Comparative Analysis of American Heart Association and European Society of Hypertension Ambulatory Blood Pressure Thresholds for Diagnosing Hypertension in Children.

Ajaya Sharma
ashar269@uwo.ca

Luis Altamirano-Diaz
Western University, laltamir@uwo.ca

Michael Grattan
mgratta@uwo.ca

Guido Filler
gfiller@uwo.ca

Ajay P Sharma
asharm57@uwo.ca

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Comparative Analysis of American Heart Association and European Society of Hypertension Ambulatory Blood Pressure Thresholds for Diagnosing Hypertension in Children

Ajaya Sharma1, Luis Altamirano-Diaz1,2,3, Michael Grattan1,2,3, Guido Filler1,3,4 and Ajay P. Sharma1,3,4

1Faculty of Medical Sciences, University of Western Ontario, London, Ontario, Canada; 2Division of Cardiology, London Health Sciences Centre, London, Ontario, Canada; 3Department of Paediatrics, London Health Sciences Centre, London, Ontario, Canada; and 4Division of Nephrology, London Health Sciences Centre, London, Ontario, Canada

Introduction: The influence of using 24-hour ambulatory blood pressure (ABP) thresholds recommended by the American Heart Association (AHA) (24-hour mean ABP >95th percentile and ABP load >25%) or the European Society of Hypertension (ESH) (mean 24-hour ABP >95th percentile or >130/80 mm Hg if mean ABP 95th percentile exceeds 130/80 mm Hg) on the diagnosis of pediatric hypertension has been understudied.

Methods: In a cross-sectional, retrospective study of 159 children from a tertiary care outpatient clinic, we classified office blood pressure (OBP) as normotension or hypertension based on the OBP thresholds recommended by the American Academy of Pediatrics (AAP) and the fourth report on the diagnosis, evaluation, and treatment of high blood pressure in children and adolescents (herein referred to as the fourth report) by the National High Blood Pressure Educational Program Working Group on High Blood Pressure in Children and Adolescents separately. Thereafter, we evaluated the agreement between the ambulatory AHA and ESH thresholds for diagnosing normotension, white-coat hypertension (WCH), masked hypertension (MH), and hypertension based on the patient’s ABP and OBP hypertension pattern.

Results: With office hypertension as per the AAP thresholds, the AHA and ESH thresholds classified 85% of subjects similarly into normotension, WCH, MH, and hypertension (κ = 0.78; 95% CI, 0.67–0.89). The agreement between the AHA and ESH thresholds did not change when OBP was reclassified by the fourth-report OBP thresholds (κ = 0.77; 95% CI, 0.65–0.88). With OBP classified by either AAP or fourth-report thresholds, the ESH thresholds diagnosed 6% to 7% more children as hypertensive, whereas the AHA threshold classified 11% more children as normotensive.

Conclusion: The AHA and ESH thresholds have good agreement in classifying OBP. However, the ESH threshold classifies more OBP as hypertensive and the AHA threshold classifies more OBP as normotensive.

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Office blood pressure (OBP) is the most commonly used tool to diagnose office hypertension in children. The OBP thresholds of the fourth report on the diagnosis, evaluation, and treatment of high blood pressure in children and adolescents (herein referred to as the fourth report) by the National High Blood Pressure Educational Program Working Group on High Blood Pressure in Children and Adolescents have been widely used to classify OBP as normotension or hypertension. However, recently the American Academy of Pediatrics (AAP) guidelines have recommended new OBP thresholds to diagnose office hypertension. In
addition to OBP, the AAP guidelines also endorsed the use of 24-hour ambulatory blood pressure monitoring (ABPM) to measure ambulatory blood pressure (ABP), which helps in further classifying OBP into normotension, white-coat hypertension (WCH), masked hypertension (MH), and hypertension. Using both OBP and ABP, patients can be classified into normotension (normal OBP and normal ABP), WCH (high OBP and normal ABP), MH (normal OBP and high ABP), and hypertension (high OBP and high ABP). In clinical practice, blood pressure medications are usually prescribed to treat only MH and hypertension.

