NO CHILD LEFT BEHIND: A QUALITY IMPROVEMENT CLINICAL IMPLEMENTATION TO IMPROVE THE TREATMENT OUTCOMES, QUALITY OF CARE, AND QUALITY OF LIFE FOR SCHOOL-AGED CHILDREN WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER AT A RURAL PRIMARY CARE PRACTICE

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ABSTRACT

Rebecca Dragomani: No Child Left Behind: A Quality Improvement Clinical Implementation to Improve Treatment Outcomes, Quality of Care, and Quality of Life and for Children with Attention Deficit Hyperactivity Disorder at a Rural Primary Care Practice
(Under the direction of Victoria Soltis-Jarrett)

Background and Rationale: Children with attention deficit hyperactivity disorder (ADHD) consistently report lower quality of life than their neurotypical peers and are at substantially increased risk for development of a comorbid psychiatric disorder. Fewer than half are prescribed an initial medication that is both efficacious and tolerable. Pharmacogenomic testing identifies medications likely to cause side effects and is available for use in routine clinical practice, although its effects on the quality of life among children who are prescribed medication for ADHD has not yet been evaluated.

Problem: Genetic differences contribute to the wide variability of response to ADHD medications but are not considered in treatment decisions. Quality of life, which correlates with the development of psychiatric comorbidities, is rarely assessed.

Purpose: The project aimed to improve the quality of care, treatment outcomes, and quality of life for school-aged children with ADHD at a primary care practice by implementing a comprehensive bundle of practice changes that individualize treatment of ADHD.

Methodology: The impact of routine pharmacogenomic testing on the incidence of ADHD medication side effects and change in behavioral symptoms was evaluated using retrospective chart review data. A convenience sample of 52 charts included 26 charts of patients who received pharmacogenomic testing (PGT) prior to being prescribed medication for ADHD and a second group of 26 patients who did not receive testing (No PGT). Quality of life was measured using cross-sectional data from 40 KINDL Quality-of-Life Questionnaires (parent-respondent). Quality of care was assessed through parent interviews.

Results: All QI initiatives were fully adopted. Pharmacogenomic testing was associated with fewer moderate and severe ADHD medication side effects (PGT 1.1 vs. No PGT 2.4) and greater differences in behavioral symptom scores (PGT -32 vs. NPGT -15.8). Mean quality-of-life scores of children with ADHD (PGT - 80.3, No PGT - 75.5, History Unknown 71.2) were higher than the benchmark averages.

Conclusion: The results support the continued use of pharmacogenomic testing prior to prescribing medication to children for ADHD, use of standardized assessments of response, and quality-of-life assessments to identify children at higher risk for the development of comorbid psychiatric disorders.

ACKNOWLEDGEMENTS

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LIST OF ABBREVIATIONS

AAP	American Academy of Pediatrics
ADHD	Attention Deficit Hyperactivity Disorder
ANOVA	Analysis of Variance
APA	American Psychiatric Association
AVG	Average (Mean)
CDC	Centers for Disease Control and Prevention
CMS	Center for Medicare and Medicaid Services
DSM	Diagnostic and Statistical Manual
EMR	Electronic medical record
HRSA	Health Resources and Services Administration
IHI	Institute for Healthcare Improvement
IRB	Institutional Review Board
JACHO	Joint Commission: Accreditation, Health Care, Certification
KINDL	KINDL Quality-of-Life Questionnaire
PGT	Pharmacogenomic testing
Pt.	Patient
N	Number
NICHQ	National Institute for Children's Healthcare Quality
NIMH	National Institute of Mental Health
NS	Not significant
QI	Quality Improvement
QoL	Quality of Life
RCT	Randomized Clinical Trial
U.S.	United States of America

VA	U. S. Department of Veterans Affairs
VS.	Versus
WA	Washington

CHAPTER 1: INTRODUCTION

Background and Significance

By the time they graduate from high school, nearly one out of every five boys and one of every eleven girls in the United States is diagnosed with attention deficit hyperactivity disorder (ADHD) (Centers for Disease Control and Prevention [CDC], 2011). Although ADHD is one of the most frequently diagnosed disorders in children (CDC, 2017), it remains one of the most poorly understood, and poorly managed, chronic health disorders worldwide (Danckaerts et al., 2010). The guidelines for the evaluation and management of ADHD among school-aged children, published by the American Academy of Pediatrics (AAP) in 2011, recommend stimulant medication, preferably with behavioral therapy, as first-line treatment for school-aged children (Perrin et al., 2011). Yet, only 41% of children will be prescribed a medication that is both efficacious and tolerable at their initial visit (American Academy of Child and Adolescent Psychiatry [AACAP], 2007). Dosing also poses challenges. Because of significant genetic variability in response, ADHD medications are not dosed by weight (Wall et al., 2012). The landmark National Institute of Mental Health (NIMH) Multimodal Treatment Study of Children with ADHD (MTA) (1999) trial found that even with meticulous titration every three days, 64% of children with ADHD suffered medication side effects. The most frequently reported side effects of ADHD medications are: sleep disturbance, decreased appetite, weight loss, nausea, abdominal pain, anxiety, tics, headaches, rebound irritability, and flattened affect (NIMH MTA, 1999; AAP 2011). Current literature indicates that 48% of children who take ADHD medications report side effects, and 21% describe their ADHD medication side effects as "very bothersome" (Cascade, Kalali, & Wigal, 2010).

Medical and scientific research has advanced our understanding of the etiology, evaluation, and treatment of ADHD over the past seven years, but little of this knowledge has been translated to routine clinical practice. Many of the challenges in the management of ADHD stem from genetic differences

among individuals, which contribute to the wide variability of response to ADHD medications and to the unpredictability of individual dosing requirements (Chou et al., 2000). ADHD is inherently complex, with a multifactorial etiology, different foci, (Kessler, 2017) multiple subtypes and presentations (Amen, 2017), and its course is influenced by socioeconomic, environmental, individual, and genetic factors (Chacko, Kofler, & Jarrett, 2014). To effectively improve outcomes of children with ADHD, treatment needs to be personalized to consider individual genetic factors that affect metabolism of medications (Barkley, 2006; Faraone & Kunwar, 2018) and patients' quality of life during treatment (Becker et al., 2011). Practical strategies to individualize treatment to improve the efficacy, tolerability, and quality of life for children with ADHD need to be implemented and systematically evaluated in clinical settings to align clinical practice with current knowledge of ADHD.

ADHD is a childhood-onset, chronic neurodevelopmental disorder, causing a sustained inability to focus, as well as impulsive and/or hyperactive behavior in two or more settings (Puper-Quakil, Ramoz, Lepagnolbestel, Gorwood, & Simonneau, 2011). The diagnostic criteria for ADHD are described in the Diagnostic and Statistical Manual of Mental Disorders Fifth Edition (DSM-5) (see Appendix A). The Vanderbilt Attention-deficit/Hyperactivity Rating Scale – Parent and Teacher Assessment forms (National Institute for Children's Health Quality [NICHQ], 2002) are among the most frequently used diagnostic tools, since the questions on the Vanderbilt Rating Scale describe behaviors that correspond to the DSM-5 diagnostic criteria for ADHD and establish their presence or absence in two or more settings (American Psychiatric Association [APA], 2013). Additional questions screen for other potential disorders that may cause the patient's symptoms, and the scoring guidelines help providers to determine whether the behaviors on the scale meet diagnostic criteria for ADHD.

The American Academy of Pediatrics (AAP) (2011) recommends prescribing stimulant medication and/or behavioral therapy, with a combination of medication and behavioral therapy as the preferred treatment. Unfortunately, the limited number of pediatric behavioral therapists, families' inability to absorb out-of-pocket expenses, and parents' difficulty taking time off work preclude

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behavioral therapy as a viable treatment option for many families. The goal of treatment of ADHD

established by the AAP (2011) is remission of ADHD behavioral symptoms, which the AAP defined as a

50% or greater reduction of symptoms and elimination of impairment (Perrin et al., 2011). Response to

treatment, with respect to frequency of symptoms, extent of impairment, and severity of medication side

effects, is assessed by the children's parents, who report their observations to their children's healthcare

providers. Unless the physical assessments are notably different or children are suffering ADHD

medication side effects at the time of their follow-up visits, the children's experiences of treatment may

not be a significant factor in treatment planning.

Problems with Standard Treatment

Pharmacological treatment of ADHD is an imprecise process that may require a series of

medication trials before treatment is therapeutic. The ADHD information webpage on the CDC website

(2017) cautions parents that children respond differently and the medication that works for one child may

not work for another child. The CDC advises parents to have patience, as their providers may need to try

several medications and different dosages before finding one that works for their child. The American

Academy of Child and Adolescent Psychiatry (AACAP) (2011) ADHD Treatment Algorithm presumes

as facts that only 41% of children will respond well to the first stimulant medication prescribed for

ADHD; another 44% of children will respond better to another stimulant in a different class. The

remaining 15% will not respond to a stimulant and should be prescribed a non-stimulant such as:

amoxetine, guanfacine XR, or clonidine, in that order (AAP, 2011). Although eventually 75-80% of

children with ADHD will tolerate and benefit from medication for ADHD, noncompliance rates are high

(AAP, 2011). Intolerable medication side effects are the most frequently cited reason for discontinuation

of ADHD pharmacotherapy (Cormier, 2012; Demidovich, Kolko, Bukstein, & Hart, 2011; Sitholey,

Agarwal, & Chamoli, 2011; Wietecha et al., 2013).

Risks of Not Treating ADHD

Undiagnosed and untreated ADHD substantially increases a child's risk for numerous undesirable

behavioral, health, and social outcomes over the lifespan (CDC, 2015). Almost half of children with ADHD are suspended from school once, and 80 to 90% are significantly behind in school by fourth grade (Johnson-Verwayne, 2015). Dalsgaard et al. (2015) found that, after adjusting for confounders, individuals who were diagnosed with ADHD at or after the age of 18 were four times as likely to die prematurely, which is consistent with the AAP (2011) report that children with ADHD are twice as likely as their neurotypical peers to die in childhood from unintentional pedestrian injuries. Epidemiological studies indicate that 75% of children with ADHD will develop a co-morbid psychiatric condition in their lifetimes (Barkley, 2006; Faraone & Kunwar, 2018).

Fortunately, ADHD is amenable to treatment. Adherence to pharmacologic therapy is associated with significant reduction in childhood accidents, motor vehicle accidents, and all substance abuse disorders among children and adolescents with ADHD (Biederman, 2003). The risk of dying before the age of 18 years in an unintentional pedestrian accident was reduced by 50-80% when children with ADHD consistently took stimulant medication to treat ADHD (AAP, 2011). Dalsgaard et al. (2015) found that diagnosis of ADHD by age six decreased the risk of premature death by 50%. Children diagnosed with ADHD who took medication achieved math scores that averaged 2.9 points higher and reading scores that were 5.4 points higher than children with ADHD who did not take medication (Scheffler et al., 2009). These scores represent learning gains of approximately 20% of a school year in math and 33% of a school year in reading (Scheffler et al., 2009).

Although ADHD is a chronic health disorder, it is not treated as the classic chronic health disorders such as diabetes, hypertension, or asthma. Healthcare providers do not typically assess children's risk of developing sequelae to ADHD, consider the impact of treatment on quality of life, or initiate care pathways aimed at reducing risk factors for known comorbidities. Treatment of ADHD in school-aged children requires long-term adherence to pharmacotherapies to reduce impairment, the development of psychiatric comorbidities (NIMH, 2015), and numerous other undesirable sequelae (Barkley, 2006; Dalsgaard et al., 2015; Faraone & Kunwar, 2018).

Social Context

Widespread public suspicion that providers are over-diagnosing ADHD and medicating children draws attention from the mainstream media with little rebuttal from the medical community. Social critics credit passage of the "No Child Left Behind Act" in 2002, which implemented national performance-based educational funding, as the greatest contributor to the soaring rates of ADHD diagnoses among school-aged children in the United States. Dr. Hinshaw and his colleagues at the University of California (2011) examined data from the National Survey of Children's Health from 2003-2007 and found that in the 20 states that did not have performance-based educational funding prior to 2002, diagnosis of ADHD increased 56% among children whose median household incomes were within 200% of the federal poverty level, compared to 3% in middle-class children, and 19% in children with the same socioeconomic status in other states (Novotney, 2014).

Performance-based educational funding encourages schools to ensure that students perform well on standardized tests. The scores of children diagnosed with ADHD are not counted in the school averages. Further, since ADHD is classified as a learning disability, schools with large populations of children with ADHD receive additional funding for accommodations such as smaller classes to provide more individualized attention. Dr. Hinshaw and his colleagues (2011) point out that children in North Carolina, one of the first states to implement performance-based educational funding, are five times more likely to be diagnosed with ADHD than children in California, where performance-based policy was more recently implemented (Novotney, 2014).

Health care providers in North Carolina may rightfully insist that they are following the practice guidelines (AAP, 2011), that multiple cultural factors account for the discrepancies in diagnosis rates, and point out that North Carolina's children are also more likely to be vaccinated (CDC, 2014), yet the air is not entirely cleared. Whatever truths underlie the geographically disproportionate rates of diagnoses, the media draws concerned attention to our system of care for children with ADHD, which is plagued with inadequacies. Attempting to address the inadequacies of the system using the same practices that created

the dysfunction only sustains it. To ensure that care for children with ADHD is truly patient-centered and health-promoting, new practice standards must be implemented, starting with standardization to ensure that consistent, comprehensive assessments are performed every visit and that patient-parent goals and patient-reported outcomes are included in treatment planning (Frankel, Haraden, Federico, & Lenoci-Edwards, 2017).

