been proposed by some (Schab & Trinh, 2004) that diet may have a greater effect on children with a diagnosis of ADHD as opposed to other conditions. Therefore, the characteristics of the sample may have an influence on the magnitude of the effect sizes. For this reason, the third research question will examine the effect sizes obtained in studies that include only children identified as having ADHD in study samples as compared to effect sizes generated from studies with samples that contain some children with ADHD and some without ADHD to determine any differences.

Also related to study sample characteristics is the inclusion criterion for the challenge component that was used in each study. Specifically, studies that identified a positive response to diet, as identified by parents or clinicians through open diet trials, as an inclusion criterion will be examined separately from those studies that did not use such a criterion. It is hypothesized that the use of diet responsive individuals and the exclusion of those who did not show an impact of diet, may impact the study effect size and over-estimate the effects of diet for the whole population of children with ADHD.

3. Method

3.1. Search Method

This meta-analysis examined the effects of diet on the behaviour of children diagnosed with ADHD. To find relevant articles, a search was conducted using the Academic Search Premier, Biomedical Reference Collection, ERIC, Global Health, Health Source – consumer edition, Health Source – Nursing/Academic edition, Medline, Google Scholar and PsycINFO databases. The search terms used were ADHD AND nutrition or diet or food AND restrict* or few foods or elimin* or oligoantigenic. The process yielded 96 citations between the years 1976 and 2012 which were then examined for study inclusion. Further, the reference lists in this corpus of studies, as well as in narrative reviews and previous meta-analyses were also reviewed to identify additional studies. This process yielded 58 studies for consideration.

3.2. Meta-Analysis Inclusion/Exclusion Criteria

In order to be considered for inclusion in this meta-analysis, the following criteria were applied to the studies: (a) either a Feingold (KP) diet or an individualized elimination diet was investigated; (b) an experimental design with either a control group or a crossover challenge was used, (c) study samples included a majority of children who had a clinical diagnosis of ADHD, or were screened for the presence of ADHD-related behaviors, or in the case of population based studies, the assumption of a heterogeneous sample was assumed, and (d) the studies were written in English.

The following exclusion criteria were applied to the studies: (a) the study used a within subject design that did not include a crossover or were open trials, (b) the study used the same children in a different study already included in the analysis; and (c) the data provided were insufficient for analysis.

3.3. Coding of Data

To assess the impact of the moderator variables to be examined, the data were coded according to (a) diet type: Feingold (KP) diets vs. individualized elimination diets (b) characteristic of measures: indirect observations of behaviour by parents, teachers, clinicians, and direct measures by neuropsychological tests, (c) sample characteristics: all children in sample show ADHD-related behaviors vs. a proportion of the sample of children show ADHD-related behaviors, and (d) response to diet: whether or not a response to the diet was a prerequisite for participating in the challenge phase of the study.

3.4. Analytic Strategy

The Comprehensive Meta-Analysis (CMA) Program (Borenstein, Hedges, Higgins, & Rothstein, 2005) was used to estimate effect sizes. This enabled the inclusion of multiple data types to be considered in the analysis. Given that one of the moderating variables to be analyzed was the characteristic of the outcome measures, it was deemed necessary to include multiple measures for several studies. However, the inclusion of more than one outcome measure, and consequently multiple effect sizes per study, likely created dependency in the effect size data (Marulis & Neuman, 2010).

Given the wide variability in diet type, sample size, challenge substance (both type and dosage) and type of outcome measure used, one true effect size common to all studies was not expected. Rather, the mean of a distribution of effects was considered to be more appropriate and, therefore, a random effects model was used for this analysis. In addition, the range in the number of effect sizes generated for each study also emphasizes the need for the use of a random effects model, as the weights of individual studies will be more balanced with this approach (Borenstein et al., 2009). However, for purposes of comparisons to previous analyses that have used a fixed effects methodology (Kavale & Forness; Nigg et al., 2012) both fixed effects and random effects models are reported.

4. Results

4.1. Overall Effect Sizes

Twenty-seven studies met the inclusion criteria with an aggregated sample size of 1198. Effect sizes are reported as standard differences between means with 95% confidence intervals.

The overall mean random effect size was .355 (95% CI, .238 to .473). The overall mean fixed effect size was .268 (95% CI, .210 to .326), but as expected there was significant heterogeneity in the size of these effects ($Q=125.64$, $p<.001$). The I^2 value determined was 63.39, meaning that 63% of the variance can be explained by between study differences, and 37% of the variance can be explained by within study random error.

Table 2 presents an overview of the studies included in this analysis and the corresponding effect sizes.

4.2. Moderator Variables

Several moderator variables were examined to help explain the heterogeneity in the overall effect sizes and to account for differences in findings from previous meta-analyses.

