Underdiagnosis of Hypertension in Children and Adolescents

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Hypertension, with an estimated prevalence of between 2% and 5%, is a common chronic disease in children. Pediatric hypertension may be secondary to another disease process or it may be essential hypertension. Secondary hypertension is more common in children than in adults, and common causes of hypertension in children include renal disease, coarctation of the aorta, and endocrine disease. However, as with adults, the majority of children and adolescents with mild to moderate hypertension have primary hypertension in which a cause is not identifiable. Hypertension in children has been shown to correlate with family history of hypertension, low birth weight, and excess weight. With the increasing prevalence of childhood weight problems, increased attention to weight-related health conditions including hypertension is warranted. Several lines of evidence suggest that blood pressure in US children and adolescents is increasing in parallel with weight. Although long-term sequelae such as myocardial infarction, heart failure, stroke, and kidney disease rarely manifest in children, hypertension during childhood has been shown to be an independent risk factor for hypertension in adulthood, and to be associated with early markers of cardiovascular disease, including left ventricular hypertrophy, intima-media thickness, arterial compliance, atherosclerosis, and diastolic dysfunction.

Context Pediatric hypertension is increasing in prevalence with the pediatric obesity epidemic. Diagnosis of hypertension in children is complicated because normal and abnormal blood pressure values vary with age, sex, and height and are therefore difficult to remember.

Objectives To determine the frequency of undiagnosed hypertension and prehypertension and to identify patient factors associated with this underdiagnosis.

Design, Setting, and Participants A cohort study of 14,187 children and adolescents aged 3 to 18 years who were observed at least 3 times for well-child care between June 1999 and September 2006 in the outpatient clinics in a large academic urban medical system in northeast Ohio. For children and adolescents who met criteria for hypertension or prehypertension at 3 or more well-child care visits, the proportion with a hypertension-related International Classification of Diseases, Ninth Revision code in the diagnoses list, problem list, or past medical history list of any visit was determined.

Main Outcome Measures Proportion of children and adolescents with 3 or more elevated age-adjusted and height-adjusted blood pressure measurements at well-child care visits and with a diagnosis of hypertension or prehypertension documented in the electronic medical record. Multivariate logistic regression identified patient factors associated with a correct diagnosis.

Results Of 507 children and adolescents (3.6%) who had hypertension, 131 (26%) had a diagnosis of hypertension or elevated blood pressure documented in the electronic medical record. Patient factors that increased the adjusted odds of a correct diagnosis were a 1-year increase in age over age 3 (odds ratio [OR], 1.09; 95% confidence interval [CI], 1.03-1.16), number of elevated blood pressure readings beyond 3 (OR, 1.77; 95% CI, 1.21-2.57), increase of 1% in height-for-age percentile (OR, 1.02; 95% CI, 1.01-1.03), having an obesity-related diagnosis (OR, 2.61; 95% CI, 1.49-4.55), and number of blood pressure readings in the stage 2 hypertension range (OR, 1.68; 95% CI, 1.29-2.19). Of 485 children and adolescents (3.4%) who had prehypertension, 55 (11%) had an appropriate diagnosis documented in the electronic medical record. Patient factors that increased the adjusted odds of being diagnosed with prehypertension included a 1-year increase in age over age 3 (OR, 1.21; 95% CI, 1.09-1.34) and number of elevated blood pressure readings beyond 3 (OR, 3.07; 95% CI, 2.20-4.28).

Conclusions Hypertension and prehypertension were frequently undiagnosed in this pediatric population. Patient age, height, obesity-related diagnoses, and magnitude and frequency of abnormal blood pressure readings all increased the odds of diagnosis.
as average blood pressure at or higher than the 90th percentile for age, sex, and height, or more than 120/80 mm Hg but less than the 95th percentile. Based on these definitions, numerous normal and abnormal cutoffs exist, which are difficult for pediatric clinicians to remember. For example, the 95th blood pressure percentile for a 13-year-old girl in the 75th percentile for height is 129/84 mm Hg, but the 95th blood pressure percentile for an 8-year-old boy in the 10th percentile for height is 112/76 mm Hg. Although normal and abnormal blood pressure value tables and electronic programs exist, it may be difficult for pediatric clinicians to integrate these tools into their workflow. Therefore, our hypothesis is that many children with hypertension or prehypertension are never diagnosed.

