Measuring knowledge and attitudes towards the utilization of pharmacogenetic testing among physicians

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Abstract

**Objective** Pharmacogenetic (PGx) testing is a relatively new available diagnostic tool, which aims to prescribe tailored medications based on genetic differences. However, this innovation has been slowly adopted by physicians. This study aims to test Rogers’ diffusion of innovation theory to assess knowledge and attitudes towards the use of PGx testing among physicians.

**Method** A sample of community physicians in South Florida was invited to complete an online survey about PGx testing. Practicing physicians who willing to sign the participation letter were included. The survey collected data on sociodemographics, knowledge of and attitudes towards PGx testing. Multiple dimensions of knowledge (i.e. prior experience) and attitude (i.e. relative advantage) were measured.

**Key findings** One hundred and forty-eight physicians participated in this study. Physicians’ actual PGx knowledge scores were averaged and significantly predicted by gender (\(P < 0.01\)), area of practice (\(P < 0.01\)) and prior experience (\(P < 0.05\)). The majority of physicians expressed optimistic attitudes towards PGx testing. Attitude scores were significantly predicted by gender (\(P < 0.05\)), the relative advantage (\(P < 0.05\)) and compatibility (\(P < 0.01\)) of testing. Barriers to PGx testing adoption including lack of insurance support, uncertainty about the clinical utility and unavailability of PGx testing at workplace were reported.

**Conclusions** Knowledge of PGx testing among physicians was moderate despite the expressed needs and favourable attitudes. Collaborative efforts to address the potential inhibitors may foster the integration of PGx testing into clinical practice. The need for additional courses and training in the field of pharmacogenetics is warranted.

**Keywords** adoption; attitudes; knowledge; pharmacogenetics; prescribers; Rogers’ theory

Introduction

Variations in the human deoxyribonucleic acid (DNA) sequence play a significant role in the development of diseases. Each individual has a unique set of genetic markers represented by DNA sequences located in specific regions of the chromosomes that may help predict his/her drug response and susceptibility to a particular disease.\(^{[1]}\)

Studying the role of genetic variability will eventually enable healthcare practitioners to customize treatments and prevention strategies to a patient’s unique genetic makeup. Several genome-wide association studies (GWAS) have been successful in identifying the association of genetic variations with chronic diseases such as type 2 diabetes mellitus (DM), Parkinson’s disease, heart disorders, obesity, Crohn’s disease and prostate cancer.\(^{[2,3]}\)

The primary aims of pharmacogenetic (PGx) research are to detect known SNPs and identify new SNPs among individuals that may largely influence their response to different medications.\(^{[4]}\) Information reported by PGx tests describes the effect of genetic differences (e.g. CYP2C19*2/2 genotype) on the physical changes (e.g. rapid metabolizer phenotype) in individual patients.\(^{[5,6]}\) Variations in the genetic sequences coding CYP450 enzymes may result in a reduced, amplified or complete loss of functionality in the
metabolizing enzymes. Consequently, inter-individual variability in drug response may account for the altered pharmacokinetic parameters.[7]

Drug-related complications are problematic for patients and healthcare systems. Adverse drug reactions (ADRs) can result in serious injuries, hospitalizations and even death. ADRs are a major contributing factor leading to mortality and morbidity.[6] The U.S. national estimate of annual emergency department visits due to ADRs reported approximately 700,000 adverse drug event cases annually between 2004 and 2005, in which 16.7% required hospitalization.[b]

A more recent prospective study reported high prevalence of patient-reported ADRs (74%) due to potentially inappropriate prescribing of medications.[10]

The treatment of chronic diseases often requires long-term use of medications. Patients with chronic diseases whose physicians do not assess their response to these drugs are more likely to have inadequate therapy management.[11,12] Moreover, the lack of time and communication between patients with chronic diseases and their healthcare providers potentially increases patients’ risk of experiencing medication-related complications.[13,14] Physicians’ knowledge about genetic variation and PGx testing may play a decisive role in the therapeutic management of patients with chronic diseases, resulting in improved quality of prescribing and improved patient safety.