Table 2: Effects Sizes of Individual Studies

Study Authors	Year	Diet Type	Sample Size	Type of Outcome Measure	Effect Size	95 % CI	p
Conners	1976	Feingold	15	Parent rating	.55	.010 to 1.097	.046
				Teacher rating	.55	.010 to 1.097	.046
Goyette et al study 1	1978	Feingold	16	Parent rating	.00	-.693 to .693	1.00
Goyette et al study 2	1978	Feingold	13	Parent rating	.71	.102 to 1.318	.02
Harley et al	1978	Feingold	9 intervention, 9 control	Parent rating	.24	-.420 to .906	.47
				Teacher rating	.11	-.550 to .760	.75
Levy et al	1978	Modified Feingold	11	Clinician rating	.00	-.836 to .836	1.00
			20	Parent rating	.00	-.620 to .620	1.00
			14	Teacher rating	.00	-.741 to .741	1.00
			17	Test	.00	-.693 to .693	1.00
Levy et al sub-analysis	1978	Modified Feingold	13	Parent rating	.94	.128 to 1.748	.02
Levy & Hobbs	1978	Feingold	7	Parent rating	.87	.003 to 1.745	.05
Mattes & Gittelman-Klein	1978	Feingold	1	Parent rating	.67	-.604 to 1.944	.30
				Teacher rating	.00	-1.24 to 1.24	1.00
Williams et al	1978	Feingold	26	Parent rating	.34	-.06 to .73	.10
				Teacher rating	.40	.004 to .804	.05
Conners study 1	1980	Feingold	16	Parent rating	-.30	-1.00 to .394	.40
Conners study 2	1980	Feingold	13	Parent rating	.38	-.39 to 1.16	.33
Conners study 3	1980	Feingold	30	Parent rating	.00	-.506 to .506	1.00
Swanson & Kinsbourne	1980	Feingold	40	Clinician rating	.00	-.620 to .620	1.00
				Test	.21	-.233 to .653	.35
Adams	1981	Feingold	18	Clinician rating	.31	-.347 to .967	.36
				Parent rating	.93	.241 to 1.616	.008
				Test	.05	-.603 to .704	.88
				Test	-.16	-.812 to .497	.64
Mattes & Gittelman	1981	Feingold	11	Clinician rating	-.35	-1.091 to .537	.44
				Parent rating	-.25	-1.091 to .587	.56
				Teacher rating	.02	-.964 to .996	.98
Spring et al	1981	Feingold	6	Parent rating	.00	-1.132 to 1.132	1.00
Egger et al	1985	Oligoantigenic	28	Clinician rating	.11	-.632 to .851	.77
				Test	-.15	-.923 to .617	.70
Kaplan et al	1989	Alberta Children's Hospital *	24	Parent rating	.60	.024 to 1.181	.04
Pollock & Warner	1990	Modified Feingold	19	Parent rating	.88	.216 to 1.548	.009
Carter et al	1993	Oligoantigenic	19	Clinician rating	.53	.048 to 1.008	.03
				Parent rating	.48	.003 to .952	.049
				Test	.48	.007 to .957	.047
Boris & Mandel	1994	Elimination Diet*	19	Parent rating	.88	.306 to 1.462	.003
Rowe & Rowe	1994	Modified Feingold	54	Parent rating	.82	.355 to 1.278	.001
Schmidt et al	1997	Oligoantigenic	49	Clinician rating	.65	.248 to 1.061	.002
				Teacher rating	-.22	-.618 to .176	.28
Dengate & Ruben	2002	Modified Feingold	27	Parent rating	.27	-.119 to .649	.18
Bateman et al	2004	Modified Feingold	277	Parent rating	.23	.395 to 2.679	.007
				Test	.07	-.095 to .239	.40
McCann et al	2007	Population-based**	153	Clinician rating	.32	.048 to .592	.02
			144	Clinician rating	.17	.066 to .274	.001
Pelsser et al	2011	Oligoantigenic	31	Parent rating	1.82	1.311 to 2.335	<.001
				Teacher rating	1.57	1.077 to 2.061	<.001

*Included in Individualized elimination diet category

**Included in Feingold (KP) diet category due to challenge with artificial food additives

4.2.1. Diet Type

All of the studies were able to be categorized as either a standardized elimination diet or an individualized elimination diet. The average effect sizes for both diet types in the random and fixed effects models are listed in Table 3. The magnitude of the average effect size in the random effects model for the individualized diet [.65 (95% CI, .293 to 1.003)] is moderate and greater than the effect size in the random effects model estimated for the standardized diet [.22 (95% CI, .145 to .297)]. An analysis of the average effect sizes in the fixed effects model yielded similar results with individualized category of diets achieving a greater mean effect size [.64 (95% CI, .490 to .787)] than the weak, mean effect size generated from studies of the standardized diets [.21 (95% CI, .144 to .268)]. However, there is significant heterogeneity in effect sizes among studies using the individualized diets (Q=60.61, p<.001) as opposed to the homogeneity found in the standardized diets (Q=37.35, p=.32). In addition, the I^2 value for the individualized elimination diets was found to be 81.85 suggesting that 82% of the variance can be explained by between study differences, and 18% of the variance can be explained by within study random error, further supporting the use of a random effects model of analysis.

