Arterial stiffening is an important event in the development of cardio- and cerebrovascular disease. It reflects a decline in elastic properties of the aorta and other large capacitance arteries.\(^1\) Aging leading to a change in arterial wall composition is the main cause for arterial stiffening.\(^2,3\) However, specific disease conditions in children and adults can lead to an excess in arterial stiffening, causing a premature increase in systolic and a decrease in diastolic blood pressure (BP) through accelerated and inappropriate pulse wave reflections.\(^4,6\) In addition, arterial stiffening could propagate the central pulsatile flow into the microvasculature and thereby lead to a constant risk for damage.\(^7\) For evaluation of these systemic changes in the central arterial tree the measurement of carotid to femoral (aortic) pulse wave velocity (aPWV) is a widely accepted procedure.\(^8\) aPWV is commonly used to assess aortic stiffness and is recommended by European Network for Noninvasive Investigation of Large Arteries and by European Guidelines on Cardiovascular Disease Prevention.\(^8,9\) High aPWV is associated with an increased cardiovascular mortality in adults with hypertension, end-stage renal disease, diabetes mellitus, and coronary heart disease.\(^10–12\) When added to standard risk factors, aPWV improves the risk prediction for cardiovascular events.\(^13\) In addition, the current guidelines from the European Society of Hypertension/European Society of Cardiology recommend aPWV assessment as part of individual cardiovascular risk evaluation and therapy guidance.\(^14\) In children and young adults, aPWV is regarded as the most widely used...
and accepted method for assessment of vascular stiffness as stated by American Heart Association Atherosclerosis, Hypertension, and Obesity in Youth Committee of the Council on Cardiovascular Disease in the Young.\textsuperscript{15}

There are different methods to assess aPWV, including Doppler ultrasound, mechanoelectrical pulse transduction, tonometry, whole body impedance cardiography and oscillometry. Besides the Compilor, the SphygmoCor system has been the most commonly used and best validated device for aPWV evaluation.\textsuperscript{16} It uses sequential tonometric recordings of pressure waves from the carotid and femoral artery to calculate transit time of the pulse wave. A major drawback is the fact that the examined subjects have to partially undress to expose the inguinal region for palpation and tonometry of the femoral artery. SphygmoCor is known to be operator-dependent, but has proved to generate highly reproducible results by multiple observers after a training period.\textsuperscript{17} Given that carotid and femoral waveforms are recorded sequentially, variability in heart rate or BP may confound the readings.

The Vicorder is a relatively new oscillometric device. This method allows simultaneous recordings of the carotid and femoral pulse waves. Compared to the SphygmoCor less operator training is required and measurements can be performed faster. However, previous studies comparing these devices in heart rate or BP may confound the readings.

The aim of this study was to assess the intra- and interobserver repeatability for aPWV measurements using a new oscillometric device (Vicorder) and to compare it with the well-established SphygmoCor device in children and adolescents. As there are no recommendations for path length assessment in children and adolescents, we determined the effect of different path length measurements on the correlation of both methods.

**METHODS**

\textit{Vicorder intraobserver repeatability study.} Intraobserver repeatability was assessed by repeated measurements in the same individuals by a single investigator (D.K.) using the Vicorder device. A total of 14 children and adolescents (mean age: 13 years, range: 8–17 years) were examined on three different points in time with at least 8 h apart to mimic a day-to-day variability. On every occasion measurements were done in triplicate with 1-min intervals.

\textit{Vicorder interobserver repeatability study.} For interobserver repeatability 14 individuals (8 children, mean age: 9 years, range: 5–17 years and 6 adults, mean age: 45 years, range: 35–64 years) were examined by three different investigators (B.M.W.S., D.K., R.Z.) in separated rooms. Investigators were not aware of distance measurements and aPWV results of the other investigators. Measurements were done in triplicate with 1-min intervals.

**Table 1 | Anthropometric data for all children included into the Vicorder–SphygmoCor comparison study in Hannover and London**