Our study was undertaken to determine the frequency of undiagnosed hypertension and prehypertension in 3- to 18-year-old children within a large, academic, urban medical system.

**METHODS**

**Patients**

This was a cohort study of all children and adolescents (N = 14,187) who received at least 3 well-child care visits, based on CPT (Current Procedural Terminology) codes between June 1999 and September 2006 at a large tertiary care health system in northeast Ohio. A child had to have at least 3 well-child care visits while aged 3 to 18 years to be included in the cohort. The age criteria coincide with the National Heart, Lung, and Blood Institute’s National High Blood Pressure Education Program Working Group on High Blood Pressure in Children and Adolescents recommendations for routine blood pressure screening in children.

**Clinicians**

The health care system in which this study was conducted had approximately 600 staff clinicians and 300 resident physicians in training annually during the study period. Pediatric clinicians included family practitioners, pediatricians (general pediatricians and combined internists and pediatricians), and a few nurse practitioners. These pediatric clinicians made up about one-sixth of the staff and practice in 10 facilities in urban and suburban Cleveland, Ohio. Our study included patients who had supervised visits with resident physicians in family practice, general pediatrics, and combined internal medicine and pediatrics training programs, which made up about one-fifth of the physicians in training.

**Data Collection**

The health care system has used an electronic medical record system (EPIC, Epicare, Epic Systems Corp, Madison, Wisconsin) in the outpatient clinics since 1999. All visit information including vital signs, clinician notes, laboratory and imaging test results, all orders (including prescriptions), and all billing (including diagnoses) are recorded in the electronic medical record. Clinicians can easily view data from prior visits. No paper records are maintained.

For our study, we looked at patient race/ethnicity, age, sex, weight, height, and blood pressure readings for all well-child care visits for each participant during the study period. Race/ethnicity was self-identified by the patient, guardian, or both as part of the patient’s routine clinical care and was assessed because of possible differences in prevalence or underdiagnosis of hypertension based on race. In addition, we obtained data on visit diagnosis codes, family history of hypertension codes, past medical history codes, and problem list codes for each participant from all visits, not just well-child care visits. Any well-child care visits without a recorded blood pressure were excluded (6%). Visits were also excluded if the patient’s recorded height for the visit was less than 30.5 cm or more than 213.4 cm or if the recorded weight was less than 1.5 kg or more than 300 kg. Height and weight measurements outside of these parameters were considered to have been entered in error. This correction eliminated less than 0.1% of the visits, indicating that the data are largely free of mistakenly entered data.

Blood pressure measurements in the electronic medical record were recorded during the normal course of clinical care. Standard nursing blood pressure measurement protocols were used. The normal procedure included intake blood pressure taken by a nurse or medically trained assistant using an automatic, appropriately sized blood pressure cuff. These values were compared with a table of normal blood pressure values. Abnormal blood pressure readings were repeated by the nurse or medically trained assistant with a manual blood pressure cuff, with continued abnormal readings to be brought to the attention of the pediatric clinician. A full range of automatic and manual blood pressure cuff sizes were available to the nurse or medically trained assistants for the initial blood pressure measurements and to the pediatric clinicians to confirm those measurements. Medically trained assistants, nurses, and clinicians were to input the most accurate blood pressure into the electronic medical record. We had no way to independently assess the accuracy of the blood pressure measurements in the electronic medical record or the degree to which the blood pressure procedures were followed. Clinicians were not routinely provided access to paper-based or electronic blood pressure references but were left to develop their own practice patterns or references for pediatric blood pressure.

The protocol for our study received full approval through an expedited review by the institutional review board of MetroHealth Medical Center.

**Statistical Analysis**

Descriptive statistics, including age-adjusted height and weight percentiles, were calculated for each participant visit using the most recent Centers for Disease Control and Prevention growth charts. The age-adjusted and height-adjusted expected systolic and diastolic blood pressures were estimated for each participant visit according
to the National High Blood Pressure Education Program Working Group on High Blood Pressure in Children and Adolescents guidelines. Blood pressure percentiles for each participant visit were then calculated based on the expected blood pressures. Stage 1 hypertension was defined as 3 or more visits with systolic or diastolic blood pressure measurements greater than or equal to the 95th percentile for sex, age, and height, and less than the 99th percentile plus 5 mm Hg. Stage 2 hypertension was defined as 3 or more visits with systolic or diastolic blood pressure measurements greater than the 99th percentile plus 5 mm Hg. Prehypertension was defined as an average systolic or diastolic blood pressure percentile between the 90th and 95th percentiles or greater than 120/80 mm Hg. Using this definition, we defined a patient as prehypertensive if he/she had 3 systolic or diastolic blood pressure readings between the 90th and 95th percentile or greater than 120/80 mm Hg.