The ABP thresholds used to diagnose ABP hypertension on 24-hour ABPM in children are different from those used to diagnose OBP hypertension. The ABP thresholds recommended by the American Heart Association (AHA) and European Society of Hypertension (ESH) are commonly used in clinical practice. The AHA threshold is based on mean 24-hour ABP $>95^{th}$ percentile and 24-hour ABP load $>25\%$. The ESH threshold is based on 24-hour mean ABP $>95^{th}$ percentile or ABP $>130/80$ mm Hg if the 24-hour mean ABP $>95^{th}$ percentile exceeds 130/80 mm Hg. Both the AHA and ESH guidelines recommend the use of ambulatory normative data initially reported by Sorgel et al. and later modified by Wuhl et al. to estimate a patient’s 24-hour mean ABP 95th percentile. The agreement between the AHA and ESH thresholds to diagnose ambulatory hypertension on 24-hour ABPM or to classify OBP into normotensive, WCH, MH, or hypertension based on the patient’s office hypertension and ambulatory hypertension pattern has remained understudied.

Therefore, our main objective was to evaluate the agreement between the AHA and ESH thresholds to diagnose ambulatory hypertension and to classify OBP into normotensive, WCH, MH, and hypertension. Based on the different thresholds, we hypothesized that a proportion of patients would be classified differently.

**METHODS**

This was a single-center, retrospective, cross-sectional study that was performed as a post hoc analysis from previously performed studies. The study involved the retrospective review of existing clinical data and was therefore considered to be exempt from the need for individual informed consent. The records of children and adolescents up to 18 years of age referred to a tertiary care outpatient hypertension clinic (London, ON, Canada) between January 2003 and December 2008 were collected. All patients older than 5 years of age in this clinic are offered routine ABPM. A standard protocol recommended by the fourth-report guidelines have been used to evaluate patients for secondary hypertension. Those who had an ABP assessment as a part of initial evaluation for hypertension were included. Those who were already on an antihypertensive medication, had less than 2 OBP recordings, had an inadequate ABPM study, or manifested a secondary etiology of hypertension on workup were excluded. Demographic data collected in patients included age at evaluation, sex, height, weight, and body mass index. Body mass index (BMI) percentiles were calculated based on the Centers for Disease Control and Prevention reference intervals ( overweight: 85th–95th percentiles; obese: $>95^{th}$ percentile).

**OBP Measurement**

The standard protocol in our hypertension clinic consists of 3 OBP measurements, which were obtained by a trained nurse using an appropriate-sized cuff, with the individual rested and seated. Elevated OBP measurement by the automated oscillometric device (V 100, Dinamap, Tampa, FL) was confirmed using the auscultatory method with a calibrated aneroid sphygmomanometer. The average of the last 2 OBP readings was used for analysis.

**ABPM Measurement**

Twenty-four-hour ABPM was performed with an oscillometric ambulatory BP monitor (model 90207 Spacelabs, Inc, Redmond, WA), which has been validated in children. A trained staff member chose an appropriate-sized cuff and supervised the ABPM per a standard protocol. The ABPM recording was considered to be successful if at least 80% valid ABPM readings, with a minimum of 1 reading per hour, were obtained during day and night. The ABP on each patient was analyzed for mean ABP and ABP load during 24 hours, and separate day and night periods. The ABP load was calculated as the percentage of ABP measurements that exceeded ABP $>95^{th}$ percentile according to the ABPM references.

**Definitions**

Definitions were as follows: (i) normal OBP: systolic or diastolic OBP less than the age-, sex-, and height-specific 95th percentile values classified by the fourth-report OBP tables and AAP thresholds separately; (ii) normal ABP: systolic or diastolic ABP less than the age-, gender-, and height-specific 95th percentile values on 24-hour mean ABP as per pediatric ABPM normative data; (iii) normotensive: normal OBP classified by the fourth-report or AAP thresholds separately and normal ABP as per AHA or ESH thresholds; (iv) white-coat hypertension (WCH):...
elevated OBP and normal ABP; and (v) masked hypertension: normal OBP and elevated ABP; hypertension: elevated OBP and elevated ABP.