Table 3: Mean Effect Sizes for Diet Type

Diet	n	k	Standard difference in means	95% CI	Z	P	Q,P	I^2
Random Effects Model								
Individualized	7	12	.65	.293, 1.003	3.58	<.001		
Standard	20	35	.22	.145, .297	5.69	<.001		
Fixed Effects Model								
Individualized	7	12	.64	.490, .787	8.42	<.001	60.61, <.001	81.85
Standard	20	35	.21	.144, .268	6.50	<.001	37.35, .32	8.97

Given that the results of the Pelsser et al. (2011) study showed much stronger effects than the others in the individualized diet category (refer to table 2) and the small number of studies in this category, this study was removed from the analysis for comparison purposes to determine if the differences between the diet types is attributed solely to this particular study. It appears that the results of the Pelsser et al. (2011)

study were reported in a way that combined the masked pediatrician behaviour ratings with non-blind parent ratings, which may partially explain the difference. The removal of this study resulted in a reduced random effects size of .43 (95% CI, .185 to .675) and a reduced fixed effects size of .41 (95% CI, .251 to .578) for the individualized diet category. In addition, the heterogeneity was also reduced, but still remained significant (Q=19.11, p=.024). Therefore, while the Pelsser et al. (2011) study did appear to partially explain the differences between the two categories of diet types, it was not the sole reason.

Both the effect sizes in the random effects model and the fixed effects model indicate that there are distinctions between the two diets with the individualized elimination diets having stronger effects. The magnitude of the average effect size is moderate for individualized elimination diets and small for the standardized diets relative to placebo controls.

4.2.2. Type of Outcome Measure

The majority of the outcome measures in this field consist of parental, teacher or clinician ratings of ADHD-related behaviours. Outcomes may vary depending on the person observing the child and by the tool used. Therefore, to determine the impact of the type of outcome measures used on effect sizes in this analysis, the category of behaviour measures, that includes parent, teacher and clinician ratings of ADHD-related behaviours, as well as a category of other measures of outcomes were used. The specific tools used in the current synthesis in each category are listed in table 4a.

Table 4b shows the mean effect sizes, using both the random and the fixed effects size models, for each of the outcome measure groupings. The magnitude of the mean effect size using the random effects model for the parental reported ratings of behaviour was moderate at .49 (95% CI: .294, .681). The clinician reported ratings of behaviour had a small mean random effect size of .25 (95% CI, 111, .394), but both the teacher reports of behaviour [.34 (95% CI, -.122,.806)] and the psychometric tests [.10 (95% CI, -.038, .234)] failed to reach significance with confidence intervals spanning zero.

Table 4a: Type of Outcome Measure Used

Outcome Measure Category	n	k	Specific Measures Used
Behaviour Measures			
Parents	22	23	Conners Rating Scale (16); Modified Conners Rating Scale (2); Rowe Behaviour Rating Inventory (2); Aggregated Parental Activity (1); ADHD Rating Scale (1); tool developed for study (1)
Teachers	8	8	Conners Rating Scale (7); ADHD Rating Scale (1)
Clinicians	9	10	Conners Rating Scales (2); Structured Observations (5); Global Hyperactivity Assessments (2)
Other Measures			
Neuropsychological Tests	6	7	Matching Familiar Figures-errors (1); Actometer (1); Paired Associated Learning Test (1); Auditory Memory tests (2); Visual Memory task (1); Aggregated tests of hyperactivity (1)

An analysis of the average effect sizes using the fixed effects size model also shows parental ratings of behaviour to yield a small, but larger effect size than when ratings are made by teachers or clinicians (.41 ; 95% CI, .305 to .680). However, using the fixed effects model, the teacher-reported ratings of behaviour was .38 (95% CI, .179, .572), which contrasted with the non-significant effect size for this same grouping when determined using the random effects model. The clinicians reports of behaviour resulted in a mean effect size, using the fixed effects size model, of .21 (95% CI, .124 to .302), and the use of direct child measures showed a mean effect size that failed to reach significance (.10; 95% CI, -.038 to .234). In contrast to the results of the random effects model, the effect size confidence intervals in fixed effects models are smaller. Therefore, effect sizes generated from teacher ratings are statistically significant and have a confidence interval that does not span zero. This is to be expected, as a random effects model accounts for both within and between studies variance and thus tends to have larger standard errors, variances, and wider confidence intervals (Borenstein et al., 2009). There was significant heterogeneity for both the parent ($Q=61.47$, $p<.001$) and teacher ($Q=34.21$, $p<.001$) ratings of behaviour, with I^2 values of 64 and 80 respectively. Therefore 64% of the variance in effect sizes generated from the parent ratings and 80% of the variance in effect sizes generated from teacher ratings can be accounted for by between study variance, and 36% and 20% respectively can be accounted for by within study random error.

The effect sizes of parental ratings of behaviour is consistent with the findings of Schab and Trinh (2004) who found the mean effects size using a random effects model in their primary analysis to be 0.441 (95% CI, .161 to .721). However, it is in contrast to the findings of Nigg et al. (2012) who determined the mean effect size determined by psychometric measures of attention (.27) to be higher than parental ratings of ADHD-related behaviours (.18). Different aspects of attention behaviour may be tapped in the different measures used in the studies included in each synthesis. In addition, the lower effect size generated by parent ratings of behaviour determined by Nigg et al. (2012) may also be attributed to fewer studies being included in the analysis, and different sample characteristics.