Problem Statement

Children with ADHD are at significant risk for developing co-morbid psychiatric disorders by early adulthood (Barkley, 2006). The literature consistently affirms that psychosocial resilience in childhood is one of the strongest predictors of good mental health (Perese, 2012). Wide variability in response to ADHD medications creates treatment challenges for healthcare providers, and insufficient information is available to assist providers with selection of the most effective medication and dose for individual patients. The trial-and-error method of treating ADHD results in high rates of ADHD medication side effects, inefficacy, and poor quality of life (Boorady, 2015). Treatment response assessments centered on discussions of the child's behavior may decrease self-esteem, hence decrease resilience and increase the already substantial risk for development of psychiatric behavioral health comorbidities. Healthcare providers are challenged to design and deliver treatment that alleviates an individual's symptoms of ADHD, improves quality of life, and promotes resilience.

Local Problem

While successful treatment of ADHD increases a child's resilience, persistent side effects of ADHD medication can *decrease* resilience by increasing anxiety or causing over-focused fixation, which inhibits social-emotional engagement and development. At the practice level, the gap between desired outcomes and actual outcomes is consistent with the national statistics that describe a wide variability of responses to standard treatments for ADHD among school-aged children. While most children with ADHD will eventually achieve symptom remission with pharmacologic treatment and report only mild medication side effects, paradoxical reactions, in which the medications exacerbate problems, are not

uncommon. Further, a significant number of children exhibit a "partial response" after multiple dosing adjustments and medication changes. Their parents report that behavioral symptoms and performance have improved significantly, removing threats of school suspension and failing grades, but symptomatic behaviors and medication side effects persist. Children with a partial response often present as anxious, agitated, or hyper-focused, with flattened affect, and parents will typically report moderate appetite loss, irritability, and insomnia. According to the AAP guidelines (2011), treatment may be considered successful if the patient's symptoms are reduced and he or she experiences no impairment. Yet, a flattened affect, anxiety, and decreased social engagement (NIMH MTA, 1999), when experienced nearly every day, may erode a child's sense of self-efficacy, stunt social-emotional development, and ultimately decrease a child's psychosocial resilience. In summary, these subtle side effects ultimately undermine the child's best defense against co-morbid disorders (Perese, 2012).

The Institute for Healthcare Improvement (IHI) recommends measuring current outcomes and establishing baseline values prior to implementing a change in treatment (Frankel et al., 2017). At the study site for this project, documentation in the patient charts regarding behavioral symptom responses and ADHD medication side effects were frequently vague. Use of the Vanderbilt Follow-up forms was inconsistent. An initial chart review revealed that as of November 1, 2017, only 49% of the patient charts in the target population contained both a Vanderbilt Rating Scales and Vanderbilt Follow-up form. When parents were called to schedule a follow-up appointment, 9 of the 57 stated that the child no longer took medication for ADHD.

Pharmacogenomic Testing

Pharmacogenomic tests may help healthcare providers select the most tolerable and efficacious ADHD medications for patients based on their individual genetic profiles (Assurex Health, 2012). The tests analyze genes involved in the metabolism and pharmacokinetics of ADHD medications by identifying genotypes and analyzing variants that affect a patient's ability to tolerate or respond as expected to medications (Assurex Health, 2012; Chou et al., 2000; de Leon, 2009). Using a complex

software algorithm, the tests predict which medications are likely to be metabolized normally and which are

likely to cause side effects, have reduced efficacy, or be metabolized at an exceptionally slow or rapid rate

(Assurex Health, 2012; Washington State Health Care Authority [WA HCA], 2016). They analyze 52

psychotropic medications, including almost all FDA-approved medications to treat ADHD (FDA, 2016), as

well as medications to treat depression, anxiety, psychotic disorders, substance use disorder, and analgesics

(Assurex Health, 2012; Hoak, 2016). The test is administered by the patient's healthcare provider, who

collects DNA from the patient in the office using a buccal swab and ships it overnight to the lab. Three

days later, the provider receives a computerized report that can guide their treatment plan (Carlat, 2015).

Pharmacogenomic tests for psychiatric medication prescribed to children are FDA-approved and

available for routine use in primary care. However, the literature indicates that the benefits of routine

pharmacogenomic testing vary dramatically among different patient populations, despite being used as a

decision support tool for treatment of the same diagnosis (Peterson, Dieperink, Ferguson, Anderson, &

Hefland, 2016).

Significance to Healthcare

The quality improvement project discussed herein is unique in many respects. It implements a

comprehensive bundle of practice changes that together furnish providers with patient-specific

information to inform treatment planning for children with ADHD. Implementation of quality-of-life

assessments inserts this issue, with its implications for psychosocial resilience, as a treatment outcome

that has not previously been stipulated as part of the standard care for children with ADHD. This fulfills

the World Health Organization's (2001) recommendation that treatment goals should include patient-

reported outcomes. Further, it is the first quality improvement project to assess the effects of

pharmacogenomic testing for psychotropic medications on quality of life. Identifying and avoiding

medications that are likely to be ineffective and/or cause side effects by identifying metabolic variants has

improved treatment outcomes and the quality of care for children with ADHD (Tan-kam, Suthisisang,

Limsila, Puangpetch, & Sukasem, 2013; Smith, Sharp, Manzardo, & Butler, 2015; Stein & McGough,

2008; Benitez et al., 2015). Several studies indicate that pharmacogenomic testing provides a moderate cost benefit by avoiding costly adverse drug reactions (Celerian Group Services Administrators [CSG], 2014; Singh, 2015; Winner et al., 2015). Assessing quality of life allows providers to identify children at greatest risk and facilitate early intervention, which has proven effective at reducing the risk of developing psychiatric comorbidities (Tolan & Dodge, 2005). Thus, this QI implementation promises to fulfill the "triple aim" of healthcare innovations: improving health outcomes, enhancing experiences of care, and controlling or reducing costs of care (Berwick, Nolan, & Whittington, 2003).

Purpose

The purpose of this project is to improve the quality of life and treatment outcomes for school-aged children with ADHD, and to reduce their risk of developing a psychiatric comorbidity, by designing, implementing, and evaluating a comprehensive bundle of practice changes: (a) standardized comprehensive and specific assessments to inform treatment planning, (b) routine pharmacogenomic testing to decrease side effects and improve efficacy, and (c) assessing quality of life as a goal of treatment.

Clinical Question

Will the acquisition of more patient-specific information, through pharmacogenomic testing, standardized comprehensive follow-up forms, and quality-of-life assessments, improve treatment outcomes, experiences of care, and quality of life, for school-aged children with ADHD at the study site?

CHAPTER 2: LITERATURE REVIEW

Literature Search

A literature search was conducted using PubMed, CINAHL, Embase, the Cochrane Library, American Psychiatric Association, and JAMA evidence databases, UptoDate, and Google Scholar, using the terms (in CINAHL) "attention deficit hyperactivity disorder" OR "ADHD" AND "pharmacogenomic test" OR "gene testing" OR "combinatorial gene testing" OR "GeneSight" and using the terms "attention deficit hyperactivity disorder pharmacogenomic test" and "ADHD gene test" in the others. Inclusion criteria included: English language; published after January 1, 2005; covering children, adolescents, and/or adults; and full text available. Exclusion criteria were: articles published before 2005; language other than English; abstract only; covering infants and neonates. The literature search was conducted to evaluate the best available evidence about the impact of pharmacogenomic testing on clinical outcomes of children with ADHD and included evidence of the effects of pharmacogenomic testing on outcomes of all psychiatric patients, as well as the impact of pharmacogenomic testing on healthcare costs for patients with psychiatric disorders. A total of 106 articles was retrieved, which was reduced to 79 after duplicates were removed. After eliminating scientific articles about single genes and medications, 32 articles remained and were reviewed.

The following sections will be presented and discussed as part of the literature review: (a) Prevalence; (b) Advances in Understanding of ADHD; (c) Pharmacogenomic Testing: Validity; (d) Pharmacogenomic Testing: Clinical Utility; (e) Generalizability of Depression Studies; (f) Known Risks; (g) Quality of Life; (h) Gaps in the Current Literature.

Prevalence

ADHD is one of the most frequently diagnosed pediatric disorders, and its prevalence continues to rise, increasing approximately 5% a year since 2006 (CDC, 2015; Holland & Riley, 2014). Children

from households with incomes less than 200% of the federal poverty level are more than twice as likely to be diagnosed with ADHD as children from households with higher median household incomes. Prevalence of ADHD is higher in the South than in other geographic regions of the United States (Novotney, 2014). School-aged boys (13.2%) are more than twice as likely as school-aged girls (5.6%) to be diagnosed with ADHD (CDC, 2015). Numerous theories, including the earlier maturity of girls (Asherson, Manor, & Huss, 2014), gender-biased wording, and the predominance of externalized behaviors described in ADHD symptom rating scales (Mahone, 2012), have been proposed as explanations for the gender disparity of ADHD diagnoses, but the persistent profound difference in prevalence among genders remains an enigma (ADHD Institute, 2016). Despite an increased prevalence of poverty among minority groups nationally, children from racial minority groups are less likely to be diagnosed with ADHD and less likely to be taking medication for ADHD (Morgan, Staff, Hillemeier, Farkas, & Maczuga, 2013). Compared to Caucasian children, African American children are 31% less likely to be diagnosed with ADHD (95% confidence interval [CI]: 60%-76%), although the gap is closing (CDC, 2014). Hispanic children are 50% less likely (95% CI: 34%-62%), and Asian and Native American children are 64% less likely (95% CI: 26%-61%) to be diagnosed with ADHD (Morgan et al., 2013).

Advances in Understanding of ADHD

Since the AAP guidelines were published in 2011, science has advanced our understanding of ADHD. In the DSM-5, the American Psychiatric Association (APA) reclassified ADHD as a neurodevelopmental disorder, as opposed to the DSM- IV classification as a disruptive behavioral disorder (APA, 2013). The DSM-5 classification reflects a growing body of scientific evidence that indicates ADHD has specific pathophysiological and neurochemical etiologies (Puper-Quakil et al., 2011). Brain mapping studies indicate that the pathogenesis of ADHD is widespread, and dysfunction occurs in multiple locations, including the frontal-parietal-cortical pathways, corpus callosum, anterior cingulate cortex, and cerebellum. These areas are responsible for functions such as cognitive processing,

attention, motor control, executive functions, response inhibition, reward, and motivation (Uneri, Senses-Dinc, & Goker, 2015).

Brain-mapping analysis indicates that ADHD is not a uniform disorder. While executive function deficits etiologically based in the frontal and pre-frontal cortex comprise the most common foci of ADHD (Kessler, 2017), there are at least seven subtypes of ADHD with varied functional deficits and presentations resulting from different etiologic foci. Treatment of the subtypes of ADHD is aimed at symptoms and does not always include a stimulant as first-line therapy (Amen, 2017). The discovery of sub-types compels the use of more comprehensive assessments and follow-up to treat appropriately. If a provider does not recognize a distinct subtype of ADHD, but assesses that the patient is failing to respond as expected to a medication that pharmacogenomic test results indicate as metabolically compatible, the test results may—indeed, should— expedite a reassessment of the disorder and a change in the treatment plan rather than the usual practice of prescribing a stimulant medication from a different class (Perrin et al., 2011).

Pharmacogenomic Testing

Validity. The validity of pharmacogenomic testing for ADHD medication selection is well-supported by a large body of scientific evidence that identifies the functions of genetic variants involved in the metabolism of psychotropic medications and allows testing to accurately match these genotypes with metabolic phenotypes (Bonvincini et al., 2016; Benitez, Jablonski, Allen, & Winner, 2015; Contini et al., 2013). Numerous studies confirm that pharmacogenomic markers accurately predict responses to the most frequently prescribed ADHD medications (Mrazek, 2009; Contini et al., 2013; Kim et al., 2013). More than 6,700 articles in the Pub Med database describe studies of gene variants related to the metabolism of ADHD medications. All pharmacogenomic tests for psychotropic medications identify variants of genes that encode the cytochrome (CYP) enzymes, which metabolize 70% of all psychotropic medications, including medications prescribed to treat ADHD: methylphenidate (Patel & Barzman, 2013; Contini et al., 2013) and amoxetine (Durham, 2014; Smith et al., 2014).

Clinical Utility. Evidence of the impact of pharmacogenomic testing for medication selection in treating ADHD is derived from smaller, open-label studies (Howland et al., 2014). Brennan et al. (2015) conducted a naturalistic clinical trial of the utility of pharmacogenomic testing for various psychiatric medications, including some used for treating ADHD, among 85 primary care patients. They concluded that all patients who received pharmacogenomic testing exhibited clinically significant improvement at three months. Stein & McGough (2008) reviewed several studies and concluded that pharmacogenomic testing for ADHD medication selection improves clinical outcomes. Three peer-reviewed case studies validate the ability of pharmacogenomic tests to correctly predict responses to ADHD medications. Madan et al. (2015), Smith et al. (2015), and Tan-kam et al. (2013) report detailed case studies of children with severe, persistent ADHD symptoms. The children achieved significant symptom remission following pharmacogenomic testing for medication selection, in conjunction with medication changes and dosage adjustments that corresponded with the test results.