Although the Food and Drug Administration (FDA) has reviewed more than 150 labels of prescription medications to include information regarding the impact of genetic variation on medication safety and efficacy,[15] the potential benefits of PGx testing in clinical diagnostic and prescribing practices have not yet recognized, possibly due to the limited knowledge and awareness among patients and physicians.

Today PGx testing could potentially play a significant role in drug selection and may help minimize ADRs associated with chemotherapeutics and psychiatric drug use,[16]; however, lack of awareness and limited knowledge among physicians have been two of the most important factors contributing to the slow adoption of PGx testing.[17,18] A large, nationally representative survey of U.S. physicians showed that the lack of adequate knowledge was probably the main factor influencing the implementation and the extent of use of PGx testing by physicians.[18]

The Everett Rogers’ diffusion of innovation model has been widely used in several disciplines since it explains the process of adopting innovations or new technology.[19,20] According to Rogers’ theory, people go through five stages of the innovation–decision process (knowledge, persuasion, adoption, implementation and confirmation) as a reaction to an innovation. During the knowledge stage, an individual attempts to learn more about the innovation, and then, the individual starts developing favourable or unfavourable thoughts about it.[20] Rogers’ theory proposes that sufficient knowledge and positive attitudes towards a particular innovation are the major stages that may influence the adoption of that innovation before it can be put into practice.

Rogers’ theory helps understand factors that influence the knowledge and attitude stages. Factors such as prior experience, perceived need for innovation, innovativeness, rurality and sociodemographic variables (e.g., age, level of education) are knowledge stage attributes. Similarly, the perceived characteristics of innovation (i.e., relative advantage, compatibility, complexity, trialability and observability) may explain an individual’s attitudes towards different innovations and also determine the rate of adoption.[20]

This study aimed to identify and evaluate the influence of knowledge, attitudes and sociodemographic characteristics of physicians on the adoption of PGx testing as a diagnostic tool in the current clinical settings. In order to achieve a better understanding of decision-making processes towards PGx testing and the strategies that help foster efficient adoption, this study was based on Rogers’ diffusion of innovation theory (2003), which has been widely accepted as a theoretical model to explore diffusion and adoption of innovations.[20]

**Methodology**

A cross-sectional, descriptive survey design was implemented to assess the knowledge and attitudes of physicians towards PGx testing. A questionnaire containing variables of interest was utilized. According to Rogers’ diffusion of innovation theory, several independent factors, such as sociodemographic variables (e.g., gender, age, ethnicity, medical specialty and types of practice setting), prior experience with PGx testing and perceived need for innovation and innovativeness can influence an individual’s knowledge of PGx testing. Other variables, including relative advantage, compatibility, complexity, trialability and observability, also work as independent variables that may affect an individual’s attitude towards PGx testing. Knowledge and attitudes towards PGx testing are independent variables that can influence the acceptance of PGx testing.

A power analysis program, G*Power 3.1, was utilized to calculate the appropriate sample size required to achieve a sufficient power.[21] Cohen’s $f^2$ was utilized for calculating the effect size within a multiple regression model in which the independent and the dependent variables are continuous.[22] Cohen’s $f^2$ value, calculated by $R^2 / (1 - R^2)$, is an adjusted coefficient of determination indicator of how well a regression equation fits the data values. After selecting a medium effect size value of $f^2 = 0.15$ and a significance level $\alpha = 0.05$, the required sample size was estimated to be 120 observations necessary to obtain 0.80 statistical power.

**Population and recruitment of prescribers**

Community physicians practicing at Nova Southeastern University (NSU) clinics involved in medication therapy decisions were asked to participate in an online survey. A letter was emailed with the survey to eligible physicians. Eligible community physicians were also recruited in person from three medical conferences held in Florida. Prescribers’ inclusion criteria included being a physician licensed to practice in Florida and currently involved in medication therapy decisions, willing to sign the participation letter and willing to complete the survey online.
Development of prescriber survey
The questions posed to prescribers were adopted from other instruments of previous studies with some modifications. Several concepts adapted from Rogers’s diffusion of innovation theory were incorporated as well. The prescriber questionnaire had 42 questions.