Table 4b: Mean Effect Sizes for Type of Outcome Measure Used

Diet	n	k	Standard difference in means	95% CI	Z	P	Q,P	I^2
Random Effects Model								
Parents	22	23	.49	.294, .681	4.944	<.001		
Teachers	8	8	.34	-.122, .806	1.494	.149		
Clinicians	9	10	.25	.111, .394	3.501	<.001		
Tests	6	7	.10	-.038, .234	1.412	.158		
Fixed Effects Model								
Parents	22	23	.41	.309, .511	7.978	<.001	61.47, <.001	64
Teachers	8	8	.38	.179, .572	3.747	<.001	34.21, <.001	80
Clinicians	9	10	.21	.124, .302	4.681	<.001	9.84, .277	19
Tests	6	7	.10	-.038, .234	1.412,	.158	3.94, .685	0

4.2.3. Sample Characteristics

To assess the hypothesis that hyperactive children may react differently than others to specific foods and/or additives, the studies were divided into two categories: those that used a sample of children identified as having ADHD, and those that included a heterogeneous sample, of which only a portion have been identified as having ADHD. Table 5 shows the mean effects sizes from this analysis.

Table 5: Mean Effect Sizes Determined by Characteristics of Sample

Category	n	k	Standard difference in means	95% CI	Z	P	Q,P	I^2
Random Effects Model								
All ADHD	20	35	.39	.229, .557	4.62	<.001		
Mix	7	12	.24	.101, .373	3.42	.001		
Fixed Effects Model								
All ADHD	20	35	.41	.310, .501	8.33	<.001	92.98, <.001	63
Mix	7	12	.19	.122, .265	5.30	<.001	20.58, .038	47

Results of the random effects model determined a mean effect size of .39 (95% CI, .229 to .557) for the sample comprised of children all of whom had been clinically diagnosed or were screened as demonstrating ADHD-related behaviours. In comparison, the average effects size in the random effects model for studies that incorporated a mixed group of children, where only some of which were diagnosed with ADHD, was .24 (95% CI, .101 to .373). The mean effect sizes using a fixed effects model yielded a similar trend in results with the overall average effect size for the ADHD group being .41 (95% CI, .310 to .501), and the mean effect size of the mixed group being even smaller at .19 (95% CI, .122 to .265). In both cases, there was significant heterogeneity with Q values that reached statistical significance.

The findings that larger effect sizes are obtained in analyses of studies that include samples of children with ADHD affirm the pattern of findings of Schab and Trinh (2004). In the Schab and Trinh (2004) synthesis, the authors distinguished studies with participants who had been diagnosed with or screened for ADHD in their primary analysis, from those that included children with other problematic behaviours, both with and without children with ADHD in the samples, in their secondary analysis. The overall average effect size in studies with samples of children with ADHD (15 studies) was .28 (95% CI, .079 to .488), whereas the studies with the mixed sample (8 studies) was found to have an overall mean effect size of .12 (95% CI, -.113 to .347).

4.2.4. Response to Diet as a Requirement for Challenge Phase

Many studies, of both the Feingold (KP) and broader elimination diets, include only those participants who responded to the diet as being eligible for the subsequent phases of the study (n = 16), whereas others did not (n = 11). This criterion of diet responsiveness selects specific children shown to have responded positively to a specific diet by either open trials and/or parent reports for the challenge trials. Therefore, the children who did not respond positively to the diet are not included in the challenge trials, and subsequently are not represented in the findings. This would tend to result in an overestimation of the results of the diet and the impact of food and additives on ADHD symptoms.

The mean effect sizes for this analysis, using both the random and fixed effects models, are provided in table 6 below, with No representing those studies that did not have response to diet as a requirement and Yes representing those that did. The mean effect size using the random effects model was greater for the Yes group (.44; 95% CI, .227 to .661) than the No group (.22; 95% CI, .128 to .306). The mean effect sizes using the fixed effects model showed a consistent trend with the results of the Yes group being moderate, but greater (.51; 95% CI, .388 to .624) than the No group (.20; 95% CI, .132 to .263). There was significant heterogeneity for the grouping that used diet responsiveness as a criterion for inclusion in the challenge phase of studies (Q=82.08, p <.001).

Table 6: Mean Effect Sizes of Response to Diet used as Requirement for Challenge Phase

Category	n	k	Standard difference in means	95% CI	Z	P	Q,P	I^2
Random Effects Model								
Yes	16	27	.44	.227, .661	4.01	<.001		
No	11	20	.22	.128, .306	4.76	<.001		
Fixed Effects Model								
Yes	16	27	.51	.388, .624	8.41	<.001	82.08, <.001	68
No	11	20	.20	.132, .263	5.89	<.001	23.49, .216	19

Yes = a positive response to the diet was required for participation in challenge

No= a positive response to the diet was not required for participation in challenge

5. Discussion

The controversy surrounding the effect of diet on ADHD-related behaviours has sparked periodic debate for decades. One of the challenges in conducting research in this area is the difficulty of having children on a restricted diet and blinding the parents to this fact. While some researchers have attempted to blind participants and parents by providing all the food for both the intervention and control group families and disguising the diets (Conners et al., 1976; Harley et al., 1978; Kaplan et al., 1984), others have not (Pelsser et al., 2009; Pelsser et al., 2012; Schmidt et al., 1997). However, many studies included an additional phase that used a double blind placebo controlled challenge trial that tested the effects of various foods or additives that had been removed from the diet. The studies in this meta-analysis included only those studies, or portions of studies, that used double blind placebo controlled trials or treatment and control diets with masked observers. The overall average effect size in the random effects model was .355 (95% CI, .238 to .473) which affirms the overall mean effect size determined by Schab and Trinh (2004) in the primary analysis portion of their meta-analysis (.283; 95% CI, .079 to .488), and in the Nigg et al (2012) synthesis (0.29; 95% CI, .016 to 0.52).