Generalizability of Depression Studies

Many of the genotype-phenotype variants that predict responses to antidepressants, such as the dopamine transporter, noradrenergic transporter, and CYP2D6 enzymes, also predict responses to ADHD medications (Mrazek, 2010). Clinical trials conducted by Breitenstein et al. in Germany (2014) and Singh (2015) in Canada indicate that pharmacogenomic-guided medication selection improved clinical outcomes for patients with a variety of psychiatric disorders. In Singh's (2015) double-blind randomized controlled trial (RCT) involving 148 patients, the pharmacogenomic-guided medication arm exhibited a 2.52 times greater rate of symptom remission ($p < 0.0001$). Pharmacogenomic testing is associated with significantly increased rates of remission from major depressive disorder in several RCTs (Altar et al., 2015; Mrazek, 2011; Hall-Flavin et al., 2011; Hall-Flavin et al., 2012; Winner et al., 2013). A meta-analysis prepared for the Centers for Medicare and Medicaid Services (CMS) found that pharmacogenomic testing for antidepressants was associated with a 73% greater improvement in depressive symptoms ($p = 0.004$) (CSG, 2014). Among 165 patients with mood disorders enrolled in an open-label clinical trial at the Mayo

Clinic, the cohort who received medications based on pharmacogenomic testing results achieved a significantly higher rate of remission at eight weeks (40.1% vs. 19.5%, p < 0.001) (Hall-Flavin et al., 2013). When Winner (2013) offered pharmacogenomic testing to patients in the control group after the study period, he found that patients who had been taking antidepressants that the pharmacogenomic test later identified as having a high probability of gene-drug interactions had reported almost no improvement (0.8%) after 10 weeks of treatment. These findings are consistent with findings by Altar et al. (2015), Breitenstein et al. (2014), and Brennan et al. (2015).

Known Risks

Systematic reviews compiling evidence of the effects of pharmacogenomic testing for psychotropic medications, including for ADHD, were performed by the U. S. Department of Veterans Affairs (VA) and the Washington State Health Care Authority (WA HCA), both of whom determined that pharmacogenomic testing posed no risk of harm (Peterson et al., 2016; WA HCA, 2016). The only potential risk of using pharmacogenomic tests for psychotropic medication selection that was identified in the literature was the potential for insurance discrimination based on genetic profile (CSG, 2014). Millennium Health and the CMS also determined that the risk of pharmacogenomic testing is negligible (CSG, 2014; Gupta, Hassainzada, & Del Tredici, 2016). Altman (2011) asserts that the evidence of non-inferiority is sufficient for a clinical implementation trial of an intervention with no known risk.

In summary, the true value of routine pharmacogenomic testing prior to prescribing medication for ADHD is not fully known. However, the potential to positively affect outcomes, as documented above, coupled with no known risk of harm, provides a compelling reason to implement routine pharmacogenomic testing prior to prescribing medication to children with ADHD, with continuation and adoption contingent upon the evaluation finding clear evidence of benefit (Gillam & Siriwardena, 2014; Orr, 2003).

Quality of Life

The World Health Organization (WHO) International Classification of Functioning, Disability and Health (2001) recommended that health outcomes be considered in terms of the biopsychosocial

model and should include patient-reported health outcomes as goals of treatment. Quality of life is a patient-reported outcome that is becoming increasingly prominent. The WHO (2001) defines "quality of life" as an individual's perception of their actual level of functionality compared to their perception of their optimal level of functionality with respect to physical and emotional health, family and social relationships, work, and self-concept (Danckaerts et al., 2010). Research in the past decade has confirmed the positive association between quality of life and health outcomes in multiple populations and at all levels of care (Danckaerts et al., 2010; WHO, 2001).

The quality of life reported by children with ADHD is persistently poor, sharing common themes of self-perceived social ineptitude, with consistently low scores in the areas of relationships with friends, family, and school and authority figures (Danckaerts et al., 2010). Vagin (2017) reports that by 12 years of age, children with ADHD hear approximately 20,000 more negative messages than their neurotypical peers. Parents of children with ADHD and children with ADHD report significantly poorer quality of life than children without chronic health disorders (Becker et al., 2011; Danckaerts et al., 2010). Danckaerts and colleagues (2010) found that children with ADHD rated their own quality of life as poorer than many children with chronic physical health disorders. The mean quality-of-life scores reported by children with ADHD were equivalent to the mean quality-of-life scores of children with cancer and cerebral palsy (Danckaerts et al., 2010). Becker et al. (2011) found that taking medication to treat ADHD increased the patient-reported KINDL Quality-of-Life (QoL) scores from a mean of 63.8, reported by children with ADHD who did not take medication, to a mean of 67.2 for children with ADHD who took two doses of methylphenidate a day. Taking methylphenidate for ADHD cut the gap between the quality-of-life scores of children with ADHD and children without ADHD by 50%.

Gaps in the Current Literature

Pharmacogenomic studies typically focus on treatment efficacy and cost-effectiveness, but so far as can be determined, this is the first quality improvement study to evaluate the effect of routine pharmacogenomic testing on patient experiences of care (incidence and severity of medication side

effects and quality of life) as primary outcomes. Since pharmacogenomic testing reliably predicts abnormal metabolism and poor responses to medications but cannot determine the most appropriate choice of medication among tolerable choices, measuring the effect of these choices on patient experiences of side effects and quality of life is possibly the most appropriate outcome measure in terms of improving patient experiences of treatment (Benitez, Jablonski, Allen, & Winner, 2015).

Although combinatorial pharmacogenomic tests have proven to be more beneficial than single-gene tests (Winner & Dechario, 2015), it is unknown whether the commercially available tests are all equally effective at identifying variants that affect metabolism of medications to treat ADHD or if some tests are superior with respect to predicting side effects, variations in metabolic rates, and/or inefficacy of medications that are approved to treat ADHD in children. Each pharmacogenomic test is patented, therefore each uses unique algorithms, tests different genes, and includes different medications in its reports (Assurex Health, 2012). All pharmacogenomic tests include genes that code for the CYP enzymes that metabolize most medications (Durham, 2014). ADHD results are primarily based on the analysis of three genes: CYP2D6, a gene that encodes enzymes that metabolize ADHD medication (NIH, 2015), COMT, a gene involved in the methylation and degradation of dopamine, epinephrine, and norepinephrine (Human Genes Database, 2015), and ADRA2A, a gene that encodes receptors responsible for neurotransmitter release (NIH, 2015).

Since studies report risk values in aggregate, without considering the variability among responses to ADHD treatment, the true value of the risk reduction among children who achieve ADHD symptom remission with a well-tolerated medication is unknown. Unfortunately, no studies compare the quality of life of children who are treated effectively for ADHD with a tolerable medication, and the quality of life reported by their neurotypical peers (Dalsgaard et al., 2015; Biederman, 2003; Charach et al., 2011). Whether reducing ADHD medication side effects and expediting symptom remission significantly improves the quality of life for children with ADHD is also unknown.

The following chapter presents an analysis of resilience theory, which provides the conceptual framework for this quality improvement project.

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CHAPTER 3: CONCEPTUAL AND THEORETICAL FRAMEWORK

Resilience Theory

The conceptual framework of this project is resilience theory. "Resilience" describes a quality that enables an individual not only to successfully navigate through adversity, significant hardship, and/or formidable challenges, but to transcend them and ultimately thrive (Perese, 2012). Conceptually, resilience theory includes an antecedent of adversity and a consequence of a positive outcome (Fletcher & Sarkar, 2013). The theory of resilience stipulates that the presence of protective attributes increases adaptive functionality and thereby increases one's ability overcome challenges (Polk, 1997). Although the factors contributing to resilience are numerous, all resilience models describe and predict outcomes based upon the balance between an individual's "risk factors" and "protective factors" (Perese, 2012). Resilience theory describes and explains factors that affect a child's psyche and predicts the effects of the factors, individually and combined, on mental health outcomes (Perese, 2012). The low level of psychosocial resilience among children with ADHD is considered both a cause and a consequence of ADHD (Regalla, Guilherme, Aguilera, Serra-Pinheiro, & Mattos, 2015). Assessments of resilience are always subjective (Santos, 2016). Nevertheless, resilience in childhood remains one of the strongest predictors of mental health in young adults (Perese, 2012; Masten, 2014), which makes resilience particularly relevant to healthcare providers who treat children with ADHD.

The concept of resilience originated in the work of Werner, Bierman & French (1971) in the context of a longitudinal study about children on the Hawaiian island of Kauai. Since World War II, resilience research has evolved primarily in the context of child development studies and the risk for the development of mental health disorders (Masten, 2014). Garmezy (1971), a psychologist, studied children at risk for the development of psychopathology and described the concept of resilience as "protective factors" that helped children to thrive despite the presence of significant risks. The tests of his model

proved not only descriptive and explanatory, but also predictive of outcomes. It was this formulation of the idea of resilience that evolved into resilience theory.

The resilience model is comprised of three dynamic components, internal forces, external forces, and circumstances (Fleming & Ledogar, 2008; Perese, 2012), that cumulatively predict an individual's ability to transcend specific challenges. Enhancing hallmark qualities that contribute to resilience, such as self-discipline and self-esteem, increases one's resiliency and supports healing and positive health outcomes (Perese, 2012). Cultivating resilience in school-aged children who are at risk addresses the "internal forces" of a child's adaptive mechanisms, such as emotional regulation, "external forces" such as recommendations for modification of the home and/or school environments, and "circumstances," such as helping children to create narratives that allow them to make sense of their experiences and process aspects of their challenges (Perese, 2012; Muller, Ward, Winefield, Tsourtos, & Lawn, 2009). Some factors of resilience among children are constant throughout the lifespan: strong parental attachments; warm, positive relationships with caregivers; and intelligence (Sapienza & Masten, 2011). Resilience in school-aged children is primarily influenced by their relationships with their parents, but is also significantly influenced by the quality of their relationships with peers, scholastic engagement, and their self-concept with respect to social competence, self-efficacy, and capacity for self-regulation (Windle, Bennett, & Noyes, 2011). Social and emotional skills programs for children (Tolan & Dodge, 2005) and positive parenting education programs (Dvorsky & Langberg, 2016) are early interventions that have increased children's quality-of-life scores and reduced the likelihood of developing psychiatric disorders by early adulthood.

Sapienza and Masten (2011) discourage "diagnosing" individuals as resilient. Resilience is dynamic (Sapienza and Masten, 2011). It can only be gauged in the moment of a challenge as a ratio: demands of the situation vis-à-vis ability to adapt to or transcend the situation. The scientific literature is consistent in its appraisals of the increased health and social risks conferred by a diagnosis of ADHD, while a growing number of people tout ADHD as an advantage rather than a handicap. In an article

entitled, "ADHD: The Entrepreneur's Superpower," Archer (2017) reports that several successful entrepreneurs credit their ADHD for the traits that they view as fundamental to their success: creativity, willingness to take risks, exceptional energy, and stamina. Masten (2014) points to the "easy baby" and "fussy baby" theory, which long held that babies with easy temperaments were more adaptive and resilient. Yet amidst the adversity of war and drought in Africa, it was the fussy babies who survived.

Resilience theory is well-aligned with the overarching goals of primary care: promotion of long-term physical and mental health by increasing protective factors, as well as identifying and decreasing risk factors of individuals (Perese, 2012). Resilience and perceived quality of life are reciprocal psychological states and consistently positively associated (Danckaerts et al., 2010). Although children's risk for development of psychiatric/behavioral health disorders is typically predicted based on measurements of resilience rather than quality of life, the KINDL Quality-of-Life Questionnaire has been validated as a reliable instrument with which to measure psychosocial resilience in school-aged children (Danckaerts et al., 2010). In this study, the KINDL Questionnaire was selected in conjunction with the practice owner and lead clinician at the clinical site. Approaching the factors of resilience by assessing quality of life empowers children to articulate their experiences of treatment and bolsters their self-esteem by indicating that their emotional responses to situations in their lives are important (Ravens-Sieber, Erhart, Willie, & Bullinger, 2008).

In the context of the resilience model, improving outcomes of school-aged children with ADHD necessitated the incorporation of long-term treatment goals focused on improving quality of life. Quality of life among children with ADHD (Becker et al., 2011) was associated with social and emotional impairments as well as academic impairments that affected self-esteem. ADHD medication side effects can improve one area, such as academic competence, but cause even greater deficits in another, such as social engagement, that may be a bigger factor in resilience. Improving children's quality of life, and subsequently, increasing their resilience, began with improving the process of selecting the most efficacious and tolerable medications to reduce their symptoms of ADHD, which in turn indicated the

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need for standardized assessment documentation. Resilience theory thus led to quality-of-life

assessments and the incorporation of patient-reported increase in quality of life as a goal of ADHD

treatment in children. Chapter 4 describes the design, implementation and evaluation of this QI project.

CHAPTER 4: METHODS

The framework for the methodology of this quality improvement project was the Institute for

Healthcare Improvement's Model for Improvement, described in the IHI's publication, "Framework for

Safe, Reliable, Effective Care" (Frankel et al., 2017). Quality improvement (QI) is defined as the

"systematic and continuous actions that lead to measurable improvement in health care services and the

health of targeted patient groups" (Health Resources and Services Administration [HRSA], 2011, p. 1).

The IHI recommends using the model to guide QI implementation processes (Frankel et al., 2017). It

facilitates vetting of QI outcomes as well as the adaptations necessary to successfully integrate an

improvement. This chapter presents the methodology used to evaluate the study and its application to the

project in the following sections: (a) Setting; (b) Study Participants; (c) Instruments;

(d) Design; (e) Data Analysis; (f) Ethical Considerations; and (g) Implementation, Procedures, &

Evaluation Methods.

Setting

The implementation site is a privately-owned family medicine practice located in a rural county

of north-central North Carolina, designated as a critical healthcare shortage area (HRSA, 2017).

Not a single pediatric psychiatrist or psychiatric mental health nurse practitioner who treats children

practices in the county. In 2016, providers at the clinical site (three physicians and two nurse

practitioners) treated a total of 5,429 patients, 879 of whom were children aged 6 to 12 years, of which

112 were children who were prescribed medication for ADHD.