**Statistical Methods**

Normality of continuous numerical data was assessed using the Kolmogorov–Smirnov test, and appropriate parametric or nonparametric methods were chosen based on the distribution. Categorical variables were compared with a \( \chi^2 \) test and continuous variables with the parametric an unpaired \( t \) test or the nonparametric Mann–Whitney U test, as appropriate. Systolic and diastolic OBP \( z \) scores and percentiles for the study subjects were calculated using the computation methodology recommended by the fourth report \(^1\) and by Rosner et al., \(^11\) as recommended by the AAP guidelines. \(^5\) The ABP \( z \) score and ABP percentile were calculated based on the ABP references by Wuhl et al. using Box–Cox transformations with age- and sex-specific estimates of the distribution median (\( M \)), coefficient of variation (\( S \)), and degree of skewness (\( L \)). \(^7\) The agreement between the ambulatory hypertension classified by the AHA and ESH threshold was estimated by the area under the curve (AUC) calculation. The AHA threshold was calculated based on 24-hour mean ABP 95th percentile and 24-hour ABP load 25%. \(^4\) The ESH threshold was calculated based on 24-hour mean ABP 95th percentile or ABP 130/80 mm Hg if 24-hour mean ABP >95th percentile exceeded 130/80 mm Hg. \(^3\) The agreement between the AHA and ESH thresholds for classifying OBP into normotensive, WCH, MH, and hypertension was evaluated by using the \( K \) coefficient and 95% confidence intervals (CIs). The \( K \) coefficient was graded per the previously published method \(^12\): 0–0.20 slight, 0.21–0.40 fair, 0.41–0.60 moderate, 0.61–0.80 good, and 0.81–1.0 very good. The \( K \) statistics and accuracy were calculated on Medcalc version 18.11 (MedCalc Software bvba, Mariakerke, Belgium). All other statistical analysis was performed IBM SPSS Statistics for Windows, version 25.0 (IBM Corp., Armonk, NY).

**RESULTS**

**Study Sample Selection and Patient Characteristics**

In the initial screening, 234 subjects who had ABPM studies during the recruitment period met inclusion criteria. Of these, 75 were excluded because of the exclusion criteria (Figure 1). The final study sample included 159 subjects, aged 5 to 18 years, with 57% of subjects ≥13 years, 40% female, and 54% overweight and/or obese subjects.

The AAP thresholds classified 57 subjects (36%; 95% CI, 27%–46%) as having office hypertension, whereas the fourth-report threshold classified 53 subjects (33%; 95% CI, 25%–44%) as having office hypertension (AUC = 0.98; 95% CI, 0.94–0.99). Of subjects <13 years of age, 42% (95% CI, 29%–61%) had office hypertension as per the AAP thresholds, and 41% (95% CI, 27%–60%) by the fourth-report thresholds. In subjects ≥13 years, 30% (95% CI, 20%–44%) had office hypertension as per the AAP thresholds and 27% (95% CI, 18%–41%) by the fourth-report thresholds. The patient characteristics are shown in Table 1. \(^12\) The groups with office normotension and hypertension as per the AAP and

![Subjects included in final analysis, n = 159](image)