The first research question posed in this synthesis pertained to whether or not there are differences in the magnitude of effect sizes for different types of elimination diets, with a differentiation made between those that are standardized from those that are tailored to individuals. The common use of the terms “elimination diets” and “restricted diets” in the literature has been found to encompass all types of diets, so this distinction adds to the literature in the field. The two main categories of elimination diet types consist of the standardized Feingold (KP) diet established by Feingold (Feingold, 1975) that restricts additives and naturally occurring salicylates from the diet, and a broader category of individualized elimination diets such as the oligoantigenic, or few foods, diet that restricts a much wider range of foods and includes a reintroduction phase that identifies culprit food specific to each individual (Egger et al., 1985). The

mean effect size for Feingold (KP) diet (.22; 95% CI; .140 to .292) was lower than the mean effect size for the other elimination diets (.65; 95% CI; .293 to 1.003). These findings are consistent with those reported by Benton (2007) in an analysis of 5 studies that used broad elimination diets (0.87; 95% CI; 0.38, 1.37).

There are several possible reasons for the differences in effect sizes between diet types. The first possible explanation is the nature of the diet itself, whereby more foods are considered potentially reactive substances and are therefore removed from the diet in the more recent elimination diets as compared to the Feingold (KP) diet. Therefore, early studies examining the efficacy of the Feingold (KP) diet used foods such as chocolate and wheat to hide the challenge substances that were later determined to cause reactions in a high percentage of children with ADHD (Carter et al., 1993; Egger et al., 1985). Therefore, it may be difficult to assume that children are not reacting to food additives when other substances impacting their behaviour are not removed from their diet. Further, Egger et al. (1985) found that the most common substances causing reaction in children were benzoic acid and tartrazine, but not a single child reacted to these alone. That is, reactions to food additives often coincided with reactions to some foods. Thus, challenge trials that test the effects of additives may not show an effect when other foods may also be provoking ADHD-symptoms in some children. The exclusion of a wider range of foods, such as in the oligoantigenic diet, followed by a systematic reintroduction of potential culprit foods specific to each individual is more likely to generate findings that have statistical and practical importance.

The second research question examined the differences in the magnitude of effect sizes in each category of outcome measure. For the purpose of analysis, the outcome measures used were separated into parental, teacher, and clinician ratings of behaviour and psychometric tests. In general, both the fixed and random effects models yielded higher effect sizes for the behavioural measures as compared to the more direct measures of neuropsychological tests, with the overall mean effect size of parental ratings being the largest (.48; 95% CI: .289, .680), which is consistent with the findings of Schab and Trinh (2004). The tools used to measure changes in behaviour, such as the Conners Behaviour Rating Questionnaire, were thought by some (Dengate & Reuben, 2002; Rowe, 1988; Rowe & Rowe, 1994) to be insensitive to the changes in

mood, specifically irritability, thought to be most influenced by diet. This would have implications of possibly underestimating the effect size of behaviour ratings if specific behaviours were not listed on the rating scales. Further, home environments may provide opportunities for a wider range of behaviours, such as sleeplessness and irritability for example, that are not as evident in other settings. The functional relevance of the changes in behaviour ratings as a result of diet is not clear, as the neuropsychological measurements of attention and hyperactivity are not reflective of the same effect. While it may be interpreted from these results that the functional importance of the impact of diet on ADHD behaviours is minimal, caution is warranted with this interpretation, as it is not clear how sensitive to changes in the specific areas of cognitive functioning influenced by diet these measures are. Further, the individual profiles characteristic of children with ADHD may also warrant individualized measures of cognition to determine the effects of diet specific to each person.

The third research question examined the type of sample included in the various studies by proportion of children with ADHD was analysed in two broad categories: (1) those studies that included only children with ADHD and (2) those studies that had samples of children with ADHD as well as children who were not diagnosed with ADHD. Studies that included only children who were non-hyperactive were excluded from this study. Schab & Trinh (2004) also separated the studies with only an ADHD sample in their primary analysis from studies with both samples of non-hyperactive children as well as those that included a proportion of children with ADHD. Similar to Schab & Trinh (2004), this analysis found differences in the overall mean effect sizes between the two groupings. The mean effect size determined for the solely ADHD grouping was larger [.39 (95% CI, .227 to .561)] than that determined for the heterogeneous grouping [.24 (95% CI, .101 to .373)], thus providing empirical support for the hypothesis that some children with ADHD are sensitive to dietary interventions. This finding has clear implications for interventions for subgroups of children with ADHD, where diet may be an important factor for consideration in a holistic approach in addressing the needs of the child.