The practice serves as a clinical training site for the UNC at Chapel Hill Schools of Nursing and

Medicine; in 2017, it was accredited as a primary care medical home by the Joint Commission for

Accreditation, Health Care, & Certification (JACHO). Continuous quality improvement (QI) and

individualization of care plans are central values of the primary care medical home model (Patient-

Centered Primary Care Collaborative, 2015). Clinicians and providers at the site were inexperienced with quality improvement projects; however, the practice's management team had undertaken structured quality improvement projects in the process of becoming a medical home and was familiar with some of the QI processes, which facilitated implementation of the data tracking and documentation improvements undertaken for this study. A collegial, non-competitive work culture at the clinical site increased teamwork and cooperation, which supported the success of the change (Damschroder et al., 2009).

Study Participants

A total of 112 children, aged 6 to 12 years old, had been diagnosed with ADHD and/or prescribed medication for ADHD by providers at the practice within the previous year.

Inclusion Criteria. Inclusion in the study necessitated that the child's initial symptoms were documented on Vanderbilt Rating Scales – Parent and Teacher Assessment forms (see Appendix C) and filed in the electronic medical record (EMR). The initial assessment needed to clearly indicate that the child met diagnostic criteria for ADHD in both the home and school settings. At least one post-treatment assessment of the child's symptoms needed to be documented on a Vanderbilt Follow-up form (see Appendix D) and available in the EMR.

Exclusion Criteria. Project exclusion criteria were incomplete documentation of the initial or follow-up ADHD visits: either the initial Vanderbilt Rating Scale – Parent and Teacher Assessment forms were missing or no Vanderbilt Follow-Up forms were filed in the patient's chart. Patients were also excluded if the initial Vanderbilt Rating Scales were more than four years old. Patients diagnosed with medical or psychiatric comorbidities other than seasonal allergies, well-controlled asthma, or well-controlled gastroesophageal reflux (GERD) were excluded from the sample.

Sample Size. The chart review sample included two groups composed of 26 children each. This satisfied the requirement that each group have a minimum of 25 patients to confer significance to a statistical test of variance. The IHI (2012) recommends that QI evaluations include a minimum of 10 patients, preferably more than 20, to ensure the results are not coincidental.

Instruments

The following instruments were used to measure outcomes:

The Vanderbilt Attention-deficit/Hyperactivity Assessment Rating Scale, which includes the Parent and Teacher Assessment forms (NICHQ, 2002) (See Appendix C) is the most frequently used instrument for screening, assessing, and measuring symptoms of ADHD in school-aged children. The NICHQ Vanderbilt Assessment Rating Scales 2002 version is available to download and distribute in the public domain, provided that NICHQ is credited. The first 18 questions of the Vanderbilt scales describe behavioral symptoms of ADHD that correspond to the DSM-5 diagnostic criteria for ADHD (APA, 2013). Additional questions screen for mood and conduct disorders that must be ruled out before diagnosing ADHD.

The Vanderbilt Follow-up form – parent respondent (NICHQ, 2002) corresponds to the Vanderbilt Rating Scales – Parent Assessment used for initial diagnosis. The follow-up form contains only the first 18 questions on the initial Vanderbilt Rating Scale, which correspond with the core behavioral symptoms of ADHD. The follow-up form also includes an ADHD medication side effects rating scale, which facilitates an efficient, yet comprehensive assessment of the patient's response to treatment and medication side effects. It can be used to measure change by comparing pre- and post-treatment behavioral symptom scores and is useful for monitoring responses over time.

The KINDL Quality-of-Life Questionnaire (KINDL.org, 2017) is a validated questionnaire for parents that evaluates the impact of chronic health disorders on a child's (aged 6-11years) quality of life (QOL). This questionnaire (see Appendix E) is comprised of 24 questions and uses a 5-point Likert scale (never, seldom, sometimes, often, all the time) with weighted responses. The questions assess perceptions of physical and emotional well-being, self-esteem, quality of familial and social relationships, school engagement, and competency (KINDL.org, 2017).

Design

Once a need for change is identified, the improvement model suggests that the project should be designed to answer three questions: what needs to change, how will we change it, and how will we know that the change is an improvement (Frankel et al., 2017)? The model emphasizes the importance of carefully planning the design of both the implementation and evaluation prior to implementing change. During the pre-implementation phase, the project's purpose, measured outcomes, measurement instruments, data collection methods, and analysis plan were determined for all three process changes to be implemented in the project: pharmacogenomic testing, standardized follow-up assessment documentation, and quality-of-life assessments. With the three essential questions answered and the project's components defined, the project was summarized in a table that confirms the logical alignment of the components (Frankel et al., 2017) to ensure that the final evaluation would answer the question: is the change an improvement?

The quality improvement bundle was implemented in three successive phases: (a) standardized ADHD follow-up assessments using the Vanderbilt Follow-up forms, (b) routine pharmacogenomic testing prior to prescribing medication for ADHD to children aged 6-12 years, and (c) administration of the KINDL Quality-of-Life Questionnaires. The changes were independently evaluated at the end of the study period to determine their impact on the quality of care, outcomes, and/or quality of life of the children treated for ADHD practice.

The IHI-based (2012) evaluation of the changes included implementing a tracking system that monitored compliance with the standardized documentation over time. A chart review was conducted to evaluate the effects of implementing routine pharmacogenomic testing prior to prescribing medication for ADHD, using patient experiences of treatment with respect to the number of moderate and severe ADHD medication side effects and the amount of behavioral change as the key areas of change. The quality of

life of children who are treated for ADHD at the clinical site was assessed by examining results of a

survey sent to the parents of the participants in the pharmacogenomics evaluation.

Table 1 summarizes the alignment of the outcomes measured, purpose of the project, methods of

measuring outcomes, data collection, and analysis of the QI evaluation.

Table 1

QI Evaluation: Alignment of Project Purpose, Outcome Measures, Methods, & Analysis

1st Outcome Measure	Definition	Alignment with Purpose	Alignment with Methods	How Data Was Collected	Analysis Plan
Number of ADHD medication side effects rated moderate and/or severe on the Vanderbilt Follow-up Form Medication Side Effects Rating Scale	Quantifies the incidence of ADHD medication side effects that are rated moderate or severe	The number of moderate and severe ADHD medication side effects indicates whether the patient's current ADHD medication is tolerable and if the side effects impair patient's functioning and or decrease quality of life. Goal: to determine whether pharmacogenomic testing prior to prescribing ADHD medication is associated with fewer moderate and severe ADHD medication side effects.	Pharmacogenomic testing (PGT) was offered to all parents of children aged 6-12 years who were prescribed medication to treat ADHD.	Parents reported the incidence of ADHD medication side effects on Vanderbilt ADHD Follow-up forms at each visit. Forms were reviewed and scored by nurses; scores were recorded in the patient's chart and in the EMR. A retrospective chart review of data from samples of children was extracted and evaluated in aggregate form.	Comparison of the mean number of moderate and severe ADHD medication side effects reported by parents of patients who had pharmacogenomic testing prior to being prescribed medication for ADHD to the mean number of such side effects reported by parents of patients who did not have pharmacogenomic testing.

2nd Outcome Measure	Definition	Alignment with Purpose	Alignment with Methods	How Data Was Collected	Analysis Plan
Change in the child's behavioral symptoms scores, determined by subtracting the behavioral symptoms score on the Vanderbilt Follow-Up forms from the behavioral symptom score on the initial Vanderbilt Rating Scale – Parent Assessment.	Change in symptoms assessment score indicated whether the medication was effectively reducing the impairment of ADHD symptoms. Efficacious response was a 50% reduction in symptoms and "no impairment" while taking medication for ADHD.	Improving treatment outcomes of children with ADHD meant ensuring that the medication was both efficacious and well tolerated. Assessing quality of life ensures that the patient experience of treatment and was also considered and that quality of life was also a goal.	Vanderbilt behavioral symptom assessments allowed monitoring of the patients' symptom responses to ADHD treatment to determine whether the treatment was effective as well as the areas in which it was not.	Parents reported behavioral symptoms using the Vanderbilt Follow-up forms at each ADHD follow up visit. Forms were reviewed and scored by nurses at check-in; scores were recorded in the patient's chart in the EMR. Retrospective chart review data from samples of children were evaluated.	Change in symptom scores were recorded for each patient and the scores of patients who had pharmacogenomic testing were compared to the scores of current patients who did not receive testing. The mean score was calculated for each group and compared to determine whether pharmacogenomic testing was associated with greater change in behavioral symptoms of ADHD.

3rd Outcome Measure	Definition	Alignment with Purpose	Alignment with Methods	How Data Was Collected	Analysis Plan
Scores on the parent-reported KINDL Quality-of-Life Questionnaire	Parental perceptions of their child's quality of life, determined by 24 questions describing the child's behaviors, which indicate the quality of parental relationships, physical and emotional wellbeing, relationships with friends, engagement in school, sense of competence, and self-efficacy.	Improving the quality of life for children with ADHD must consider not only the effect of medications on symptoms of ADHD but also on the individual's quality of life with respect to psychosocial and emotional experiences. Improved quality of life was measured by parental reports of their child's quality of life.	Improving the quality of life for children with ADHD involved improving the care processes to deliver care that was responsive to the patients' and parents' needs.	Study: The KINDL Quality-of-Life Questionnaire was mailed to parents of patients in the study groups, with a stamped envelope for anonymous return to the practice. Implementation: all parents of children aged 6-12 years, treated for ADHD were asked to complete a KINDL Quality-of-Life Questionnaire at least annually.	Scoring according to KINDL manual. Review of data, with comparison to benchmark values to determine if a child experienced poor quality of life and required further evaluation.

Data Analysis

Data was analyzed to evaluate each outcome. Retrospective chart review data was analyzed using a non-randomized control group design and basic descriptive statistics (mean, range, outliers) to compare outcomes of the two groups (Siriwanda, 2009; Frankel et al., 2017). Data was analyzed by calculating each quality-of-life score, per the formula in KINDL manual (see Figure 1), and comparing outcomes to the established benchmark data and by reviewing common themes (see Table 5).

Ethical Considerations

No identifiers from patient charts were recorded during the data collection. Only the doctoral student evaluator and practice managers know the identities of the patients who were included in the sample. Since the clinical site is a private practice, patient charts are stored on an electronic medical record (EMR) within a closed network system. The student and practice managers only accessed the EMR while physically present at the implementation site. Patients were assigned codes that were used to assign them to groups (see Table 3). The doctoral student's computer was assessed by the graduate school technical security supervisor; all data on the computer is encrypted and password protected. The study was approved by the Office of Human Research Ethics Institutional Review Board (IRB) of the University of North Carolina at Chapel Hill (17-2556).

Implementation and Evaluation Procedures

The three process changes of the quality improvement project were implemented in accordance with the IHI model for improvement (Frankel et al., 2017; Demming, 2011), although, unlike PDSA cycles, the changes were implemented universally. Standardized ADHD follow-up documentation was implemented practice-wide. All children with ADHD, aged 6-12 years, were expected to present with their parent for follow-up of ADHD treatment with a completed Vanderbilt Follow-up form. All such children who were either failing their current therapy or initiating therapy for ADHD were offered the opportunity to have pharmacogenomic testing prior to being prescribed medication for ADHD.

Phase 1: Implementation of the Vanderbilt Follow-up Form

Frankel et al. (2017) are adamant about the necessity of implementing standardized documentation of assessments, stating that to rely on the memory and altruism of providers results in mediocre care.

Implementation Procedure. The Vanderbilt Follow-up Parent Assessment forms were implemented as standard documentation for every follow-up visit. When patients presented for ADHD follow-up appointments, parents brought the completed Vanderbilt follow up form (NICHQ, 2002), which includes the same 18 questions, and rate their child's symptoms while on the medication, and report any ADHD medication side effects that their child has experienced since the last visit. During the intake evaluation, nurses review both the symptoms and medication side effects reported on the Vanderbilt Follow-up forms and record values in the electronic medical record (EMR). ADHD symptoms and medication side effects are quantified and documented. The patient's symptoms are quantified as the difference between the total symptom score on the initial Vanderbilt Rating Scale Parent Assessment form, and the total symptoms score on the Vanderbilt Follow-up Parent Assessment form. The following procedures were initiated to support the implementation process.

A. Vanderbilt Follow-up forms were mailed to the parents of all patients, aged 6-12 years, who were scheduled for follow-up appointments within the next two months, with an appointment reminder and a request to complete the form and bring it to their appointment.

B. To ensure consistent use, the office administrators maintained a supply of Vanderbilt Assessment Scales and Follow-up forms. The Vanderbilt Follow-up forms were saved on the shared drive, accessible to all staff when needed.

C. Upon check-out, the front desk staff provided parents with a Vanderbilt follow-up form. The receptionists asked parents to bring it to their next appointment.

D. When patients returned for follow-up, the front desk staff asked the parent if they had completed the Vanderbilt Follow-Up form. If they had not, the receptionist gave the parents a

Vanderbilt Follow-up form on a clipboard and asked them to fill it out and return it before they were taken back for assessment.

E. To ensure compliance with documentation, the practice manager performed a random chart audit of five charts, then tracked the documentation of all patient visits for follow-up treatment of ADHD of patients between the ages of 6 and 12 years.

Phase 2: Implementation of Routine Pharmacogenomic Testing

Pharmacogenomic testing was offered to all children with ADHD, aged 6-12 years, before being prescribed medication for ADHD. The implementation of pharmacogenomic testing in clinical practice was as described in the paragraph below. (See Appendix B for the QI implementation protocol.)

Implementation Procedure. Providers educated parents and patients about the pharmacogenomic test, its benefits and limitations, potential co-pays, and explained that medication would be prescribed after reviewing the results of the test. Nurses or providers obtained consent, then obtained a DNA sample using a buccal swab and packaged the sample. Front desk administrators copy the patient's insurance cards and sent the sample to the lab. Providers ordered the test and completed the pre-authorization form online. Three days later, test results were posted to the company portal, and the provider was notified that the results were available. Providers reviewed the results and selected a medication and starting dose that was most appropriate based on the information available, including family history, patient physical characteristics, severity and symptoms of ADHD, the patient's insurance, and the pharmacogenomic test results. Nurses contacted parents to inform them that the results had arrived and the provider had selected a medication and offered to leave the prescription at the front desk.