Six healthcare professionals agreed to participate in testing the survey. For face and content validity purposes, they were asked to explain their reactions to the wording, order and clarity of the questions. An average completion time of 6.5 min was reported. Changes to the questionnaire were made based on the feedback provided; these modifications reduced average time of completion to 4 min. The attitude and knowledge items showed Cronbach’s alpha scores of 0.78 and 0.60 respectively.

Data collection and statistical analysis
All prescriber questionnaires were administered and answered online. The questions were programmed into the Snap Survey software (Snap Surveys Ltd: Portsmouth, NH, USA; https://www.snapsurveys.com). Potential participants were invited to complete an online survey about PGx testing during the period July to October 2016. The survey was terminated after receiving 150 responses. The prescriber survey was anonymous; all identifiable information was removed from the responses before downloading them.

Data analyses were performed using IBM Statistical Package for the Social Sciences (SPSS, version 24.0, IBM Corp., Armonk, NY, USA) and Stata (version 14, StataCorp LP, College Station, TX, USA). A generalized path analysis was conducted to predict the causal connections of the factors that influence the acceptance of PGx testing among physicians.

Ethical considerations
After reviewing the study design, an exemption was granted from NSU Institutional Review Board (IRB). The prescriber survey, invitation e-mail and participation letter were submitted and approved by NSU before the implementation of the study in compliance with the Health Insurance Portability and Accountability Act (HIPAA). The data did not include direct physicians identifiers.

Results
Sample characteristics
Of the initial 1000 physicians contacted via e-mail, there were 850 deliverable messages and 60 participants successfully completed and submitted the online survey. In addition, 70 physicians were contacted at regional conferences and 20 were contacted at NSU’s Health Professions Division. In two surveys, the majority of the questions were blank, either due to a software error or due to lost Internet connection that led to data loss. These surveys were deleted. A total of 148 physicians completed the online survey for a response rate of 15.7%. Most of them were men and White, and they were evenly distributed in terms of age groups (see Table 1).

Prescribers’ knowledge of pharmacogenetic testing
The mean score was 3.40 out of 6.00, with a standard deviation of 1.53. Younger, non-White and female respondents practicing in suburban areas had higher mean scores than their counterparts. While the majority of physicians knew that PGx testing can determine whether response to the same medication may vary among people with genetic differences, almost one-half knew about the availability of PGx testing (see Table 2).

Prescribers’ attitudes towards pharmacogenetic testing
The mean score was 4.97 out of 8.00, with a standard deviation of 2.04. Older, White and female participants practicing in urban areas had relatively higher mean attitude scores. The majority of physicians expressed favourable attitudes towards the perceived benefits of PGx testing. However, concerns about potential genetic discrimination in health insurance companies and unauthorized access to testing results were reported (see Figure 1).

Rogers’s diffusion of innovation-based questions
Only 20% of physicians said that they had ever ordered PGx testing for a patient, and about a third replied that they had ever talked with a patient about PGx testing. Most participants expressed the need for PGx testing, especially when genetic information is included in the package inserts and when the practice guidelines become available.

<table>
<thead>
<tr>
<th>Table 1: Percentage distribution of selected demographic variables of prescribers in the sample (n = 148)</th>
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<tbody>
<tr>
<td><strong>Variables</strong></td>
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<tr>
<td>----------------</td>
</tr>
<tr>
<td>Gender</td>
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<tr>
<td>Male</td>
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<tr>
<td>Female</td>
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<tr>
<td>Age (years)</td>
</tr>
<tr>
<td>25–39</td>
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<tr>
<td>40–49</td>
</tr>
<tr>
<td>50–59</td>
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<tr>
<td>60 or older</td>
</tr>
<tr>
<td>Ethnicity</td>
</tr>
<tr>
<td>White/Caucasian</td>
</tr>
<tr>
<td>Hispanic/Latino</td>
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<tr>
<td>Black or African American</td>
</tr>
<tr>
<td>Other</td>
</tr>
<tr>
<td>Medical specialty</td>
</tr>
<tr>
<td>Internal medicine</td>
</tr>
<tr>
<td>Family medicine</td>
</tr>
<tr>
<td>Others (emergency medicine, paediatrics, dermatology, pain management, psychiatry)</td>
</tr>
<tr>
<td>Type of practice setting</td>
</tr>
<tr>
<td>Urban</td>
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<tr>
<td>Suburban</td>
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<td>Rural</td>
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Likewise, the majority of prescriber agreed on the relative advantages of using PGx testing to avoid the risk of non-response to an essential drug and to select a medication that better controls a patient’s health condition. In general, attitudes towards the perceived need, relative advantage and compatibility of PGx testing had more favourable responses than attitudes towards its trialability and complexity (see Figure 2).