Findings for the analysis of how subjects were selected for the challenge phase of the trial, the fourth research question of this analysis, were not unexpected. That is, it seems logical that diet responsive subjects would be more likely to respond to challenge

substances, and studies that used diet responsiveness as determined by open diet trials or parental reports as a criterion for participation in the challenge trials would yield an overall higher effect size than studies that did not. Differences in mean effect sizes for the two groups were evident with diet responsiveness as a criterion yielding an overall mean effect of .44 (95% CI, .227 to .661) as compared to those trials that did not use this criterion [.21(95% CI, .122 to .299)]. The studies that used this criterion can therefore be considered to be reflective of a subgroup of the ADHD population reported to be responsive to diet. Further, the categorization of studies in this manner resulted in a mix of diet types in each category (both the Feingold and the individualized elimination diets) which, as previously discussed, also had an impact on effect size. This supports the idea that it is likely a combination of factors such as diet types, sample characteristics, and the type of outcome measurement used that impacting the magnitude of effect sizes.

Taken together, the findings of this analysis of the literature suggest that interventions addressing ADHD related behaviours might include an individualized elimination diet as part of a holistic plan prior to the use of medication, as a subgroup of children with ADHD may benefit from this approach. This has been recommended by and is supported by others in the field (Hill & Taylor, 2001).

6. Limitations

The results of this analysis must be considered in light of limitations. The inclusion of more than one effect size for several studies for the purpose of analyzing the various outcome measures resulted in heavier weighting of some studies in the results. There were also numerous studies that reported outcomes in a narrative fashion that were consequently excluded from this analysis. Similarly, some studies reported findings that were non-significant without sufficient data to include in this synthesis. It is difficult to determine the extent to which some individuals are influenced by diet when the results are reported in aggregate. For example, Egger et al (1985) found that four participants responded so adversely to the challenge phase that they could not continue the trial, but this information is not reported in the aggregate results. Therefore, results that are not statistically significant may have clinical significance for some individuals.

Further, how ADHD has been defined and diagnosed has varied over the time span of the studies included in this synthesis, meaning the studies with samples of children diagnosed as having hyperkinetic syndrome in the 1970's according to DSM-II criteria have different characteristics than the studies with samples of children diagnosed with ADD-H and ADHD according to different versions of the DSM. Therefore, while a difference in magnitude of effect sizes between samples of children defined as hyperactive and samples with only some of the children defined as hyperactive was found, this finding is somewhat diluted by the variances in the way the disorder has been described and the different diagnostic criteria used for identification.

7. Implications for Future Research

The main finding from this synthesis is that for some children with ADHD, their diet can be modified on an individual basis to exclude foods that are likely to increase hyperactive behaviour. What is evident from the research to date is that a number of children with ADHD seem to have their symptoms reduced by the removal of one or more substances they ingest, including some foods and additives. An oligoantigenic diet may be an option to try before starting a course of medication for children living in families who are able to support their child's adherence to the diet for several weeks and who are supervised by a pediatric dietician (Hill & Taylor, 2001). However, further research in this area is needed, as there are relatively few double blind placebo controlled studies using an oligoantigenic approach.

While many of the studies to date have explored allergies and food sensitivities as the mechanism causing food related ADHD symptoms, another possibility that is of growing interest is the relationship between intestinal bacteria and behaviour (Finegold, 2008; MacFabe et al., 2007). Research exploring the effects of intestinal flora that is out of balance, or an overgrowth of harmful bacteria, on ADHD symptoms and the results of a diet that re-establishes a balanced system would be beneficial to the field.

What also appears to be lacking in the literature to date is the child's perception of their changes in mood and behaviour. It would be interesting to explore whether a children's awareness and self-regulation of diet can influence their behaviour.

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Appendices

Appendix A.

Studies Considered in Systematic Review

Study	Diet	Sample Size	Study Design	Inclusion Criteria	Outcome Measure
Palmer, Rapoport & Quinn, 1975	No diet	79	Survey	Participation in a study of hyperactive boys	questionnaire
Conners et al, 1976	Feingold	15	Double blind crossover	DSM II criteria for hyperkinesis	CRS – parents, teachers
Cook & Woodhill, 1976	Feingold	15	Open trial	Diagnosis of hyperkinesis	questionnaire
Salzman, 1976	Feingold	15	Open trial	Learning and behavioural problems and sensitivity to salicylates, artificial colours and flavours	Behaviour ratings
Stein, 1976	Feingold	2	Case Study	Referral to therapeutic nursery	Parent, teacher, and pediatrician observations
Brenner, 1977	Feingold	32 – diet 15 – control	Open trial with control group	DSM II – minimal cerebral dysfunction hyperkinetic syndrome	Parent and teacher reports
Goyette et al, 1978	Feingold	16	Double blind placebo controlled challenge crossover	DSM II criteria for hyperkinesis; 25% reduction of symptoms on diet	CRS – parent and teacher; zero input tracking analyzer; auxiliary distraction task
		13	Double blind placebo controlled challenge crossover	(8) DSM II criteria for hyperkinesis; 25% reduction of symptoms on diet (5) DSM criteria, borderline response to diet	CRS – parent and teacher
Harley et al, 1978a	Feingold	36 intervention 34 control	Double blind crossover	Referral to clinic for hyperactivity; CRS score > 15; or diagnosis of hyperkinesis	CRS – parent and teacher; EEG; observations; neuropsychological measures
Harley et al, 1978b	Feingold	9	Double blind placebo controlled challenge crossover	Chosen from first study based on a positive response to the diet	CRS – parent and teacher; structured observations; battery of neuropsychological measures