Modifications to Side Effect and Behavioral Symptom Scoring. During meetings, several providers determined that modifications to scoring the documentation were necessary. Mild side effects such as an occasional mild headache would not affect treatment planning and might not even have been side effects of the medication. The difference between moderate and severe were difficult to define.

Hence, only moderate and severe medication side effects were counted, and they were counted as single instances, without weighted scores.

Additionally, patients who screened positive for some of the mood or conduct disorder symptoms on the initial Vanderbilt Rating Scale may have appeared (inaccurately) to have greater symptom improvement than children who did not exhibit conduct or mood disorder symptoms, because the initial Vanderbilt Assessment score counted those behaviors in the total while the Vanderbilt Follow-up only considered items 1-18, the behavioral symptoms of ADHD. The difference in behavioral scores was therefore based only upon the difference in the score of items 1-18 on the initial Vanderbilt Rating Scale (parent) and the Vanderbilt Follow-up (parent) forms.

Evaluation Procedure. The number of ADHD medication side effects rated "moderate" and "severe" on each Vanderbilt follow-up form in the charts of patients in each sample group was recorded without identifiers in Excel. The change in behavioral symptom scores was also calculated for each patient, and recorded in the EMR. The difference in behavioral symptoms was calculated as the difference between the first 18 questions on the initial Vanderbilt Rating Scale – Parent Assessment and the Vanderbilt Follow-up forms. The means and range of each group were compared. Demographic data was collected to ensure similarity in age and gender mix of the study sample populations.

Implementation of the Quality-of-Life Questionnaire

Information in the initial KINDL Quality-of-Life Questionnaire survey, in which the identities of the respondents and children were unknown, indicated a need for further evaluation and referrals. This prompted the practice to implement the KINDL Quality-of-Life Questionnaire as an annual assessment for all children between the ages of 6-12 years with ADHD.

Implementation Procedure. Nurses provided the questionnaire to parents on a clipboard, to complete in the room during the review of the current complaint and health information. Once the KINDL Questionnaire had been reviewed and scored, providers placed a practice alert in the patient's hub and the note appeared in a yellow box, "2018 KINDL completed on [date]." If the score was within the standard

deviation of the normal range and no responses raised red flags, the questionnaire was filed in the chart. If the score was low or responses raised questions, the primary care providers assessed further and referred the child to a pediatric psychiatrist for further evaluation.

Implementation of the Quality-of-Life Survey

The quality-of-life survey assessed the quality of life of children with ADHD and the potential effect of pharmacogenomic testing on quality of life. The practice initially surveyed the quality of life of children with ADHD using the KINDL Quality-of-Life Questionnaire (KINDL.org, 2017; see Appendix D) by mailing it to 40 parents of children with ADHD, allowing parents to respond anonymously when returning the forms. Some parents called to learn their child's score and the interpretation of the score. This generated discussion about quality of life that proved valuable.

Survey Evaluation Procedure. The survey was returned by 18 of 40 parents. Upon receipt of the surveys, the quality-of-life score for each child was calculated according to the formula provided in the KINDL Quality-of-Life Questionnaire Manual (see Figure 1). Mean scores were calculated for each study group and for the study population. The mean scores of patients who had pharmacogenomic testing were compared to the scores of patients who did not have pharmacogenomic testing. Scores of the total population were compared to the baseline reference values of other school-aged children with ADHD, established by the OBSEER trial (see Table 3), and to the values of neurotypical school-aged children without chronic health disorders, established in the BELLA trial (see Table 3). Figure 1 presents the formula for calculating quality-of-life scores using the KINDL.

Figure 1. Formula for Calculating KINDL Quality-of-Life Scores

Sum score = sum of sub-scale items (4 questions)

Sub-scale score = sum of sub-scale items / number of sub-scale items (24)

Total sub-scale score = sum of 24 items/24

Transform to 100 = <u>sub-scale score – lowest possible score</u>
                                Possible range of raw score

Quotient X 100

Figure 1. Formula used to calculate individual scores of parent KINDL Quality-of-Life Questionnaires. (Ravens-Sieber, Erhart, Willie, & Bullinger, 2008, pp. 18-22).

Evaluation of the Quality of Care

The value of quality of care is subjective and measured in the context of individual experiences and expectations. The success of this project's efforts to improve quality of care was based on information provided by parents of patients in interviews following their child's follow-up visits for treatment of ADHD. Parents were informed of the quality improvement implementation and the study and asked to provide feedback about what was helpful as well as make suggestions for improvement. During staff meetings, providers and clinical staff at the implementation site also evaluated the impact of the interventions, which were considered in the final evaluation.

CHAPTER 5: RESULTS

The three practice improvements were fully implemented: 1) implementation of standardized comprehensive assessments of symptom response and ADHD medication side effects using the Vanderbilt Follow-up form, 2) routine pharmacogenomic testing for ADHD medication prescribed to children, and 3) annual quality-of-life assessments of children with ADHD using the KINDL Quality-of-Life Questionnaire. This report describes the outcomes as of December 1, 2017, although implementation at the clinical site is ongoing. The results of the quality improvement implementation evaluations are reported in accordance with the Squire 2.0 (2018) reporting guidelines for quality improvement projects.

Evaluation of Documentation Compliance

Between October 5, 2017, and December 1, 2017, documentation compliance improved. Initially, only 49% of the charts of current school-aged patients with ADHD contained both the Vanderbilt Rating Scales Parent and Teacher Assessments and the Vanderbilt Follow-up forms. However, based on the last audit, the clinic is incorporating the QI documentation model into their charting and clinical practices. On December 1, 2017, 77% of visits for ADHD in the past month contained documentation of the appropriate behavioral symptoms and/or medication side effects on Vanderbilt forms, which were scanned into the patient documents. Problems that persisted included: (a) no name on the form, which prevents administrators from filing the form into a patient's chart; (b) no date, which prevents the data from being useful since it cannot be related to a specific course of treatment; (c) inconsistent use of the ADHD follow-up visit template in the EMR; and (d) proper scoring of the Vanderbilt Follow-up forms. In-services were planned to review scoring and interpretation of the Vanderbilt Assessment Scales, the diagnostic criteria for ADHD, and the necessity for entering scores in the EMR using the template.

Providers' responses to the standardized documentation were unanimously positive. Providers

agreed that quality of care is enhanced by using the Vanderbilt Follow-up forms because the standardized assessments are more comprehensive than the previous practice of asking open-ended questions about symptoms, side effects, and performance. Providers also agreed that their treatment plans are more thorough and more patient-specific because the forms provide comprehensive assessment information within two minutes, which allows time for the providers to focus discussions on specific concerns. Since maintaining JACHO accreditation as a primary care medical home is contingent upon demonstration of continuous quality improvement, the responsibility for ensuring compliance with the documentation is managed by the practice's internal QI committee.

Results of the Pharmacogenomic Testing Evaluation

The evaluation of pharmacogenomic testing was conducted by using retrospective chart review data to evaluate whether pharmacogenomic testing prior to prescribing medication for ADHD was associated with a significant difference in the reported number of medication side effects and the amount of behavioral change. The chart review included charts of 52 patients aged 6-12 years who were treated at the practice for ADHD in 2016. The two study groups comprised 46% of the population of children aged 6-12 years who were treated for ADHD at the implementation site in 2016 (n = 112). The patient charts were divided into two groups according to their history (PGT) or absence of history (No PGT) of pharmacogenomic testing for psychotropic medications; the first 26 patients in each group who met study inclusion criteria were selected as study participants.

Demographic data. Each sample was comprised of 26 patients. The PGT group was comprised of 20 boys and 6 girls; patients ranged in age from 6-13 years old, with a mean age of 9 years. The No PGT group was comprised of 18 boys and 8 girls, with a mean age of 9 years, 6 months. Racial composition was: 4 bi-racial children (2 African American-Caucasian, 2 Hispanic-Caucasian), 4 Hispanic, 20 African American, and 24 Caucasian children. The total number of visits per patient ranged from 1-7, with an average of 2.5 visits per patient.

Medication Side Effects. Pharmacogenomic testing prior to prescribing medication for ADHD was associated with lower mean incidences of parent-reported moderate and severe ADHD medication side effects. The average number of side effects experienced by patients in each group was compared (see Table 2). The PGT group reported an average of 1.1 moderate or severe side effects, with a range of 0-4, whereas the mean number of moderate or severe side effects reported by the No PGT group was 2.4 with a range of 0-6.

Behavior Change. The study participants who received pharmacogenomic testing also had a greater improvement in behavioral symptoms after taking medication for ADHD. The difference in behavioral symptoms indicated by the Vanderbilt initial assessment and the follow-up assessment behavioral symptom scores was (PGT -32 vs. No PGT -15.8) (see Table 2).

Table 2 presents the data collected in the retrospective chart review, indicating the difference in behavioral scores and the number of moderate and severe ADHD medication side effects reported by participants in each group.

Table 2

Evaluation of the Effects of Pharmacogenomic Testing on Changes in Behavioral Symptoms and Incidence of Moderate or Severe ADHD Medication Side Effects for Children Receiving and Not Receiving Pharmacogenomic (PGT) Testing

Group	Change in Symptoms	# of SE	Group	Change in Symptoms	# of SE
PGT-1	-17	0	NO PGT-1	-11	2
PGT-2	-25	0	NO PGT-2	-38	2
PGT-3	-34	0	NO PGT-3	-26	4
PGT-4	-48	0	NO PGT-4	-22	0
PGT-5	-69	0	NO PGT-5	0	0
PGT-6	-60	3	NO-PGT-6	6	0
PGT-7	-37	2	NO PGT-7	-20	1
PGT-8	-17	0	NO PGT-8	-5	6
PGT-9	-30	1	NO PGT-9	-2	1
PGT-10	-24	0	NO PGT-10	-20	1
PGT-11	-37	5	NO PGT-11	-20	1
PGT-12	-36	3	NO PGT-12	-8	8
PGT-13	-43	2	NO PGT-13	-6	6
PGT-14	-45	2	NO PGT-14	-4	5
PGT-15	-36	2	NO PGT-15	-25	6

Group	Change in Symptoms	# of SE	Group	Change in Symptoms	# of SE
PGT-16	-17	0	NO PGT-16	-6	0
PGT-17	-15	2	NO PGT-17	-17	2
PGT-18	-18	3	NO PGT-18	-7	2
PGT-19	-15	0	NO PGT-19	-27	5
PGT-20	-24	1	NO PGT-20	-38	1
PGT-21	-19	0	NO PGT-21	-12	3
PGT-22	-51	0	NO PGT-22	-30	0
PGT-23	-45	1	NO PGT-23	-20	0
PGT-24	-31	1	NO PGT-24	-7	4
PGT-25	-17	1	NO PGT-25	0	3
PGT-26	-22	0	NO PGT-26	-64	3
MEAN	**-32**	**1.1**	**MEAN**	**-15.8**	**2.4**

Note. **Changes in Vanderbilt Behavioral Scores** = Initial Rating Scale (Parent) score - Follow-up (Parent) score; **Number of ADHD Medication Side Effects** = Number of side effects are reported as "moderate" or "severe"

Results of Quality-of-Life Assessments

Demographics. The sample was comprised of 18 patients, including 11 boys and 7 girls. Patients ranged in age from 6 to 13 years old, with a mean age of 9 years old.

Survey Results. The parent KINDL questionnaire was completed by 18 of 40 parents. The mean quality-of-life score of the study population was 75.6. The results of the survey as well as the population and subgroup totals are reported in Table 3. Although the values of the PGT group were higher, the small sample size (n = 3) prohibits generalization of the results (IHI, 2012). The unidentified respondents are more likely to have been patients who had not received pharmacogenomic testing, and if those three scores were added to the established No PGT average, the group score would be lowered to 74.7. Table 3 depicts the quality-of-life scores of the study participants.

Table 3

Results of the KINDL Quality-of-Life Questionnaire Survey of Study Participants

PGT Group (N = 3)   Avg. 80.3
Pt. Scores: 93, 74, 74

No PGT Group (N = 12)   Avg. 75.5
Pt. Scores: 79, 84, 91.6, 58, 61.5, 73.9, 70.8, 73, 78.1, 94.7, 72, 69.8, 71.6

Unknown Affiliation (N = 3)   Avg. 71.2
80.2, 72, 61.5

Study Population (N = 18)   Avg. 75.6

Range: 58 – 94.7

Average NPGT Group score after eliminating highest and lowest scores: 75.5

Trends in Responses. The KINDL questionnaire respondents consistently affirmed positive

parenting and family relationships and physical well-being for their children, especially in response to

questions in which parents rated their child as "always" or "often" full of energy, "never" feeling alone,

and "never" feeling afraid. The scores dipped in response to the self-esteem item, "my child has lots of

good ideas," which was most frequently responded to with "sometimes" or "often," although one parent

responded "rarely."

Responses varied in parents' assessments of their children's self-esteem and scholastic

engagement. Parents also reported a variety of responses to the question asking whether their child "felt

different from other children" and was "interested in the lessons taught at school." These three low scores

(58, 61.5, 61.5) are on par with the average KINDL parent-rated quality-of-life score of children with

ADHD as reported in the OBSEER study (Becker, 2011, pp. 61-65). To put these numbers in

perspective, the KINDL.org site (2017) posts 0.85 as the normal value for children aged 6-11 years

without chronic health disorders, as established by the multi-centered KIGGS trial in Germany.