**Figure 1.** Study sample selection. ABPM, ambulatory blood pressure monitoring. OBP, office blood pressure.

**Table 1. Patient Characteristics**

| Characteristic                  | Office normotension | Office hypertension | Office normotension | Office hypertension |
|--------------------------------|---------------------|---------------------|---------------------|---------------------|
| Age, yr, mean (SD)             | 13.26 (3.76)        | 12.49 (4.26)        | 13.32 (3.73)        | 12.31 (4.32)        |
| Age <13 yr, n = 68, n (%)      | 39 (38)             | 29 (51)             | 40 (38)             | 28 (53)             |
| Age ≥13 yr, n = 91, n (%)      | 63 (62)             | 28 (49)             | 66 (62)             | 25 (47)             |
| Male, n = 96, n (%)            | 64 (63)             | 32 (56)             | 67 (63)             | 29 (55)             |
| Female, n = 63, n (%)          | 38 (37)             | 25 (44)             | 39 (37)             | 24 (45)             |
| BMI z score, mean (SD)         | 0.95 (1.13)         | 1.15 (1.19)         | 0.93 (1.14)         | 1.19 (1.16)         |
| Normal BMI, n = 73, n (%)      | 49 (48)             | 24 (42)             | 52 (49)             | 21 (40)             |
| Overweight and/or obese, n = 66, n (%) | 53 (52) | 33 (58) | 54 (51) | 32 (60) |

AAP, American academy of Pediatrics; BMI, body mass index; Fourth report, fourth report on the diagnosis, evaluation, and treatment of high blood pressure in children and adolescents by the National High Blood Pressure Educational Program Working Group on High Blood Pressure in Children and Adolescents; OBP, office blood pressure.

*Definitions: AAP OBP threshold: OBP threshold proposed by AAP guidelines; fourth-report OBP threshold: OBP threshold proposed by fourth-report guidelines.*
fourth-report thresholds had an equal representation of adolescents, female subjects, and overweight and/or obese subjects. However, the adolescents ≥13 years had a higher representation of male subjects (63% vs. 49%) and overweight and/or obese subjects (62% vs. 47%) than those <13 years of age.

**Diagnosis of Ambulatory Hypertension by the AHA and ESH Thresholds**

The agreement between the AHA and ESH thresholds for classifying ABP on ABPM is shown in Table 2. Both the AHA and ESH thresholds classified 90% subjects similarly for diagnosing ambulatory hypertension (AUC = 0.90; 95% CI, 0.84–0.94; P < 0.001). The ESH threshold required the use of ABP >130/80 mm Hg in 25 subjects (16%; 95% CI, 10%–23%) who were ≥13 years. The AUC for classifying ABP was separately analyzed based on the age (<13 years vs. ≥13 years), sex and BMI (normal weight vs. overweight and/or obese). The AUC between the AHA and ESH thresholds remained largely unchanged on subgroup analysis. However, the AUC between the AHA and ESH thresholds was relatively higher in subjects <13 years, in female subjects, and in normal weight subjects.

**Classification of OBP by the AHA and ESH Thresholds**

The agreement between the AHA and ESH thresholds for classifying OBP into normotension, WCH, MH, and hypertension is shown in Table 3. With OBP classified by the AAP thresholds, the AHA and ESH thresholds classified 85% subjects similarly (K = 0.78; 95% CI, 0.67–0.89). The agreement between the AHA and ESH thresholds did not change when OBP was reclassified based on the fourth-report OBP thresholds (K = 0.77; 95% CI, 0.65–0.88). As shown in Table 3, the agreement between the AHA and ESH thresholds remained largely unchanged for classifying OBP in subgroup analysis based on age (age <13 years vs. ≥13 years), sex, and BMI (normal weight, overweight and/or obese) when either AAP or fourth-report thresholds classified OBP.

Among subgroups, we found stronger agreement between the AHA and ESH thresholds in subjects <13 years, with 90% subjects classified similarly (K = 0.87; 95% CI, 0.74–0.99 by the AAP thresholds, and K = 0.86; 95% CI, 0.73–0.99 by the fourth-report thresholds) as compared to those ≥13 years, with 81% subjects classified similarly (K = 0.69; 95% CI, 0.52–0.86 by the AAP thresholds, and K = 0.65; 95% CI, 0.46–0.85 by the fourth-report thresholds). The female subjects had stronger agreement between the AHA and the ESH thresholds (K = 0.90; 95% CI, 0.81–0.98 by the AAP thresholds, and K = 0.86; 95% CI, 0.72–1.00 by the fourth-report thresholds) than the male subjects (K = 0.70; 95% CI, 0.53–0.86 by the AAP thresholds, and K = 0.70; 95% CI, 0.53–0.87 by the fourth-report thresholds). Similarly, normal weight children had a stronger agreement between the AHA and ESH thresholds (K = 0.87; 95% CI, 0.78–0.97 by the AAP thresholds, and K = 0.83; 95% CI, 0.68–0.97 by the fourth-report thresholds) than the overweight and/or obese children (K = 0.71; 95% CI, 0.53–0.88 by the AAP thresholds, and K = 0.72; 95% CI, 0.55–0.89 by the fourth-report thresholds).