Patients were considered to have been diagnosed with hypertension if the problem list, list of diagnoses, or past medical history list from any visit contained 1 of the following International Classification of Diseases, Ninth Revision (ICD-9) codes related to hypertension: elevated blood pressure without hypertension (code 796.2); hypertension (code 401.xx); hypertension, not otherwise specified (code 401.9); hypertension, benign (code 401.1); and hypertension (code 997.91) or heart disease due to hypertension, not otherwise specified (code 402.9). We first calculated the prevalence of prehypertension, stage 1 hypertension, and stage 2 hypertension in the cohort. Then, for those patients who met criteria for hypertension (stage 1 or stage 2) or prehypertension, the fraction with a diagnosis of hypertension present in the electronic medical record was determined.

Multivariate logistic regression analysis was performed to determine the association between various factors and having a hypertension or elevated blood pressure diagnosis in the electronic medical record. The following factors were included in the regression models: age, number of elevated blood pressure readings beyond 3, weight-for-age percentile, height-for-age percentile, male sex, African American race, Hispanic/Latino ethnicity, presence of an obesity-related diagnosis, and family history of hypertension. The following ICD-9 codes were used to define an obesity-related diagnosis: obesity, not otherwise specified (code 278.00); overweight (code 278.02); overweight for pediatric patient (code 278.002); and weight gain, abnormal (code 283.1). In addition, the number of blood pressure readings in the stage 2 hypertension range was included in the regression model for those children and adolescents with hypertension. Models were selected based on our a priori hypotheses of factors, which may have been associated with having a diagnosis of hypertension. We report the adjusted odds ratios (ORs) and 95% confidence intervals for the regression results.

To assess the accuracy of the problem lists, visit diagnosis lists, and past medical history lists, we also performed a manual review of the electronic medical records from 50 randomly selected patients with undiagnosed hypertension. All well-child care visits from the electronic medical records of these patients were manually searched for mention of elevated blood pressure or hypertension.

SAS version 9.13 was used for all data processing and analysis.

**RESULTS**

Study inclusion criteria were met by 14,187 participants, with a total of 53,911 patient visits. At the most recently recorded visit for all participants, mean (SD) age was 8.8 (3.8) years, mean weight-for-age percentile was the 66th percentile, mean height-for-age percentile was the 60th percentile, 50% of the participants were African American, and 49% were female (Table 1).

Criteria for hypertension were met for 507 children (3.6%). Of the children with hypertension, only 131 (26%) had a diagnosis of hypertension or elevated blood pressure documented in the electronic medical record. Hence, 376 of 507 participants (74%) had undiagnosed hypertension. Elevated blood pressure without hypertension (ICD-9 code 796.2) was the only code present in 51 of the 131 diagnosed with hypertension; therefore, only 80 of the 507 participants (15.8%) had a true hypertension diagnosis in the electronic medical record. In addition, 17 of the 507 participants (3%) with hypertension had stage 2 hypertension, and 10 of these 17 (59%) had an elevated blood pressure or hypertension-related diagnosis present in the electronic medical record. Therefore, 7 of the 17 participants (41%) had undiagnosed stage 2 hypertension. Family history of hypertension was documented in 18% of the 507 patients with hypertension. Criteria for prehy-
Hypertension were met by 485 children (3.4%). Of these children, 55 (11%) had a diagnosis of hypertension or elevated blood pressure documented in the electronic medical record.