However, the KIGGS study is not translated to English. The literature in English consistently refers to

the "normal" reference values established by the BELLA trial, which is 76.3 in neurotypical children,

aged 6-11 years, without chronic health disorders (Becker et al., 2011, p. S271).

Study Participants Compared to Benchmark Averages. The quality-of-life scores of the

population of school-aged children with ADHD treated at the implementation site are on par with

reference values of parent-reported KINDL Quality-of-Life Questionnaire scores of neurotypical children

without chronic health disorder diagnoses (76.3). The scores of children with ADHD at the study site

exceed the established benchmark average quality-of-life scores for children aged 6-11 years with ADHD

(62.9) as reported on the parent KINDL (Becker, et al., 2011). Benchmark reference values are reported

in Table 4.

Table 4

Comparison of Benchmark Quality-of-Life Scores Using the KINDL Questionnaire: Children without Chronic Health Disorders (BELLA) vs. Children with ADHD (OBSEER) (Adapted from: Becker et al., 2011, p. S271)

	BELLA (n = 2,863)	**OBSEER** (n = 721)	**d**	**T**
Total Score	**76.3 (SD 10.1)**	**62.9 (SD 13.3)**	**1.1**	**30.51**
Physical well-being	76.5 (17.3)	71.4 (18.3)	0.3	6.52
Emotional well-being	80.8 (12.8)	67.6 (17.6)	0.9	22.51
Self-esteem	68.8 (14.2)	55.1 (18.5)	0.8	21.84
Family	77.7 (14.3)	62.2 (19.4)	0.9	24.95
Friends	78.0 (13.4)	60.2 (20.9)	1.0	24.31
School	76.0 (16.0)	60.9 (18.7)	0.9	20.10

Evaluation of the Quality of Care

Client Feedback. Parents' perceptions of the quality and experiences of care were obtained

through a series of informal interviews at the clinical site. Responses to the implementation of

pharmacogenomic testing have been consistently very positive. A typical response was that of a mother

who reported that she had cried throughout her first three visits because she was upset at the thought of

medicating her son, but was also fearful of the consequences of not effectively treating his symptoms.

After treatment as described in this study, she remarked that she was very pleased by the quality of care

her son received and felt reassured that the ADHD treatment prescribed was safe, appropriately

monitored, and in his long-term best interests, which took a weight off her shoulders. She stated that

"The pharmacogenomic testing was part of the whole care package," which indicated to her that the care

was individualized, careful, and caring. One strong vote of confidence came when she recommended our

practice to a friend whose son had been diagnosed with ADHD and whose father had refused to allow him

to take medication. After the friend's son was brought in by his father, a provider confirmed the son's

diagnosis of ADHD and administered the pharmacogenomic test. The father was adamantly against his son taking medication to treat ADHD. He appreciated our approach however, and came back and agreed to try medication after it was pointed out that the medication might help his son to have better impulse control in situations outside of school. His son's pharmacogenomic report indicated that he was an abnormal metabolizer of all FDA-approved medications for treatment of ADHD in children. This spared the child and family at least one, if not two, unnecessary trials of different classes of stimulants. The child's father remarked that he "felt more comfortable moving forward.… Now I understand why I had such a hard time. It's not that all the medicines do that." He later agreed that, "He [his son] is on the right medicine."

CHAPTER 6: DISCUSSION

The quality improvement project achieved its purpose. Parents of children with ADHD, providers, and administrative and clinical staff at the implementation site all positively appraised the changes implemented so far and stated that the changes improved both the quality and the outcomes of care. Despite the missing documentation and subsequently skewed distribution of the study groups, which precluded statistical significance for the chart review results, implementing routine pharmacogenomic testing was judged valuable by providers at the clinical site because the study population was comprised of 46% of the target population and the groups were demographically similar, eliminating other confounders. The small sample size of the quality-of-life survey (18 of 40) prohibits generalization of its results, yet the consistency of the relatively high quality of life reported by parents of children with ADHD is encouraging. Although the KINDL Quality-of-Life Questionnaire scores are primarily attributable to the children's family and social networks, the consistency of the positive scores among survey respondents indicates that the system is working effectively to support the healthy development of resilience among an exceptionally large percentage of children with ADHD.

Attributes

This quality improvement project was unique in many respects. Implementation of the quality-of-life evaluations inserted this dimension, with its implications for psychosocial resilience, into the equation for measuring outcomes in children with ADHD. QoL has not previously been stipulated as a standard treatment outcome for children with ADHD. However, providers at the implementation site unanimously agreed that the development of resilience via improved QoL should be considered a treatment goal for school-aged children with ADHD. That formal consensus supported the implementation of the quality-of-life survey assessment for all children with ADHD and compelled a discussion with parents about the long-term goals of treatment.

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The obvious and most compelling benefit of assessing quality of life is to improve outcomes by identifying patients with poor quality of life to facilitate the early interventions necessary to forestall development of comorbid behavioral health disorders (Danckaerts et al., 2010). Discussion among healthcare providers and with parents about quality-of-life assessments improves the quality of care. Talking about a child's quality of life in a warm and supportive manner invites parents to partner with their child's healthcare providers in promoting the factors leading to resilience. In addition, the discussion opens potentially therapeutic channels of communication between parents and children about situations that the child finds problematic, providing an opportunity for children to be heard and validated. The discussion allows healthcare providers to partner with the parents, demonstrate "positive parenting," and encourage children to articulate their concerns and solve problems. Assessments indicating a good quality of life are valuable because they briefly shift the focus of the discussion away from the reports of a child's behavior and performance last week, to considering the goals of treating ADHD, such as healthy development and quality of life, both of which support resilience and promote lifelong good health.

Small-Scale Quality Improvement Evaluations. Quality improvement with continuous monitoring has become an important means of translating evidence into practice and of improving the outcomes and quality of healthcare (IHI, 2012). Routinely offering pharmacogenomic testing before prescribing medication to treat ADHD in children is an example of a quality improvement implementation that may further our knowledge and change our practices. The refinement of our methods will further validate quality improvement findings as legitimate evidence, which will empower individuals and small practices with the means of transforming at least one piece of the system of healthcare.

Rogers' (2003) discussion of the diffusion of innovations describes, explains, and predicts how, why, and at what rate new ideas and practices are adopted within a society. The theory has been widely applied to the adoption of healthcare innovations because it is a translational theory that predicts the perception of the external validity of innovations (Cain & Mittman, 2002). His theory can be used to

explain the slow adoption of pharmacogenomic testing among the medical community, which is due to the lack of large, randomized, controlled clinical trials. The theory of the diffusion of innovations asserts that smaller organizations with leaders who are visionary and respected opinion leaders will serve as the innovators and early adopters of innovations in a society, while larger organizations will be more risk-averse, late-majority adopters (Cain & Mittman, 2002). Small practices are positioned to take the lead in the adoption of innovations in healthcare because they are more flexible and able to adapt systems to incorporate innovations. A sense of community allows for the more cooperative work flow necessary to implement new processes into clinical routines.

Limitations

This study was limited by the small sample sizes and prior history of poor documentation, particularly when patients were satisfied with their outcomes, which skewed the distribution of the No-PGT pharmacogenomic testing sample. Those unavoidable factors prevented the inclusion of a larger number of patients who would meet the study criteria and the more balanced distribution of samples that would have followed. Problems with documentation were revealed by the QI evaluation, addressed, and resolved, thus improving both the quality of care and the efficiency of delivery. The study only viewed quality of life from the parental perspective due to the time limitations of the study period and the potential time required by the IRB to authorize the inclusion of child respondents.

Recommendations for Future Studies

The IHI (2012) advocates the creation of a learning-oriented healthcare system in which healthcare providers share mistakes as well as successes to advance the evolutionary plane of knowledge. Quality improvement clinical implementation projects are fraught with unanticipated challenges and missteps that must be addressed before the desired change can be implemented and proven to be an improvement. QIs are typically real-world implementations led by individuals without research backgrounds in settings over which they have limited control. Yet learning from others about what not to do in a situation or how to anticipate a problem would be helpful to others in the field. In a transparent system, these non-academic QI leaders would be able to share their procedures, findings, and mistakes in

the literature, which could then be read by individuals with similar interests, who might thereby be forewarned not repeat the same mistakes in a similar project. To be truly helpful, future studies should focus not only on the results of the evaluations but also detail the processes involved as often-inexperienced clinicians and teams work to implement changes at the practice level, leaving a trail so that others following in their footsteps would be able to go farther.

Future studies should attempt to accurately characterize the value of successfully treating ADHD in children by selecting a much larger sample of children with confirmed diagnosis of ADHD who take medication for the condition, children who report improvement of ADHD symptoms and no moderate or severe medication side effects. Their outcomes should then be compared to those of neurotypical children who do not have ADHD. Numerous studies report that treatment for ADHD is associated with lower risk of developing substance abuse and/or eating disorders, dying in a motor vehicle accident compared to peers with ADHD who do not take medication (Biederman, 2003; Charach et al., 2011, Dalsgaard et al., 2015; Ruiz et al., 2017). However, existing the studies do not indicate the remission status of the children taking ADHD medication. Hence, there is a possibility—even a probability—that the results may be skewed, with children with ADHD who are successfully treated enjoying a high level of risk reduction, while children who have responded poorly to their current medication or who only experience a moderate reduction or no reduction of risks, reported in aggregate, pull the risk reduction level down.

CHAPTER 7: CONCLUSION

Overall, the evaluation results of this quality improvement implementation indicate that the project has successfully furthered its goals of improving the quality of life and quality of care for school-aged children with ADHD at the implementation site. The high quality-of-life scores reported by the survey respondents, fewer incidences of moderate and severe ADHD medication side effects, and greater change in behavioral symptom scores in the group of patients who received pharmacogenomic testing all support an appraisal of the changes as improvements. Despite an inability to generalize the findings based on the limited data available at the time of the evaluation, providers agreed that the findings justified continuing implementation of the innovations in their clinical practice. The 52 study participants accounted for 46% of the total population of children between the ages of 6 and 12 years who were treated at the practice in 2016. Ignoring the findings and reverting to the previous routine, they felt, would defy common sense.

Although the evaluation results found that the changes were improvements, the hypothesis underlying the study design was never proven as true or untrue. This is significant because it leaves uncertainty about the approach that healthcare providers should take to address the issues of quality of life and resilience. Further, it leaves uncertainty about the value of individual interventions even within the same population. The underlying hypothesis of the project was that the relative lack of resilience among children with ADHD, reflected in consistent reports of poor quality of life, is largely attributable to the unremitting symptoms of ADHD and ADHD medication side effects. ADHD side effects often decrease a child's social and academic engagement and thus subsequently decrease resilience. However, the literature consistently finds that improving the long-term health of children with ADHD begins by furthering resilience (Perese, 2012; Masten, 2014). Since resilience is inextricably connected to quality of life, improving quality of life would be a means of promoting resiliency in children. This project was

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designed to improve quality of life, starting by decreasing the number and severity of ADHD medication side effects, improving treatment efficacy, and formally assessing quality of life as a treatment outcome.

Since the implementation of quality-of-life assessments and standardized follow-up assessments is readily available, this hypothesis may be tested in future studies. Charting points on a scatter plot may reveal a linear relationship between the number of moderate and severe ADHD medication side effects on the vertical axis and quality-of-life scores on the horizontal axis (IHI, 2012). Another avenue worth further exploration is the issue of whether pharmacogenomic testing improves the quality of care, in part, by providing reassurance to parents and providers that the treatment plan is optimized, even when the results themselves do not significantly alter the provider's choice of treatment.

Some of the implications for clinical practice were discovered during the QI process rather than being anticipated at the design stage. Quality-of-life assessments, for example, potentially improve outcomes by identifying patients with poor quality of life and fewer factors contributing to resilience. This improvement is possible because assessing a child's quality of life in a warm and supportive manner invites parents to partner with health care providers, which promotes the positive reinforcement of resilience and raises awareness of the larger goals of treating the child's ADHD symptoms.

Quality improvement projects are implemented with the understanding that modifications will no doubt occur and with plans for continuous monitoring and improvement (Frankel et al., 2017). In this project, this process, by design, generated information about how to improve the delivery of care to maintain efficiency as well as to improve quality. The evaluations, rather than damaging the project, rallied the support of the administrative staff, helping to spur the design of a systematic data collection, chart auditing, and a QI evaluation process that will allow the next evaluation to be truly meaningful. This report assesses the outcomes of the QI implementation as of December 1, 2017, but the implementation is ongoing; the site's internal quality improvement team has assumed responsibility for continuing to collect data for ongoing evaluation of outcomes in collaboration with their JACHO representative.

DSM-5 Diagnostic Criteria for Attention-Deficit/Hyperactivity Disorder

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A.   A persistent pattern of inattention and/or hyperactivity-impulsivity that interferes with functioning or development, as characterized by (1) and/or (2)

1.   **Inattention**: Six (or more) of the following symptoms, which have persisted for at least 6 months, to a degree that is inconsistent with developmental level, and that negatively impact social and academic/occupational activities. **Note**: The symptoms are not solely a manifestation of oppositional behavioral, defiance, hostility, or failure to understand tasks or instructions. For older adolescents and adults (age 17 and older), at least five symptoms are required.

  a.   Often fails to give close attention to details or makes careless mistakes in schoolwork, at work, or during other activities (e.g., overlooks or missing details, work is inaccurate).

  b.   Often has difficulty sustaining attention in tasks or play activities (e.g., has difficulty remaining focused during lectures, conversations, or lengthy reading).

  c.   Often does not seem to listen when spoken to directly (e.g., mind seems elsewhere, even in the absence of any obvious distraction).

  d.   Often does not follow through on instructions and fails to finish schoolwork, chores, or duties in the workplace (e.g., starts tasks but quickly loses focus and is easily side-tracked).

  e.   Often has difficulty organizing tasks and activities (e.g., difficulty managing sequential tasks; difficulty keeping materials and belongings in order; messy, disorganized work; has poor time management; fails to meet deadlines).

  f.   Often avoids, dislikes, or is reluctant to engage in tasks that require sustained mental effort (e.g., schoolwork or homework; for older adolescents and adults, preparing reports, completing forms, reviewing lengthy papers).

  g.   Often loses things necessary for tasks or activities (e.g., school materials, pencils, books, tools, wallets, keys, paperwork, eyeglasses, mobile telephones).

  h.   Is often easily distracted by extraneous stimuli (for older adolescents and adults, may include unrelated thoughts).

  i.   Is often forgetful in daily activities (e.g., doing chores, running errands; for older adolescents and adults, returning calls, paying bills, keeping appointments).