We then analyzed the difference in the classification of OBP by the AHA and ESH thresholds. As compared with the AHA thresholds, the ESH thresholds diagnosed 6% more children with hypertension when the AAP thresholds classified OBP and 7% more children with hypertension when the fourth-report OBP thresholds classified OBP. The increase in the diagnosis of hypertension remained consistent in subgroup analysis based on age, sex, and BMI (Table 3). The diagnosis of WCH by the AHA and ESH thresholds was similar except for 4% higher WCH by the ESH thresholds in female subjects. Masked hypertension was diagnosed more frequently by the ESH threshold, by 2% to 5%. On the contrary, the AHA threshold classified more children as normotensive, by 11%, with OBP classified by either AAP thresholds or fourth-report OBP thresholds.

**DISCUSSION**

The results from the current study showed that the use of AHA and ESH thresholds to interpret 24-ABPM have a good agreement for diagnosing normotension, WCH, MH, and hypertension, when the office hypertension was diagnosed by either AAP or fourth-report OBP thresholds. The agreement between the 2 ABP thresholds remained relatively stronger in children younger than 13 years. However, the ESH thresholds classified more subjects with hypertension and MH than the
AHA thresholds, and the AHA thresholds diagnosed more subjects with normotension than the ESH thresholds. We are unaware of any previous study that compared the AHA and ESH thresholds for diagnosing hypertension in children.

The good agreement between the 2 ABP thresholds can be explained by the use of $95^{th}$ ABP percentile in both AHA and ESH thresholds. The $95^{th}$ ABP percentile for these ABP thresholds in turn is based on the common German ABP data reported by Sorgel et al.6 and Wuhl et al.7 Based on the AUC, both the ABP thresholds diagnosed ambulatory hypertension on ABPM similarly in 90% of subjects. Consequently, the good agreement between the 2 ABP thresholds to diagnose ambulatory hypertension translated into a similar diagnosis of normotension, WCH, MH, and hypertension when patients’ ambulatory and office hypertension were analyzed together. The good agreement between the AHA and ESH thresholds despite the use of either AAP or fourth-report OBP thresholds for diagnosing office hypertension was a significant observation in our study, given the previous studies demonstrating 3% to 5% more OBP hypertension by the AAP thresholds than the fourth-report thresholds.13–16 These studies did not evaluate the influence of 24-hour ABPM on further characterization of OBP. Although we also found a consistent increase in OBP hypertension by the AAP thresholds

Table 3. Agreement between AHA and ESH thresholds for classifying OBP (classified by the AAP and fourth-report OBP thresholds) into normotension, white-coat hypertension (WCH), masked hypertension (MH), and hypertension ($n = 159$)