Results of multivariate logistic regression analysis performed for the cohorts with hypertension and prehypertension are shown in Table 2. Patient characteristics significantly associated with having a diagnosis of hypertension included a 1-year increase in age over age 3, number of elevated blood pressure readings beyond 3, and an obesity-related diagnosis, and the number of blood pressure readings in the stage 2 hypertension range. The OR for height-for-age percentile would be interpreted as a 1.9% increase in the odds of having a diagnosis of hypertension for a 1% increase in height-for-age percentile. This can be approximately extrapolated as a 19% increase in the odds of diagnosis for a 10% increase in height-for-age percentile. Factors not significantly associated with having a diagnosis of hypertension in the electronic medical record included weight-for-age percentile, African American race or Hispanic/Latino ethnicity, sex, and family history of hypertension.

Patient characteristics significantly associated with having a diagnosis of prehypertension included a 1-year increase in age over age 3 and number of elevated blood pressure readings beyond the required 3. Factors not significantly associated with having an elevated blood pressure-related diagnosis included height-for-age percentile, weight-for-age percentile, sex, African American race or Hispanic/Latino ethnicity, and family history of hypertension (Table 2).

On manual review of 50 randomly selected charts of patients with undiagnosed hypertension, the pediatric clinician made a note of an abnormal blood pressure in the text of the electronic medical record clinic note, without making the equivalent notation in the problem list, past medical history, or visit diagnosis list, in 4 charts (8%). Including these additional chart notations as correct identification and assuming an equivalent documentation rate across all charts, the diagnosis rate for hypertension would increase from 25.8% to 31.8% and, for prehypertension, from 11.3% to 18.6%.

### Table 2. Logistic Regression Analysis of Factors Associated With Having a Correct Diagnosis of Hypertension and Prehypertension in Children Aged 3 to 18 Years

<table>
<thead>
<tr>
<th>Variable</th>
<th>Hypertension</th>
<th>Prehypertension</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Demographic factors</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age, per 1-y increase over age 3 y</td>
<td>1.09 (1.03-1.16)</td>
<td>1.21 (1.09-1.34)</td>
</tr>
<tr>
<td>Male sex</td>
<td>1.15 (0.73-1.80)</td>
<td>1.20 (0.61-2.36)</td>
</tr>
<tr>
<td>African American race</td>
<td>1.04 (0.62-1.75)</td>
<td>1.20 (0.59-2.45)</td>
</tr>
<tr>
<td>Hispanic/Latino ethnicity</td>
<td>1.31 (0.61-2.83)</td>
<td>0.75 (0.22-2.53)</td>
</tr>
<tr>
<td><strong>Anthropometric factors</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Weight-for-age percentile, per 1% increase</td>
<td>1.00 (0.98-1.01)</td>
<td>1.02 (0.99-1.04)</td>
</tr>
<tr>
<td>Height-for-age percentile, per 1% increase</td>
<td>1.02 (1.01-1.03)</td>
<td>1.00 (0.99-1.02)</td>
</tr>
<tr>
<td>Obesity-related diagnosis</td>
<td>2.61 (1.49-4.55)</td>
<td>1.90 (0.90-4.00)</td>
</tr>
<tr>
<td><strong>Clinical factors</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No. of elevated blood pressure readings</td>
<td>1.77 (1.21-2.57)</td>
<td>3.07 (2.20-4.28)</td>
</tr>
<tr>
<td>beyond 3</td>
<td></td>
<td></td>
</tr>
<tr>
<td>No. of blood pressure readings in stage 2</td>
<td>1.68 (1.29-2.19)</td>
<td>NA</td>
</tr>
<tr>
<td>hypertension range</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Family history of hypertension</td>
<td>1.21 (0.70-2.11)</td>
<td>1.28 (0.60-2.76)</td>
</tr>
</tbody>
</table>

Abbreviations: CI, confidence interval; NA, not applicable.

- Listed odds ratios were adjusted for variables in the same column during logistic regression analysis.

### COMMENT

Our study documents the underdiagnosis of pediatric hypertension and prehypertension in a large pediatric population during an extended period of time. The prevalence of hypertension in our study is consistent with other studies in which the reported prevalence of hypertension in children ranges from 2% to 5%. Although the data to make the diagnosis were present in the patients’ records, pediatric clinicians did not appropriately identify hypertension and prehypertension in these children. This low diagnosis rate could be accounted for by 2 primary factors: (1) lack of knowledge of normal blood pressure ranges and (2) lack of awareness of a patient’s previous blood pressure readings. Because normal blood pressure in children is a function of age, sex, and height percentile, clinicians typically cannot remember normal blood pressures for the wide range of children observed in the typical primary care setting. Although tables exist with normal values, using these references for every blood pressure during well-child care visits could be time consuming. Additionally, even if a particular blood pressure is found to be abnormally high, investigating prior blood pressure readings is often difficult because the prior blood pressure readings, as well as the age and height percentile of the child at the time of those readings, need to be found.