2.   **Hyperactivity and impulsivity**: Six (or more) of the following symptoms have persisted for at least 6 months to a degree that is inconsistent with developmental level and that negatively impacts directly on social and academic/occupational activities. **Note**: The symptoms are not solely a manifestation of oppositional behavioral, defiance, hostility, or failure to understand tasks or instructions. For older adolescents and adults (age 17 and older), at least five symptoms are required.

  a.   Often fidgets with or taps hands or feet or squirms in seat.

  b.   Often leaves seat in situations when remaining seated is expected (e.g., leaves his or her place in the classroom, in the office or other workplace, or in other situations that

require remaining in place).

    c.   Often runs about or climbs in situations where it is inappropriate. (**Note**: In adolescents or adults, may be limited to feeling restless.)

    d.   Often unable to play or engage in leisure activities quietly.

    e.   If often "on the go," acting as if "driven by a motor" (e.g., is unable to be or uncomfortable being still or extended time, as in restaurants, meetings; may be experienced by others as being restless or difficult to keep up with).

    f.   Often talks excessively.

    g.   Often blurts out an answer before a question has been completed (e.g., completes people's sentences; cannot wait for turn in conversation).

    h.   Often has difficulty waiting his or her turn (e.g., while waiting in line).

    i.   Often interrupts or intrudes on other (e.g., butts into conversation, games, activities; may start using other people's things without asking or receiving permission; for adolescents and adults, may intrude into or take over what others are doing).

B.   Several inattentive or hyperactive-impulsive symptoms were present prior to age 12 years.

C.   Several inattentive or hyperactive-impulsive symptoms are present in two or more settings (e.g., at home, school, or work; with friends or relatives; in other activities).

D.   There is clear evidence that the symptoms interfere with, or reduce the quality of, social, academic, or occupational functioning.

E.   The symptoms do not occur exclusively during schizophrenia or another psychotic disorder and are not better explained by another mental disorder (e.g., mood disorder, anxiety disorder, dissociative disorder, personality disorder, substance intoxication or withdrawal).

American Psychiatric Association. (2013). *Diagnostic and statistical manual of mental disorders* (5th ed.). Arlington, VA: American Psychiatric Publishing

APPENDIX B
ADHD QI IMPLEMENTATION PROTOCOL

Information about Our QI Implementation

As many of you know, our practice has begun implementation of a quality improvement (QI) initiative to improve the quality of care, outcomes, and quality of life for school-aged children with attention deficit hyperactivity disorder (ADHD).

ADHD in childhood is a significant risk factor for the development of other psychiatric disorders later in life. Resilience is the strongest predictors of good mental health later in life. A stimulant medication may increase focus and decrease impulsivity, and be "efficacious" while a child may be suffering a flattened affect, and persistent anxiety, which leads to social inhibition, disengagement, and decreased self-efficacy. These factors of resilience in school-aged children are crucial to strengthening psychosocial resilience, exhibited in a child's social skills, initiative, pride, and belief in his or her competence. We hope to increase resilience by decreasing the medication side effects and by increasing our awareness of the child's experience of treatment of the balance between efficacy and social engagement.

The guidelines for the management of school-aged children with ADHD in primary care were published in 2011, prior to the reclassification of ADHD in the DSM-5 as a neurodevelopmental disorder, rather than a behavioral disorder. The treatment of ADHD in school-aged children continues to reflect the conception of ADHD as a behavioral disorder, with a goal of decreasing impairment by remission of the externalized behaviors that characterize ADHD. As a primary care medical home, our goal is to provide comprehensive, patient-centered care to improve the health and wellbeing of individuals over their lifespans, accomplished, essentially, by identifying and reducing risk factors and increasing protective factors, such as resilience.

To avoid medication side effects, and taking medications that may not work, we have implemented routine offering of the GeneSight ADHD test for all kids aged 6-12 who are newly treated in our practice. We have implemented the Vanderbilt Follow-up form, to assess the child's response to pharmacotherapy on the behaviors identified as problematic in the initial assessment, and, to identify moderate or severe side effects that may necessitate a dosing adjustment or medication change. Our goal is to reduce symptoms to the point where the child feels competent, without suffering medications side effects. The child should feel that he or she can do what they need to with respect to their schoolwork, and exercise age-appropriate impulse control, yet eat dinner and fall to sleep at bedtime.

When the child has been treated for at least 3 months, we will ask parents to complete the KINDL Quality-of-Life Questionnaire. This questionnaire corresponds with the factors of resilience and helps us to identify kids who need extra support so that we can intervene early. If the child is maintaining psychosocial resilience during his ADHD treatment, and ensures that our treatment plan is not only keeping him out of trouble in school now, it is also supporting his wellness for years to come.

ADHD Quality Improvement Implementation Protocol

1. Upon diagnosis of ADHD, providers will give parents the option of having their child tested with the GeneSight pharmacogenomic test before prescribing medicine to treat their ADHD. The test can be offered to the parents of every child aged 6-12 years who will be prescribed medication for ADHD.

If parents bring the child in for an initial ADHD evaluation, and describe behavior that meets diagnostic criteria for ADHD, which has occurred in two or more settings for at least six months, and the child's

clinical presentation is consistent with ADHD, providers will order the GeneSight test when they provide parents the parent and teacher Vanderbilt assessment forms. This will avoid a delay in treatment once the diagnosis is confirmed.

If the child's diagnosis is unclear, providers will wait to test until the parent and child return with both Vanderbilt forms, and confirm the diagnosis, but will provide the information about the GeneSight test at the initial visit.

*The provider may order the test, and a proxy may complete the information on the GeneSight website from the provider's notes.

2. Parents will be educated about the benefits of test, and its limitations at the initial ADHD visit at NSMC. We should give them the information from Assurex Health regarding their financial responsibility at the first visit.

*Explanation of the risks and benefits, and financial responsibility follows the protocol.

3. At each ADHD follow-up visit, all parents of children aged 6-12 will complete the Vanderbilt Follow-Up form, which will be reviewed by providers prior to prescribing the next medication. If they did not bring it with them, the ladies at the front desk will provide the form for them to complete when they arrive.

4. Nurses will review the ADHD Follow-Up form to ensure that it is complete, and scored correctly, ad will enter scores for:
- A. the behavioral section
- B. the total number of moderate or severe medication side effects

*The performance score is contextual information only and is not scored.

5. **Once the treatment plan is determined, and the patient is only returning for 3-month follow-up appointments, parents will be asked to complete the KINDL Quality-of-Life Questionnaire** to assess the child's quality of life and ensure that he is developing psychosocial resilience while he is treated for ADHD.

NICHQ Vanderbilt Assessment Scales

Used for diagnosing ADHD

NICHQ
National Institute for
Children's Health Quality

VANDERBILT ASSESSMENT FORM – PARENT

Each rating should be considered in the context of what is appropriate for the age of your child.

When completing this form, please think about your child's behaviors in the past <u>6 months.</u>

Is this evaluation based on a time when the child:
☐ was on medication ☐ was not on medication ☐not sure?

	Symptoms	Never	Occasion-ally	Often	Very Often
1.	Does not pay attention to details or makes careless mistakes with, for example, homework	0	1	2	3
2.	Has difficulty keeping attention to what needs to be done	0	1	2	3
3.	Does not seem to listen when spoken to directly	0	1	2	3
4.	Does not follow through when given directions and fails to finish activities (not due to refusal or failure to understand)	0	1	2	3
5.	Has difficulty organizing tasks and activities	0	1	2	3
6.	Avoids, dislikes, or does not want to start tasks that require ongoing mental effort	0	1	2	3
7.	Loses things necessary for tasks or activities (toys, assignments, pencils, or books)	0	1	2	3
8.	Is easily distracted by noises or other stimuli	0	1	2	3
9.	Is forgetful in daily activities	0	1	2	3
10.	Fidgets with hands or feet or squirms in seat	0	1	2	3
11.	Leaves seat when remaining seated is expected	0	1	2	3
12.	Runs about or climbs too much when remaining seated is expected	0	1	2	3
13.	Has difficulty playing or beginning quiet play activities	0	1	2	3
14.	Is "on the go" or often acts as if "driven by a motor"	0	1	2	3
15.	Talks too much	0	1	2	3
16.	Blurts out answers before questions have been completed	0	1	2	3
17.	Has difficulty waiting his or her turn	0	1	2	3
18.	Interrupts or intrudes in on others' conversations and/or	0	1	2	3

	Symptoms	Never	Occasionally	Often	Very Often
	activities				
19.	Argues with adults	0	1	2	3
20.	Loses temper	0	1	2	3
21.	Actively defies or refuses to go along with adults' requests or rules	0	1	2	3
22.	Deliberately annoys people	0	1	2	3
23.	Blames others for his or her mistakes or misbehaviors	0	1	2	3
24.	Is touchy or easily annoyed by others	0	1	2	3
25.	Is angry or resentful	0	1	2	3
26.	Is spiteful and wants to get even	0	1	2	3
27.	Bullies, threatens, or intimidates others	0	1	2	3
28.	Starts physical fights	0	1	2	3
29.	Lies to get out of trouble or to avoid obligations (i.e., "cons" others)	0	1	2	3
30.	Is truant from school (skips school) without permission	0	1	2	3
31.	Is physically cruel to people	0	1	2	3
32.	Has stolen things that have value	0	1	2	3
33.	Deliberately destroys others' property	0	1	2	3
34.	Has used a weapon that can cause serious harm (bat, knife, brick, gun)	0	1	2	3
35.	Is physically cruel to animals	0	1	2	3
36.	Has deliberately set fires to cause damage	0	1	2	3
37.	Has broken into someone else's home, business, or car	0	1	2	3
38.	Has stayed out at night without permission	0	1	2	3
39.	Has run away from home overnight	0	1	2	3
40.	Has forced someone into sexual activity	0	1	2	3
41,	Is fearful, anxious, or worried	0	1	2	3
42.	Is afraid to try new things for fear of making mistakes	0	1	2	3
43.	Feels worthless or inferior	0	1	2	3
44.	Blames self for problems, feels guilty	0	1	2	3
45.	Feels lonely, unwanted, or unloved; complains that "no one loves him or her	0	1	2	3
46.	Is sad, unhappy, or depressed	0	1	2	3
47.	Is self-conscious or easily embarrassed	0	1	2	3

Performance	Excellent	Above Average	Average	Somewhat of a Problem	Problematic
48. Overall school performance	1	2	3	4	5
49. Reading	1	2	3	4	5
50. Writing	1	2	3	4	5
51. Mathematics	1	2	3	4	5
52. Relationship with parents	1	2	3	4	5
53. Relationship with siblings	1	2	3	4	5
54. Relationship with peers	1	2	3	4	5
55. Participation in organized activities (e.g., teams)	1	2	3	4	5

Comments:

For Office Use Only

Total number of questions scored 2 or 3 in questions 1–9: _____

Total number of questions scored 2 or 3 in questions 10–18: _____

Total Symptom Score for questions 1–18: _____

Total number of questions scored 2 or 3 in questions 19–26: _____

Total number of questions scored 2 or 3 in questions 27–40: _____

Total number of questions scored 2 or 3 in questions 41–47: _____

Total number of questions scored 4 or 5 in questions 48–55: _____

Average Performance Score: _____

TEACHER ASSESSMENT

Today's Date: _____   Child's Name: _____   Teacher's Name: _____

Directions: Each rating should be considered in the context of what is appropriate for the age of the child you are rating and should reflect that child's behavior since the beginning of the school year. Please indicate the number of weeks or months you have been able to evaluate the behaviors: _____.

Is this evaluation based on a time when the child:

☐ was on medication   ☐ was not on medication   ☐ not sure?