<table>
<thead>
<tr>
<th>Anthropometric variables</th>
<th>Values</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total population</td>
<td>N 156</td>
</tr>
<tr>
<td>Gender</td>
<td></td>
</tr>
<tr>
<td>Boys</td>
<td>73 (47%)</td>
</tr>
<tr>
<td>Girls</td>
<td>83 (53%)</td>
</tr>
<tr>
<td>Age (years)</td>
<td>Mean ± s.d. 11.1 ± 2.9</td>
</tr>
<tr>
<td></td>
<td>Range 6.3–18.3</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>Mean ± s.d. 41.1 ± 15.3</td>
</tr>
<tr>
<td></td>
<td>Range 21.5–83.4</td>
</tr>
<tr>
<td>Weight SDS</td>
<td>Mean ± s.d. 0.4 ± 1.0</td>
</tr>
<tr>
<td></td>
<td>Range −2.1 to 3.1</td>
</tr>
<tr>
<td>Height (m)</td>
<td>Mean ± s.d. 1.5 ± 0.2</td>
</tr>
<tr>
<td></td>
<td>Range 1.2 to 1.9</td>
</tr>
<tr>
<td>Height SDS</td>
<td>Mean ± s.d. 0.4 ± 1.1</td>
</tr>
<tr>
<td></td>
<td>Range −3.7 to 4.7</td>
</tr>
<tr>
<td>BMI</td>
<td>Mean ± s.d. 18.7 ± 3.4</td>
</tr>
<tr>
<td></td>
<td>Range 13.7–31.1</td>
</tr>
<tr>
<td>BMI SDS</td>
<td>Mean ± s.d. 0.2 ± 0.9</td>
</tr>
<tr>
<td></td>
<td>Range −2.3 to 2.5</td>
</tr>
<tr>
<td>Systolic blood pressure (mm Hg)</td>
<td>Mean ± s.d. 110 ± 11</td>
</tr>
<tr>
<td></td>
<td>Range 89 to 152</td>
</tr>
<tr>
<td>Systolic blood pressure SDS</td>
<td>Mean ± s.d. 0.5 ± 0.8</td>
</tr>
<tr>
<td></td>
<td>Range −1.3 to 4.3</td>
</tr>
<tr>
<td>Diastolic blood pressure (mm Hg)</td>
<td>Mean ± s.d. 62 ± 8</td>
</tr>
<tr>
<td></td>
<td>Range 45–96</td>
</tr>
<tr>
<td>Diastolic blood pressure SDS</td>
<td>Mean ± s.d. 0.0 ± 0.7</td>
</tr>
<tr>
<td></td>
<td>Range −1.6 to 2.8</td>
</tr>
<tr>
<td>Heart rate/min</td>
<td>Mean ± s.d. 80 ± 12</td>
</tr>
<tr>
<td></td>
<td>Range 53–112</td>
</tr>
</tbody>
</table>

Values are shown as mean ± s.d. Percentages are given for gender and ranges for all other parameters.

B.M.W.S., body mass index.
Anthropometric data and BP for comparison study. Weight and height were measured in a standardized manner. SDS values for weight, height and body mass index were calculated based on the 2000 CDC Growth Charts (http://www.cdc.gov/nchs/data/series/sr_11/sr11_246.pdf). BP measurements were performed before SphygmoCor and Vicorder readings after 5 min of rest in supine position using a semiautomated device (Dinamap Pro 100 or Dinamap Carescape v100; General Electric Company, Munich, Germany). BP SDS values were calculated as previously described.23

Measurement of aPWV for comparison study. All participating individuals were measured with SphygmoCor and Vicorder consecutively during one visit, but in random order. Settings and measurement conditions were according to the recommendations of the Task Force III on clinical applications of arterial stiffness.24 Vicorder measurements were done in triplicate in Hannover and in duplicate in London; mean values were used for further analysis. SphygmoCor measurements were accepted if the standard deviation of the measured carotid time delay was <6% of the mean and if the standard deviation of the femoral time delay was <10% of the mean. aPWV (m/s) was calculated as carotid to femoral path length (m) divided by the pulse transit time (s).

A detailed measurement procedure description for SphygmoCor and Vicorder is provided in the Supplementary Data online.

Measurement of carotid to femoral path length. The carotid to femoral path was determined using a measuring tape. We determined two distances that were composites of different length measurements, which are illustrated in Figure 1. Distance A is the composite of the direct distance from suprasternal notch (SSN) to femoral recording site minus the distance from SSN to carotid recording site. Distance B is an alternative length determination that more accurately follows the real path of the arterial tree by measuring (SSN to umbilicus (Umb)) + (Umb to femoral recording) – (SSN to carotid recording site).

Statistical analysis. For intra- and interobserver repeatability as well as for the comparison of values obtained by both devices Bland–Altman plots were generated.25 For construction of Bland–Altman plots of the intra- and interobserver repeatability, mean values (shown on the x-axis) were calculated based on three measurements, differences were calculated between the highest and the lowest values out of the three measurements.

As further measures of agreement for intra- and interobserver repeatability, we calculated the coefficient of variation (CV, calculated as SDw/M·× 100%) and the intraclass correlation coefficient (ICC). According to Shrout and Fleiss ICC(3,k)26 was used and ICC calculated as (SDB 2–SDE 2)/SDB 2 with SDB 2 being the between observer variance and SDE 2 being the residual variance. ICC was calculated with PASW Statistics 18.0.0 (SPSS, Chicago, IL). An ICC of 0.5–0.6 is interpreted as moderate association, 0.7–0.8 as strong association and >0.8 as almost complete association. In addition, we state the limit of agreement (LoA) that indicates the confidence limits around the mean difference.