We found that several patient factors were associated with increased adjusted odds that hypertension or prehypertension would be recognized. Specifically, older and taller children were more likely to have their abnormal blood pressure identified. The normal blood pressure range for children increases with age and height. Therefore, older and taller children with high blood pressure are more likely to have their blood pressure be more than 120/80 mm Hg, which is above the normal blood pressure value for adults. The knowledge of this normal adult blood pressure among pediatric clinicians may account for the increase in abnormal blood pressure identification in these patients.

Some risk factors for abnormal blood pressure increased the chance of identification of abnormal blood pressure. Presence of an obesity-related diagnosis was significantly associated with an
increased adjusted odds of hypertension diagnosis among patients with hypertension and, although not significant, a similar trend was noticed in patients with prehypertension. These trends probably occur because pediatric clinicians look more carefully for abnormal blood pressure in overweight children, since abnormal blood pressure is a common comorbid condition occurring in upward of 30% of overweight children. A positive family history of hypertension, however, did not increase the adjusted odds of identification of abnormal blood pressure in either group. This is probably related to the fact that, except for the visit at which the family history is obtained, the clinician is not generally aware of the positive family history and therefore does not factor this into the care of the child.

The frequency and magnitude of abnormal blood pressure readings also correlated with increased adjusted odds of identification of abnormal blood pressure. As the relative magnitude of the abnormal blood pressure increased, indicated by the presence of increased numbers of blood pressure readings in the stage 2 hypertension range, the adjusted odds of diagnosis also increased. One reason for this could again be that as the abnormal blood pressure approaches and surpasses the normal cutoff for adults of 120/80 mm Hg, the pediatric clinician recognizes the blood pressure as abnormal. Additionally, as the number of abnormal blood pressure readings increased, the adjusted odds of diagnosis also increased, which is most likely because the pediatric clinician has more opportunities to recognize the abnormal blood pressure.

One potential limitation of our study is that it did not examine clinician characteristics that may be related to the rate of appropriate abnormal blood pressure diagnosis. Given the duration of the study period and the involvement of resident physicians, generally more than 1 clinician was involved in the visits for each patient. Also, any number of relatively unique clinician characteristics (years of experience, training status, training background, percentage of practice time, patient panel characteristics) could affect diagnosis rates. Our study was designed only to investigate the overall diagnosis rates and patient characteristics affecting diagnosis rates.

Another potential limitation of our study is our reliance on the problem lists, past medical history lists, and visit diagnosis lists as the gold standard for the positive identification of a child with abnormal blood pressure. However, our manual review showed few charts with only text notations of an abnormal blood pressure. In the era of decreasing continuity of clinicians and increasing use of electronic medical records, one may argue that a pure text comment should not be considered sufficient documentation of a diagnosis.

In our study, blood pressure measurement followed routine clinical procedures as opposed to more rigorous measurement techniques. Although there may be more accurate ways to measure blood pressure, the blood pressure measurement protocols we used are similar to those in many institutions. We do not have data on how frequently blood pressures were correctly obtained; however, we do know that among children aged 3 to 18 years observed in our system, 94% of well-child care visits had a blood pressure documented. Our results may not be generalizable to other practice settings with single or smaller groups of clinicians in which different blood pressure measurement techniques are used.

Diagnoses of hypertension and prehypertension were based on blood pressure readings taken at the well-child care visits. We thought this was appropriate for 2 reasons. We did not want to include visits in which blood pressure readings may have been artificially elevated secondary to acute conditions, such as pain or asthma exacerbation, rather than true hypertension and current consensus guidelines call for screening blood pressure measurement at well-child care visits from ages 3 to 18 years. Reliance on well-child care visits alone for blood pressure measurements decreased the potential sample size of our study, as all children had to have at least 3 well-child care visits to be included in our cohort. In addition, bias may have been introduced by potentially selecting a population more likely to get well-child care. However, the group of patients not included due to having less than 3 primary care visits had less than 2% difference in mean age, height percentile, weight percentile, and percentage age female compared with the study group.