Prescriber inferential statistics

Research question 1B analysis

The empirical evidence indicated that gender ($F(1, 141) = 5.39, P < 0.05$), type of practice setting ($F(2, 140) = 4.81, P < 0.01$), prior experience ($F(1, 131) = 8.38, P < 0.01$), perceived need ($F(2, 145) = 3.4, P < 0.01$) and sources of communication ($F(3, 144) = 4.5, P < 0.01$) showed significant differences in scores of knowledge about PGx testing by physicians. Post hoc Tukey’s tests were performed to determine which groups differed from each other.

The results showed that the mean PGx testing knowledge score of participants who perceived two needs for the testing was significantly higher than the score of those who expressed no need, and the mean scores of participants who used one or two resources were significantly greater than those who did not report any source of health information.

A multiple linear regression model was generated using the significant predictors found in the one-way ANOVA tests (gender, type of practice setting, prior experience, perceived need and sources of communication). The forward, backward and stepwise regression versions revealed that gender, type of practice setting and prior experience were significant variables that best fit the data (see Table 3). The adjusted coefficient of multiple determination value was 0.22.

Research question 2B analysis

Gender ($F(1, 141) = 5.98, P < 0.05$), relative advantage ($F(2, 145) = 6.52, P < 0.01$), compatibility ($F(2, 145) = 11.5, P < 0.01$) and observability ($F(1, 146) = 6.52, P < 0.05$) were significantly related to the total attitude score. Post hoc Tukey’s tests were performed to determine which groups differed from each other. They showed that the mean score of participants who agreed on two relative advantages of PGx testing was significantly higher than the mean of those who did not report advantages. The mean score of participants who agreed or strongly agreed with the statement about compatibility of PGx testing was significantly higher than the mean of those who disagreed or strongly disagreed.

Figure 1 Percentage of favourable responses by prescribers pertaining to attitudes towards pharmacogenetic (PGx) testing. The attitude scale had five response options: Strongly Disagree (SD), Disagree (D), Neutral (N), Agree (A) and Strongly Agree (SA).
The predictors found to be significant in the one-way ANOVA tests were utilized as independent variables in the estimation of a regression equation. Forward selection, backward elimination and stepwise regressions were conducted. All three models revealed that coefficients for gender, relative advantage and compatibility were significant (see Table 4). The adjusted coefficient of multiple determination value was 0.21.

Table 3 Predictors of prescribers’ knowledge of pharmacogenetic testing

<table>
<thead>
<tr>
<th>Predictors</th>
<th>Regression coefficient</th>
<th>Standard error</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender</td>
<td>0.798**</td>
<td>0.267</td>
</tr>
<tr>
<td>Type of practice setting</td>
<td>-0.742**</td>
<td>0.255</td>
</tr>
<tr>
<td>Prior experience</td>
<td>0.771*</td>
<td>0.314</td>
</tr>
<tr>
<td>Perceived need</td>
<td>0.255</td>
<td>0.179</td>
</tr>
<tr>
<td>Communication channels</td>
<td>0.159</td>
<td>0.134</td>
</tr>
<tr>
<td>Independent term</td>
<td>3.500</td>
<td>0.374</td>
</tr>
</tbody>
</table>

*P < 0.05.  **P < 0.01.