CRS: Conners Rating Scale

EEG: Electroencephalogram

Study	Diet	Sample Size	Study Design	Inclusion Criteria	Outcome Measure
Levy et al, 1978	Feingold	10-20 – varied by test	Double blind placebo controlled challenge crossover	IQ>80; parent reports of inattention, overactivity, impulsivity and aggression; clinical judgement of hyperactivity	CRS; test measuring motility, attention, impulsivity, perceptual-motor, memory, WISC sub-tests
Levy & Hobbes, 1978	Feingold	7	Double blind placebo controlled challenge crossover	DSM II criteria for hyperkinesis; 25% reduction of symptoms on diet	CRS - parent
Mattes & Gittelman-Klein, 1978	Feingold	1	Double blind placebo controlled challenge crossover	Diagnosis of hyperkinesis; Improvement on diet reported by parents	A-CRS - parent
Rapp, 1978	Modified Feingold	24	Open challenge	Diagnosis of hyperkinesis; non-asthmatic	Abbott Hyperkinesis Index – Parents; medical questionnaire - parents
Rose, 1978	Feingold	2	Double blind placebo controlled challenge crossover	Diagnosis of hyperkinesis; Previously on Feingold Diet; discontinuation of stimulant medication	Informal daily log – parents; structured observations of on task, out of seat, aggressive behaviours
Williams et al, 1978	Feingold	26	Double blind placebo controlled challenge crossover	Diagnosis of hyperkinesis; on stimulant medication for 3 months	A-CRS – parent and teacher; CRS – parent and teacher
Tryphonas & Trites, 1979	No diet – allergy testing	120	Correlation study: Blood samples testing IgE antibodies and correlated with CRS	3 groupings: Hyperactive: diagnosis and CRS scores; Learning Disability – normal intelligence and academic delay; Emotional Inattentive – restlessness and inattentive associated with anxiety	RAST tests; CRS – parent and teacher

A-CRS: Abbreviated Conners Rating Scale

CRS: Conners Rating Scale

RAST – Phadebas Radioallergosorbent kits to test for the presence of IgE antibodies

Study	Diet	Sample Size	Study Design	Inclusion Criteria	Outcome Measure
Conners, 1980a;b	Feingold	16	Double blind placebo controlled challenge crossover	Baseline scores of > 15 on CRS; 25% reduction in symptoms on CRS - parents	CRS – parent and teacher; zero-input tracking analyzer
		18		Same as above	CRS – parent
		30		Not indicated	CRS - parent
Swanson & Kinsbourne, 1980	Feingold	40	Double blind placebo controlled challenge crossover	Referred to clinic for hyperactivity	CRS Paired Associate Learning Test
Weiss et al, 1980	Feingold	22	Double blind placebo controlled challenge crossover	On Feingold diet – none had diagnosis of hyperkinesis	Parental observations of target behaviours
Adams, 1981	Feingold	18	Double blind placebo controlled challenge crossover	Pre-diet CRS > 15 and improved by diet	Measures of overall activity; fine motor; gross motor; auditory and visual memory
Mattes & Gittelman, 1981	Feingold	11	Double blind placebo controlled challenge crossover	Referred by Feingold Association; 6 met DSM III criteria for ADD-H	CRS – parent and teacher; Children's Diagnostic Scale; Distractibility test; structured observations
Spring et al, 1981	Feingold	6	Double blind placebo controlled challenge crossover	Improvement in hyperactive behaviours after diet	Abbreviated Hyperactivity Rating Scale; global behaviour judgment
Thorley, 1984	Diet free of artificial additives	10	Double blind placebo controlled challenge crossover	At residential school for children with Intellectual Impairments (mean IQ 52)	CRS – teachers and care staff; Porteus maze; paired associated learning test; actometer
Egger et al, 1985	Oligoantigenic	28	Double blind placebo controlled challenge crossover	Diagnosis of hyperkinetic syndrome or overactivity as part of another behavioural disturbance	A-CRS; Matching Familiar Figures; Porteus Maze; Actometer; structured observations