Mean values of different measurements were compared using paired t-test. Values are expressed as mean ± s.d. The level of significance was set to P < 0.05.

Figure 1 | Schematic illustration of path length determination. We used two path length measurements to calculate aortic pulse wave velocity (aPWV). These path lengths were composites of different distance measurements: (1) Distance from suprasternal notch (SSN) to the recording point at the carotid artery (Car), which was in case of the SphygmoCor the point of transducer placement at the Car, (a) whereas for the Vicorder it reflected the mid of the neck cuff (CarCuff) (b). (2) Distance from SSN to umbilicus (Umb). (3) Distance from Umb to the recording point at the femoral artery (SphygmoCor: transducer placement over femoral artery (Fem); Vicorder: mid of the femoral cuff (FemCuff)). (4) Direct distance from SSN to the recording point at the Fem (differences between SphygmoCor and Vicorder see above).
RESULTS

Vicorder intraobserver repeatability study
Mean aPWV using distance A (Figure 1) was 4.8 ± 0.5 m/s. Mean difference between repeated measurements was 0.3 ± 0.5 m/s. The CV between measurements was 5.6% and ICC was 0.8. The LoA was −0.7 to 1.2 m/s (Figure 2). Taken together, these measures show a good agreement of the measurements.

Vicorder interobserver repeatability study
Mean aPWV using distance A was 5.2 ± 1.4 m/s for all participants, 4.3 ± 0.6 m/s for children and 6.4 ± 1.3 m/s for adults. Mean difference between the observers’ measurements was 0.2 ± 0.6 m/s. CV between three observers was 5.8%, ICC was 0.5. The LoA was −1.0 to 1.4 m/s (Figure 3).

Similar results for intra- and interobserver repeatability were found using distance B (see Figure 1 and Supplementary Figures S1 and S2 online).

Vicorder–SphygmoCor comparison study
Using distance A, mean aPWV was 4.8 ± 0.7 m/s for the SphygmoCor and 4.5 ± 0.6 m/s for the Vicorder. The mean difference of aPWV values between both devices was 0.4 ± 0.7 m/s (P < 0.001) and the mean percentage deviation was 13.0%. The Bland–Altman plot with the LoA ranging from −1.0 to 1.7 m/s reflects a good agreement between both methods (Figure 4a).

Using distance B, an even better agreement between both devices was seen with a lower percentage deviation of 11.8% and a LoA ranging from −1.0 to 1.6 m/s (Supplementary Figure S3).

Of note, the distance measurements are always longer for the Vicorder device. This is an inherent difference between the two instruments as the SphygmoCor records the pulse wave directly on the femoral artery as it traverses through the inguinal canal, whereas the Vicorder records a femoral wave form at the upper thigh where the cuff is applied. This is also reflected in the significant difference in transit time, that was 80.2 ± 11.1 ms for the SphygmoCor and 110.9 ± 11.6 ms for the Vicorder (P < 0.001).

As obesity and hypertension are associated with higher aPWV values, we reanalyzed the data set by including only individuals with either a body mass index below the 85th percentile of either a body mass index below the 85th percentile. Results showed that values from obese nor from hypertensive individuals resulted in outliers in the Bland–Altman plot (Supplementary Figures S4–S6).

DISCUSSION
This study shows that aPWV measurements in healthy children and adolescents obtained by the oscillometric Vicorder...
device are in good agreement with results from the conventional tonometric SphygmoCor that is currently most often used for aPWV measurements. Our results support the good intraobserver repeatability seen by others and extend these observations by showing also an excellent interobserver repeatability. Based on our findings we recommend measuring the distance from SSN to the femoral recording site (via Umb, rather than direct) and subtract the distance from SSN to carotid recording site.

Despite the good agreement between the measurements performed with the Vicorder and the SphygmoCor, aPWV values measured by Vicorder were significantly lower. Similar to what has been reported by others we found significantly higher transit times for the Vicorder compared to the SphygmoCor. Most of this difference is explained by the longer path that the pulse wave travels in case of the Vicorder device because of the different recording points. The remaining difference between both devices can probably be attributed to the different detection (tonometer vs. cuff) and recording systems (simultaneous vs. sequential) rather than to different algorithms for transit time calculation. When looking at these absolute differences between the Vicorder and the SphygmoCor, one has to realize that former comparison studies between different devices such as the SphygmoCor, the Complior, or the Arteriograph always have shown a shift toward higher or lower values depending on the device used. Interpretation of aPWV values therefore depends on the device and the distance used.