Although the blood pressures used in our study were from well-child care visits only, the ICD-9 codes used to determine whether a child was diagnosed came from all visits. For example, if a diagnosis code for hypertension or elevated blood pressure was associated with a nephrology visit or a non–well-child primary care visit, it would be included in the analysis. Some practitioners may have rechecked a patient’s elevated blood pressure at a separate non–well-child care visit. In this case, the blood pressure measurement from the recheck visit would not be included in our analysis but any ICD-9 abnormal blood pressure codes would be. A child with hypertension based on ICD-9 codes who did not have 3 abnormal readings during well-child care visits would not be counted among the 507 children with a diagnosis of hypertension.

In our population, we also investigated the diagnosis of hypertension in children without 3 well-child care visits with abnormal blood pressures. There were 900 children in our cohort who had at least 3 abnormal blood pressure measurements during all outpatient visits in the study period but did not have 3 abnormal blood pressure measurements at well-child care visits. Of these 900 children, only 155 had an ICD-9–associated abnormal blood pressure code, leading to a diagnosis rate in this population of 17.2%. Some cases exist in which clinicians may be more likely to look for abnormal blood pressure readings and diagnosis of hypertension, such as follow-up abnormal blood pressure visits and obstetric-gynecologic visits. However, in well-
child care visits, clinicians should be focused on screening and prevention of diseases including hypertension and most non–well-child care visits are for specific issues that would not focus the clinician’s attention to the patient’s blood pressure. Additionally, there may be acute circumstances, such as pain or asthma exacerbation, in which the blood pressure could be acutely high from a normal baseline and so it would be inappropriate to diagnose the child with chronic hypertension at that time. The fact that these 900 cases would also make the prevelance of hypertension in our population 9.9% (1407/14 187), up to double that of published prevalence in other studies of normal children, supports the idea that some of the abnormal blood pressures using this expanded criterion could represent false-positive findings.

All patients in our study whom we labeled with hypertension had elevated blood pressure at 3 separate well-child care visits and met current consensus criteria for a diagnosis of hypertension. Our study represents true underdiagnosis of hypertension as these patients’ hypertension was not recognized by clinicians throughout our health care system.

Identification of elevated blood pressure in children meeting prehypertension or hypertension criteria is important because of the increasing prevalence of pediatric weight problems and because secondary hypertension is more common in children than adults, requiring identification and appropriate work-up. If abnormal blood pressure is not identified by a patient’s pediatric clinician, it may be years before the abnormal blood pressure is detected, leading to end-organ damage. Because effective treatments for abnormal blood pressure exist, these long-term sequelae can be avoided with early diagnosis.

Although this study identifies the problem of undiagnosed hypertension in children, it also points to the potential of electronic medical records to help address this issue. The relatively poor identification of abnormal blood pressure could be remedied by a clinical decision support algorithm built into an electronic medical record that would automatically review current and prior blood pressures, ages, heights, and sex to determine if abnormal blood pressure criteria had been met. The algorithm could indicate if any abnormal blood pressure ICD-9 codes already existed and prompt the pediatric clinician that the child appears to have undiagnosed abnormal blood pressure. In addition, the clinical decision support algorithm could provide guideline-based evaluation, treatment, and parent/patient education materials to the clinician.

CONCLUSION
Hypertension and prehypertension are well-defined, prevalent, asymptomatic, chronic conditions in children and adolescents. Based on the data in this study, these conditions appear to be frequently undiagnosed by pediatric clinicians. Early, appropriate diagnosis is important because established evaluation guidelines and effective treatment for abnormal blood pressure exist.

Author Contributions: Drs Hansen and Kaelber had full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.

Study concept and design: Hansen, Gunn, Kaelber. Acquisition of data: Kaelber. Analysis and interpretation of data: Hansen, Gunn, Kaelber. Drafting of the manuscript: Hansen, Gunn, Kaelber. Critical revision of the manuscript for important intellectual content: Hansen, Gunn, Kaelber. Statistical analysis: Hansen, Kaelber. Administrative, technical, or material support: Kaelber. Study supervision: Kaelber.

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REFERENCES