Table 4 Predictors of prescribers’ attitudes towards pharmacogenetic testing

<table>
<thead>
<tr>
<th>Predictors</th>
<th>Regression coefficient</th>
<th>Standard error</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender</td>
<td>0.078*</td>
<td>0.037</td>
</tr>
<tr>
<td>Relative advantage</td>
<td>0.061*</td>
<td>0.026</td>
</tr>
<tr>
<td>Compatibility</td>
<td>0.155**</td>
<td>0.044</td>
</tr>
<tr>
<td>Observability</td>
<td>0.061</td>
<td>0.038</td>
</tr>
<tr>
<td>Independent term</td>
<td>-0.730</td>
<td>0.060</td>
</tr>
</tbody>
</table>

*P < 0.05.  **P < 0.01.

The predictors found to be significant in the one-way ANOVA tests were utilized as independent variables in the estimation of a regression equation. Forward selection, backward elimination and stepwise regressions were conducted. All three models revealed that coefficients for gender, relative advantage and compatibility were significant (see Table 4). The adjusted coefficient of multiple determination value was 0.21.
model indicated a good fit model for the collected data. The coefficient of multiple determination values for the predictors were as follows: 0.19 for knowledge, 0.23 for attitudes and 0.18 for adoption of PGx testing. The goodness-of-fit scores pertaining to path analysis of prescribers’ adoption of PGx testing were estimated. The root mean square error of approximation (RMSEA) was <0.08 and chi-square ($\chi^2$) was >0.05 indicating that a good model fit was obtained. The results of the path analysis showed that participants who scored higher on the perceived characteristics of innovation subscale and on the perceived need items were more likely to accept PGx testing (see Table 5).

**Discussion**

**Prescribers’ knowledge of pharmacogenetic testing**

Few physicians knew about the impact of genetic variability on drug response and were unfamiliar with the availability of PGx testing for Plavix (clopidogrel, Sanofi-Aventis U.S. LLC, Bridgewater, NJ, USA). However, physicians’ overall knowledge of PGx testing in the sample was greater than the knowledge of physicians who participated in other studies.\(^{17,26–30}\) Compared to other studies,\(^{18,27,28,31}\) the percentage of physicians who reported receiving formal education in genetics was higher. This might reflect the growth of the PGx field and the surge in interest to know more about it.

Physicians’ overall knowledge of PGx testing was significantly associated with gender, perceived need, prior experience, type of practice setting and sources of communication. Physicians’ age, ethnicity, duration of practice and type of specialty were not significantly associated with overall knowledge of PGx testing, which might be explained by the fact that participants received comparable education and training programmes in genetics. Also the findings may reflect uniform genetics education and training across different specialties.

This study suggests that physicians’ active role in PGx information seeking is required. Physicians who used at least one source of genetic information had a higher level of overall PGx knowledge than physicians who did not report any source. This finding was consistent with other studies.\(^{18,26–28,30}\) Sources of genetic information included genetics training in medical school, CME courses, undergraduate genetics courses, genetics-related seminars or workshops, and grand rounds. Furthermore, physicians with high overall PGx testing knowledge score had perceived the need for PGx testing in reducing ADRs and preventing ineffective therapies. Stanek et al. (2012), Stanek et al. (2013) and Haga et al. (2012a) reported similar findings.

Finally, the results of multiple linear regression model revealed the strength of the relationship between overall knowledge of PGx testing and three significant predictors: gender, prior experience and type of practice setting. Female physicians practising in suburban areas with prior experience had a higher overall PGx testing knowledge score. Practicing in suburban areas might have provided physicians with a greater degree of exposure to PGx testing. More research is needed to investigate the factors that may result in a greater awareness of inter-individual variation in drug response among suburban-practice physicians. The findings of this work agreed with the results of several studies indicating that an association existed between prior experience with PGx testing and the level of knowledge.\(^{18,28,30}\)

**Prescribers’ attitudes towards pharmacogenetic testing**

The findings suggest that physicians’ attitudes towards PGx testing are becoming more receptive, and this may be due to the increase in the availability of PGx testing and more perceived benefits of genetic tests in improving medication safety and efficacy. Supporting the findings of other studies,\(^{17,18,28,32,33}\) concerns about the cost of PGx testing, patients’ confidentiality and the clinical utility of these tests were reported. Rogausch et al. (2006) revealed more reserved attitudes towards PGx testing among healthcare professionals when considering the potential discrimination by health insurance companies and employers. In this study, however, the levels of concern shared by physicians were much lower.