Symptoms	Never	Occasionally	Often	Very Often
1. Fails to give attention to details or makes careless mistakes in schoolwork	0	1	2	3
2. Has difficulty sustaining attention to tasks or	0	1	2	3

	Symptoms	Never	Occasionally	Often	Very Often
	activities				
3.	Does not seem to listen when spoken to directly	0	1	2	3
4.	Does not follow through on instructions and fails to finish schoolwork (not due to oppositional behavior or failure to understand)	0	1	2	3
5.	Has difficulty organizing tasks and activities	0	1	2	3
6.	Avoids, dislikes, or is reluctant to engage in tasks that require sustained mental effort	0	1	2	3
7.	Loses things necessary for tasks or activities (school assignments, pencils, or books)	0	1	2	3
8.	Is easily distracted by extraneous stimuli	0	1	2	3
9.	Is forgetful in daily activities	0	1	2	3
10.	Fidgets with hands or feet or squirms in seat	0	1	2	3
11.	Leaves seat in classroom or in other situations in which remaining seated is expected	0	1	2	3
12.	Runs about or climbs excessively in situations in which remaining seated is expected	0	1	2	3
13.	Has difficulty playing or engaging in leisure activities quietly	0	1	2	3
14.	Is "on the go" or often acts as if "driven by a motor"	0	1	2	3
15.	Talks excessively	0	1	2	3
16.	Blurts out answers before questions have been completed	0	1	2	3
17.	Has difficulty waiting in line	0	1	2	3
18.	Interrupts or intrudes on others (e.g., butts into conversations/games)	0	1	2	3
19.	Loses temper	0	1	2	3
20.	Actively defies or refuses to comply with adult's requests or rules	0	1	2	3
21.	Is angry or resentful	0	1	2	3
22.	Is spiteful and vindictive	0	1	2	3
23.	Bullies, threatens, or intimidates others	0	1	2	3
24.	Initiates physical fights	0	1	2	3
25.	Lies to obtain goods for favors or to avoid obligations (e.g., "cons" others)	0	1	2	3
26.	Is physically cruel to people	0	1	2	3
27.	Has stolen items of nontrivial value	0	1	2	3
28.	Deliberately destroys others' property	0	1	2	3
29.	Is fearful, anxious, or worried	0	1	2	3
30.	Is self-conscious or easily embarrassed	0	1	2	3
31.	Is afraid to try new things for fear of making mistakes	0	1	2	3
32.	Feels worthless or inferior	0	1	2	3
33.	Blames self for problems; feels guilty	0	1	2	3
34.	Feels lonely, unwanted, or unloved; complains that "no one loves him"	0	1	2	3

	Symptoms	Never	Occasionally	Often	Very Often
35.	Is sad, unhappy, or depressed	0	1	2	3

	Performance	Excellent	Above Average	Average	Somewhat of a Problem	Problematic
	Academic Performance					
36.	Reading	1	2	3	4	5
37.	Mathematics	1	2	3	4	5
38.	Written expression	1	2	3	4	5
		1	2	3	4	5
	Classroom Behavioral Performance	1	2	3	4	5
39.	Relationship with peers	1	2	3	4	5
40.	Following directions	1	2	3	4	5
41,	Disrupting class	1	2	3	4	5
42.	Assignment completion	1	2	3	4	5
43.	Organizational skills	1	2	3	4	5

Comments:

Please return this form to: _____

Fax number: _____

For Office Use Only

Total number of questions scored 2 or 3 in questions 1–9: _____

Total number of questions scored 2 or 3 in questions 10–18: _____

Total Symptom Score for questions 1–18: _____

Total number of questions scored 2 or 3 in questions 19–28: _____

Total number of questions scored 2 or 3 in questions 29–35: _____

Total number of questions scored 4 or 5 in questions 36–43: _____

Average Performance Score: _____

VANDERBILT FOLLOW-UP FORM – PARENT RESPONDENT

Parent's Name: _____Parent's phone number: _____

<u>Directions:</u> Each rating should be considered in the context of what is appropriate for the age of your child. Please think about your child's behaviors since the last assessment scale was filled out when rating his/her behaviors.

This evaluation should be based on a time when the child was on medication.

	Symptoms	Never	Occasion-ally	Often	Very Often
1.	Does not pay attention to details or makes careless mistakes with, for example, homework	0	1	2	3
2.	Has difficulty keeping attention to what needs to be done	0	1	2	3
3.	Does not seem to listen when spoken to directly	0	1	2	3
4.	Does not follow through when given directions and fails to finish activities (not due to refusal or failure to understand)	0	1	2	3
5.	Has difficulty organizing tasks and activities	0	1	2	3
6.	Avoids, dislikes, or does not want to start tasks that require ongoing mental effort	0	1	2	3
7.	Loses things necessary for tasks or activities (toys, assignments, pencils, or books)	0	1	2	3
8.	Is easily distracted by noises or other stimuli	0	1	2	3
9.	Is forgetful in daily activities	0	1	2	3
10.	Fidgets with hands or feet or squirms in seat	0	1	2	3
11.	Leaves seat when remaining seated is expected	0	1	2	3
12.	Runs about or climbs too much when remaining seated is expected	0	1	2	3
13.	Has difficulty playing or beginning quiet play activities	0	1	2	3
14.	Is "on the go" or often acts as if "driven by a motor"	0	1	2	3
15.	Talks too much	0	1	2	3
16.	Blurts out answers before questions have been completed	0	1	2	3
17.	Has difficulty waiting his or her turn	0	1	2	3
18.	Interrupts or intrudes in on others' conversations and/or activities	0	1	2	3

	Performance	Excellent	Above Average	Average	Somewhat of a Problem	Problematic
19.	Overall school performance	1	2	3	4	5
20.	Reading	1	2	3	4	5
21.	Writing	1	2	3	4	5

	Performance	Excellent	Above Average	Average	Somewhat of a Problem	Problematic
22.	Mathematics	1	2	3	4	5
23.	Relationship with parents	1	2	3	4	5
24.	Relationship with siblings	1	2	3	4	5
25.	Relationship with peers	1	2	3	4	5
26.	Participation in organized activities (e.g., teams)	1	2	3	4	5

Comments:

For Office Use Only
Total Symptom Score for questions 1–18: _____
Average Performance Score for questions 19–26: _____

The information contained in this publication should not be used as a substitute for the medical care and advice of your pediatrician. There may be variations in treatment that your pediatrician may recommend based on individual facts and circumstances.

Child's Name: _____ Parent's Phone Number: _____

Side Effects: Has your child experienced any of the following side effects or problems in the past week?	Are these side effects currently a problem?			
	None	Mild	Moderate	Severe
Headache				
Stomachache				
Change of appetite—explain below				
Trouble sleeping				
Irritability in the late morning, late afternoon, or evening—explain below				
Socially withdrawn—decreased interaction with others				
Extreme sadness or unusual crying				
Dull, tired, listless behavior				
Tremors/feeling shaky				
Repetitive movements, tics, jerking, twitching, eye blinking—explain below				
Picking at skin or fingers, nail biting, lip or cheek chewing—explain below				
Sees or hears things that aren't there				

Total number of moderate or severe side effects: _____

Explain/Comments:

Adapted from the Pittsburgh side effects scale, developed by William E. Pelham, Jr, PhD

These scales should NOT be used alone to make any diagnosis. You must take into consideration information from multiple sources. Scores of 2 or 3 on a single Symptom question reflect often-occurring behaviors. Scores of 4 or 5 on Performance questions reflect problems in performance.

The initial assessment scales, parent and teacher, have 2 components: symptom assessment and impairment in performance. On both the parent and teacher initial scales, the symptom assessment screens for symptoms that meet criteria for both inattentive (items 1–9) and hyperactive ADHD (items 10–18). To meet DSM-IV criteria for the diagnosis, one must have at least 6 positive responses to either the inattentive 9 or hyperactive 9 core symptoms, or both. A positive response is a 2 or 3 (often, very often).

The initial scales also have symptom screens for 3 other co- morbidities—oppositional-defiant, conduct, and anxiety/depression. These are screened by the number of positive responses in each of the segments separated by the "squares." The specific item sets and numbers of positives required for each co-morbid symptom screen set are detailed below. The second section of the scale has a set of performance measures, scored 1 to 5, with 4 and 5 being somewhat of a problem/problematic. To meet criteria for ADHD there must be at least one item of the Performance set in which the child scores a 4 or 5;

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i.e., there must be impairment, not just symptoms to meet diagnostic criteria. The sheet has a place to record the number of positives (4s, 5s) and an Average Performance Score.

Parent Assessment Scale	Teacher Assessment Scale
Predominantly Inattentive subtype ■ Must score a 2 or 3 on 6 out of 9 it ems on questions 1–9 AND ■ Score a 4 or 5 on any of the Performance questions 48–55	Predominantly Inattentive subtype ■ Must score a 2 or 3 on 6 out of 9 it ems on questions 1–9 AND ■ Score a 4 or 5 on any of the Performance questions 36–43
Predominantly Hyperactive/Impulsive subtype ■ Must score a 2 or 3 on 6 out of 9 items on questions 10–18 AND ■ Score a 4 or 5 on any of the Performance questions 48–55	Predominantly Hyperactive/Impulsive subtype ■ Must score a 2 or 3 on 6 out of 9 it ems on questions 10–18 AND ■ Score a 4 or 5 on any of the Performance questions 36–43
ADHD Combined Inattention/Hyperactivity ■ Requires the above criteria on both inattention and hyperactivity/impulsivity	ADHD Combined Inattention/Hyperactivity ■ Requires the above criteria on both inattention and hyperactivity/impulsivity
Oppositional-Defiant Disorder Screen ■ Must score a 2 or 3 on 4 out of 8 behaviors on questions 19–26 AND ■ Score a 4 or 5 on any of the Performance questions 48–55	Oppositional-Defiant/Conduct Disorder Screen ■ Must score a 2 or 3 on 3 out of 10 items on questions 19–28 AND ■ Score a 4 or 5 on any of the Performance questions 36–43
Conduct Disorder Screen ■ Must score a 2 or 3 on 3 out of 14 behaviors on questions 27–40 AND ■ Score a 4 or 5 on any of the Performance questions 48–55	Anxiety/Depression Screen ■ Must score a 2 or 3 on 3 out of 7 items on questions 29–35 AND ■ Score a 4 or 5 on any of the Performance questions 36–43
Anxiety/Depression Screen ■ Must score a 2 or 3 on 3 out of 7 behaviors on questions 41–47 AND ■ Score a 4 or 5 on any of the Performance questions 48–55	

Quality of Life Questionnaire for Children

Dear Parent,

We really appreciate your taking the time to complete this questionnaire about your child's well-being and health-related quality of life.

Since it is a matter of **your** own assessment of your child's well-being, please complete the questionnaire yourself according to the instructions, i.e. without asking your child.

☐   Read each question carefully.

☐   Think about how your child has been feeling during the past week.

☐   Put a cross in the box corresponding to the answer **in each line** that fits your child best.

For example:

During the past week ... ☐	Never	seldom	some-times	often	all the time
. ...my child has slept well	☐	☐	☐	☐	☐

My Child is a: ☐   Girl   ☐ Boy

Age: _Years

You are: ☐   Mother   ☐ Father   ☐ Other_____?

Date of fill out: ___/____/____(day / month / year)

1. Physical Well-being

During the past week ...	never	seldom	some-times	often	all the time
1. … my child felt ill	☐	☐	☐	☐	☐
2. … my child had a headache or tummy- ache	☐	☐	☐	☐	☐
3. … my child was tired and worn-out	☐	☐	☐	☐	☐
4. ... my child felt strong and full of energy	☐	☐	☐	☐	☐

2. Emotional Well-being

During the past week ...	never	seldom	some-times	often	all the time
1. ... my child had fun and laughed a lot	☐	☐	☐	☐	☐
2. ... my child didn't feel much like doing anything	☐	☐	☐	☐	☐
3. ... my child felt alone	☐	☐	☐	☐	☐
4. ... my child felt scared or unsure of him-/ herself	☐	☐	☐	☐	☐

3. Self-esteem

During the past week ...	never	seldom	some-times	often	all the time
1. ... my child was proud of him-/herself	☐	☐	☐	☐	☐
2. ... my child felt on top of the world	☐	☐	☐	☐	☐
3. ... my child felt pleased with him-/ herself	☐	☐	☐	☐	☐
4. ... my child had lots of good ideas	☐	☐	☐	☐	☐

4. Family

During the past week ...	never	seldom	some-times	often	all the time
1. ... my child got on well with us as parents	☐	☐	☐	☐	☐
2. ... my child felt fine at home	☐	☐	☐	☐	☐
3. ... we quarreled at home	☐	☐	☐	☐	☐
4. ... my child felt that I was bossing him/ her around	☐	☐	☐	☐	☐

5. Social Contacts

During the past week ...	never	seldom	some-times	often	all the time
1. ... my child did things together with friends	☐	☐	☐	☐	☐
2. ... my child was liked by other kids	☐	☐	☐	☐	☐
3. ... my child got along well with his/ her friends	☐	☐	☐	☐	☐
4. ... my child felt different from other children	☐	☐	☐	☐	☐

6. School

During the last week in which my child was at school ...	never	seldom	some-times	often	all the time
1. ... my child easily coped with schoolwork	☐	☐	☐	☐	☐
2. ... my child enjoyed the school lessons	☐	☐	☐	☐	☐
3. ... my child worried about his/her future	☐	☐	☐	☐	☐
4. ... my child was afraid of bad marks or grades	☐	☐	☐	☐	☐

PARENT ASSESSMENT Follow-up — Calculate Total Symptom Score for questions 1–18. Calculate Average Performance Score questions 19–26.

TEACHER ASSESSMENT Follow-up — Calculate Total Symptom Score for questions 1–18. Calculate Average Performance Score for questions 19.

The parent and teacher follow-up scales have the first 18 core ADHD symptoms, not the co-morbid symptoms. The section segment has the same Performance items and impairment assessment as the initial scales, and then has a side-effect reporting scale that the average of the Performance items answered as measures of improvement over time with treatment. Parent Assessment Follow-up can be used to both assess and monitor the presence of adverse reactions to medications prescribed.

Dear Rebecca Dragomani,

Thank you for your interest in the KINDL instruments.

We have now received your complete signed collaboration form and are very happy to collaborate with you.

You should be able to find the questionnaires as well as the manual for the questionnaires (in English) on our website: http://kindl.org/english/.

For a better documentation on our side and to assure that requests regarding the KINDL are being dealt with as quickly as possible we do assign ID numbers to every request.

In your case, it is number **1437**.

It would be very helpful for us if you could state this number every time you contact us. This becomes even more important if eventually some other person from your team needs to contact us. By knowing the number, we are than able to quickly connect people to the right projects and hopefully reply to requests even faster. In case of any questions, please feel free to contact us again.

With kind regards,

Toni Maria Klein
Office of Quality of Life Measures in Children | Wissenschaftliche Assistentin

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