A-CRS: Abbreviated Conners Rating Scale

ADD-H: Attention Deficit Disorder – with hyperactivity

CRS- Conners Rating Scale

Study	Diet	Sample Size	Study Design	Inclusion Criteria	Outcome Measure
David, 1987	Individualized diet	24	Double blind placebo controlled challenge crossover	Referral to hospital unit for asthma and eczema; parent reports of adverse reactions to foods and additives; 6 met DSM III criteria for ADD	Unstructured parent and nurse observations
Gross et al, 1987	Feingold	39	Placebo controlled crossover diet challenge	Attendance at school for children with learning disorders	Structured observations of video tapes of meals
Rowe, 1988	Feingold	9	Double blind placebo controlled challenge crossover	Referral for suspected hyperactivity; 6 months of improved behaviour on diet; absence of diagnosed psychiatric illness	Daily behaviour checklists – parents and teachers
Kaplan et al, 1989	Alberta Children's Hospital Diet	24	Placebo controlled crossover diet challenge	DSM III criteria for ADD-H	A-CRS – parents and day care; plus additional items added by parents
Wilson & Scott, 1989	Additive free diet	29	Double blind placebo controlled challenge crossover	Improvements in physical and behavioural symptoms as a result of diet	Daily symptom scores
Pollock & Warner, 1990	Additive free diet	19	Double blind placebo controlled challenge crossover	Referral to pediatric allergy clinic; parental reports of improved behaviour as a results of diet; 1 child diagnosed as hyperkinetic	A-CRS – parents; weekly overall perception of improvement - parents
Sarantinos, Rowe & Briggs, 1990	Artificial colouring free diet	13	Double blind placebo controlled repeated measures	ADD according to DSM III-R	A-CRS- parents; Behavioural Rating Inventory
Breakey, Hill & Connell, 1991	Modified Feingold	516	Open Challenge	Outpatients of clinic for children and adolescents with emotional; problems	Parent reports of response to challenge
Egger, Carter et al, 1992	Oligoantigenic	21	Double blind placebo controlled repeated measures	History of enuresis, headaches or hyperkinesis; 13 from Egger et al (1985) study	Standard diary card

A-CRS: Abbreviated Conners Rating Scale

ADD: Attention Deficit Disorder

ADD-H: Attention Deficit Disorder with hyperactivity

Study	Diet	Sample Size	Study Design	Inclusion Criteria	Outcome Measure
Egger & Stolla, 1992	Oligoantigenic	40	Double blind placebo controlled challenge crossover	DSM-III-R criteria of ADHD; positive response to diet	Standard diary card; skin prick tests; serum IgE
Carter et al, 1993	Oligoantigenic	19	Double blind placebo controlled challenge crossover	DSM III criteria for ADD-H; positive response to diet	CRS- parents; structured observations; Paired Associated Learning Test; Matching Familiar Figures Test
Boris & Mandel, 1994	Elimination Diet	19	Double blind placebo controlled challenge crossover	DSM-III-R criteria for ADHD	A-CRS- parents
Rowe & Rowe, 1994	Modified Feingold	54	Double blind placebo controlled repeated measures	Referred to Royal Children's Hospital for assessment of hyperactivity	Behaviour Rating Inventory; A-CRS
Schmidt et al, 1997	Oligoantigenic	49	Placebo controlled crossover diet challenge; comparison to open medication trial	Diagnosis of ADHD/Conduct Disorder according to DSM-III-R	Paired Associate Learning Test; Continuous Performance Task; A-CRS –teachers; structured observations
Uhlig et al, 1997	Oligoantigenic	12	Placebo controlled challenge crossover	ADHD – DSM-IV; score > 15 on A-CRS; positive response to diet	A-CRS; EEG
Dengate & Ruben, 2002	Modified Feingold	27	Double blind placebo controlled challenge crossover	Score of 85% or higher on RBRI; positive response to diet	RBRI – parents and teachers; A-CRS – parents and teachers
Bateman et al; 2004	Modified Feingold	277	Double blind placebo controlled challenge crossover	Screened for presence of hyperactivity using EAS Activity Scale and WWP-Activity Scale	Aggregated test of hyperactivity; aggregated parental hyperactivity ratings

A-CRS: Abbreviated Conners Rating Scale

ADD-H: Attention Deficit Disorder with hyperactivity

ADHD: Attention Deficit/Hyperactivity Disorder

CRS: Conners Rating Scale

EAS Activity Scale: Emotionality, Activity and Sociability

EEG: Electroencephalogram

RBRI: Rowe Behavioural Rating Inventory

WWP Activity Scale: Weiss-Werry-Peters

Study	Diet	Sample Size	Study Design	Inclusion Criteria	Outcome Measure
McCann et al, 2007	Population based study – no diet	297	Double blind placebo controlled challenge crossover	Open recruitment in childcare settings	Global Hyperactivity Aggregate comprised of: Abbreviated ADHD rating scale IV (teachers); Abbreviated WWP (parents); classroom observation code; Conners Continuous Performance task
Pelsser et al, 2009	Oligoantigenic	24	Open trial diet intervention vs control	DSM-IV criteria for ADHD	A-CRS; ADHD DSM-IV rating scale
Pelsser et al, 2011	Oligoantigenic	29	Placebo controlled challenge crossover – masked pediatrician ratings	Diagnosis of ADHD	A-CRS; ADHD DSM IV rating scale; SDQ; SPI

A-CRS: Abbreviated Conners Rating Scale
ADHD: Attention Deficit Hyperactivity Disorder
WWP: Weiss-Werry-Peters Activity Scale
SDQ: Strengths and Difficulties Questionnaire
SPI: Structured Psychiatric Interview