A low variation in intra- and interobserver repeatability is crucial for the use of any medical device for clinical and research use. Our results show that aPWV values obtained with the Vicorder device show an excellent intra- and interobserver repeatability. The intraobserver repeatability was very good with a CV of 5.6%, but is higher than what is presented by Hickson and colleagues. In their study, they found an intraobserver CV of 2.8% when three measurements were obtained within 15 min. In our intraobserver study, we measured the same children on three different occasions, which very well explains the greater variability, but probably reflects the daily clinical situation more appropriately. Contrary to these findings, a group from the Netherlands recently reported poor results with the Vicorder, mainly due to difficulties in recordings from the carotid site. The LoA for our measurements ranged from $-0.7$ to $1.2$ m/s meaning that differences below $-0.7$ m/s and $>1.2$ m/s are definitely due to real changes of arterial stiffness and do not reflect random variation. In a recently published study using the SphygmoCor device, the authors reported a CV of $<7\%$ and a significant difference between healthy and diabetic children of $1.3$ m/s, which could have been also detected using the Vicorder based on our data. Our study on interobserver repeatability resulted in a good CV of $5.8\%$ and the LoA reached from $-1.0$ to $1.4$ m/s. We were able to show that part of the variation is caused by variations in path length measurement (data shown in Supplementary Data online).

Even though carotid to femoral aPWV has an enormous impact on cardiovascular risk assessment within the past decades, there is no overall consensus on how to measure the distance traveled by the pulse wave. Any definition of the path length measured on the body surface should be the best estimate of the true length of the blood vessel that the pulse wave travels through. We and others showed that distance values are crucial for aPWV calculation, but are also an evident source of error. The simplest way to estimate the path length seems the direct measurement between the SSN and the femoral recording site. Therefore, this distance has been used in many of the epidemiological outcome studies in adults. Unfortunately this is subject to inherent variations based on the patients’ body shape, leg position (abducted or externally rotated), and potential variations in the angle of measurement used by the observer. An overestimation of aPWV by up to $30\%$ can result, but this can be reduced by subtracting the neck segment, i.e., the distance from SSN to carotid recording site. This is apparently closer to the true length of the aorta as proven by invasive and MRI measurements and is thereby proposed to be used on all aPWV measurements for the purpose of standardization.

In addition, current reports suggest that this length (our distance A) is clinically most relevant. Because of the greater variation in body segments in children and to best describe the aortic tree, we chose to additionally partition the distance between the SSN and the femoral recording site by two distance measurements from SSN to Umb and from Umb to the femoral recording site (our distance B). Using this approach, we found the least variation between the two devices.

After using the Vicorder and the SphygmoCor in a large cohort of healthy young individuals, we found the Vicorder relatively easy to use and that it was as well tolerated as the SphygmoCor by children and adolescents. Results were in very good agreement with the currently most often used and established method and proved to be highly reproducible with a reasonable amount of training. Thus, the Vicorder device seems to be suitable for use in children in a clinical setting and in large population based studies.

The Vicorder device might be useful in detecting early target organ damage and could help to select patients at high risk for cardiovascular disease in the clinical setting with patients of all ages. It could contribute to reach the goal of several International Societies to promote the use of arterial stiffness as a standard tool for clinicians and as a surrogate end point for therapy modification and initiation of secondary prevention strategies. Since significant differences in aPWV of the two major devices SphygmoCor and Complior have been stated to be clinically relevant, values gathered by different techniques are clearly not interchangeable. It is obvious that apart from the recently published aPWV normal values for children and young adults using the PulsePen device and the large normal value database created with several devices throughout Europe, normal values with age and height percentiles have to be gathered for pediatric patients of all ages for different devices. This study should encourage pediatricians to cooperate across borders to generate a database for children, promoting clinical use of arterial stiffness measurement for high-risk groups.
Supplementary material is linked to the online version of the paper at http://www.nature.com/ajh

Acknowledgments: We are indebted to our fellow working group members Ingrid Fleischmann, Meike Hömme, Birgit Berenkamp, Margit Überheide, Carolin Schilthorn, Julian Lünig, and Ulrike Drenenberg for their contribution to the success of this comparison study at the public school site in Hannover. We also thank our colleagues Doris Franke, Mikro Zviniaik, Lars Pape, and Jochen Ehrich and their children as well as all the children and adolescents from the Integrierte Gesamtschule Roderbruch for their participation. This work was supported by Federal Ministry of Education and Research (reference number: 01EO08002), the KfH-Stiftung Präventivmedizin, ERA-EHTA. For the large comparison study in children and adolescents that was carried out by the investigators from Hannover Medical School, each of the two local suppliers (AtCor Medical as well as SMT Medical) provided one additional device (SphygmoCor and Vicorder) for study purposes.

Disclosure: We have no association with the investors, manufacturers, or distributors of SphygmoCor or Vicorder. The authors declared no conflict of interest.