The results of the regression analysis indicated that physicians’ total attitude score towards PGx testing was predicted significantly by gender, relative advantage and compatibility. The lack of statistical significance of medical specialty might be due to a possible selection bias or because participants did not perceive the benefits of PGx to be directly related to their specialties. The lack of statistical significance of urban–rural practice setting might be attributed to receiving equal access to genetic information.

Female physicians in this study had more favourable attitudes than male physicians towards the clinical application of PGx testing; this may be due to their higher level of knowledge about PGx testing compared to their male counterparts. However, other studies showed that male physicians had more favourable attitudes than female physicians towards PGx testing.\(^{54,35}\)

In addition, a significant relationship was found between attitudes towards PGx testing and relative advantage, compatibility and observability. Haga et al. (2012a) also reported an impact of the relative advantage of PGx testing towards predicting potential ADRs and improving therapeutic outcomes on physicians’ attitudes and their decision to accept PGx testing. The significant effect of the observability variable, however, disappeared after conducting regression analysis. In this study, trialability and complexity were not significantly associated with attitudes towards PGx testing. This is possibly due to the lack of experience with PGx testing and physicians’ time constraints, which may prevent them from accepting the desired clinical tool.

**Adoption of pharmacogenetic testing among physicians**

The results of the path analysis showed that the adoption of PGx testing by physicians was significantly influenced by the perceived characteristics of PGx testing as well as the perceived need for innovation. Over 50% of physicians were willing to accept PGx testing. This finding may be
attributed to the fact that physicians have become more confident about the PGx testing results. Supporting the results of other studies,[18,26–39] this study showed that lack of knowledge and poor attitudes towards PGx testing negatively impacts the PGx-based prescribing decisions among physicians. Other reported factors contributing to the low use of PGx tests included lack of insurance support (43.2%), uncertainty about the clinical utility (38.6%), unavailability of PGx testing at workplace (37.5%) and waiting time on testing results (22.7%). Yet, improving the perceived characteristics of PGx testing (e.g. relative advantage, complexity) and its clinical need would potentiate the widespread utility of these genetic tests.

Limitations
The relatively low response rate of physicians might have limited the generalizability of the findings. Some might not have participated due to the inconvenience of responding via e-mail. Underrepresentation in some medical specialties was a limitation. The Cronbach’s alpha score of the knowledge scale items was almost 0.6, due to removing several items, which might have influenced the Cronbach’s alpha score without providing additional information, were removed from the scale. However, avoiding a long questionnaire was important to increase participants’ response rate and minimize survey fatigue.

Conclusion
Advances in the field of PGx in modern medicine are increasingly becoming a transformation point in the way chronic conditions are treated, medications are prescribed, and in developing trusting relationships among patients, pharmacists and physicians. The findings also showed that general knowledge of, and attitudes towards, the use of PGx testing increased physicians’ tendency to select the technique and implement it on their patients to improve health outcomes. Physicians’ acceptance of these tests was exclusively linked to their prior experience with, and perceived need for, genetic testing as well as perceived characteristics of PGx testing. There is a need for educational initiatives and training to increase physicians’ knowledge and competency in interpreting and communicating PGx testing results to their patients. Moreover, PGx companies need to improve the characteristics of PGx testing and alleviate currently foreseen barriers.

Declarations
Conflict of interest
The Author(s) declare(s) that they have no conflicts of interest to disclose.

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Authors’ contributions
I, Dr Muflih, am the principal investigator who provided direct and substantial contribution towards the design of the work, data collection, analysis and interpretation of data as well as drafting the work. Dr. Bleidt contributed significantly to the design of the work and supervising the process of data collection and analysis as well as critically revising the content of the work. Drs. Lafferty and Alvarez provided substantial contribution towards interpretation of the data and confirmed that the integrity of research objectives is appropriately explored. Dr. Shawaqleth contributed to a significant level to the study design and data analysis used. All authors have access to the data. They have revised, discussed, and approved the findings and significantly contributed to the final work.

Note
1. Nova Southeastern University IRB number 2016-77.

References