| Characteristics | OBP classified similarly by AHA and ESH thresholds, n (%) | OBP classified as hypertension by AHA thresholds, n (%) | OBP classified as hypertension by ESH thresholds, n (%) | OBP classified as WCH by AHA thresholds, n (%) | OBP classified as WCH by ESH thresholds, n (%) | OBP classified as MH AHA thresholds, n (%) | OBP classified as MH ESH thresholds, n (%) | OBP classified as normal by AHA thresholds, n (%) | OBP classified as normal by ESH thresholds, n (%) |
|-----------------|----------------------------------------------------------|-------------------------------------------------------|-------------------------------------------------------|---------------------------------------------|---------------------------------------------|---------------------------------------------|---------------------------------------------|-------------------------------------------------|---------------------------------------------|
| Whole group, n = 159 | 135 (85) | 36 (23) | 48 (29) | 22 (14) | 24 (15) | 28 (18) | 34 (21) | 73 (46) | 55 (35) |
| Age <13 yr, n = 68 | 61 (90) | 22 (32) | 25 (37) | 9 (13) | 11 (16) | 11 (16) | 12 (18) | 26 (38) | 20 (30) |
| Age ≥13 yr, n = 91 | 74 (81) | 14 (15) | 13 (14) | 13 (14) | 17 (19) | 22 (24) | 47 (52) | 35 (38) | |
| Male, n = 96 | 80 (83) | 18 (19) | 27 (28) | 14 (15) | 13 (14) | 19 (20) | 22 (23) | 45 (47) | 34 (35) |
| Female, n = 63 | 55 (87) | 18 (29) | 19 (30) | 8 (13) | 11 (17) | 9 (14) | 12 (19) | 28 (44) | 21 (33) |
| Normal weight, n = 73 | 64 (88) | 18 (25) | 21 (29) | 8 (11) | 10 (14) | 13 (18) | 15 (21) | 34 (47) | 27 (37) |
| Overweight and/or obese, n = 86 | 71 (83) | 18 (21) | 25 (29) | 14 (16) | 14 (16) | 15 (17) | 19 (22) | 39 (45) | 28 (33) |

AAP, American Academy of Pediatrics; AHA, American Heart Association; ESH, European Society of Hypertension; fourth report, on the diagnosis, evaluation, and treatment of high blood pressure in children and adolescents by the National High Blood Pressure Educational Program Working Group on High Blood Pressure in Children and Adolescents; OBP, office blood pressure.

*Definitions: AAP OBP thresholds: OBP thresholds proposed by AAP guidelines; fourth-report OBP thresholds: OBP thresholds proposed by fourth-report guidelines; AHA thresholds: mean 24-h mean ABP >$95^{th}$ percentile and 24-h ABP load >25%; ESH thresholds: 24-h mean ABP >$95^{th}$ percentile or ABP >130/80 mm Hg if 24-h mean ABP >$95^{th}$ percentile exceeds 130/80 mm Hg.*
over those diagnosed by the fourth-report thresholds, our observations suggest a relatively lesser role of diagnosing office hypertension by either OBP thresholds on further characterization of OBP into WCH, MH, normotension, and hypertension by the AHA or ESH thresholds on 24-hour ABPM.

Despite a good agreement between the AHA and ESH thresholds for classifying OBP, more children and adolescents were diagnosed as hypertensive by the ESH thresholds, whereas more children and adolescents were diagnosed as normotensive by the AHA thresholds. This difference is important as it has therapeutic implications, given that only those individuals with MH and hypertension, unlike WCH (despite office hypertension) are treated with blood pressure medications. The difference in the classification of OBP by the 2 ABP thresholds can be explained by the use of ABP load >25% in the AHA thresholds and fixed ABP threshold of 130/80 mm Hg if 24-hour mean ABP 95th percentile exceeds 130/80 mm Hg in the ESH thresholds. The use of a fixed ABP threshold in 16% of those individuals ≥13 years of age explains the widening difference in the agreement between the AHA and ESH thresholds in adolescent subjects. A higher representation of male and overweight and/or obese subjects in adolescents also weakened the agreement between the AHA and ESH thresholds in those ≥13 years. In the absence of outcome-based studies on the AHA and ESH thresholds, our observations suggest that the use of ESH threshold for classifying OBP will lead to more investigations pertaining to secondary etiologies of hypertension and greater use of antihypertensive medications, whereas the use of AHA threshold will diagnose fewer subjects with hypertension.

Strengths of our study included the consistent use of a standardized protocol and methodology for OBP and ABP measurement, as recommended by the fourth-report guidelines. As well, the OBP thresholds used to interpret OBP were those recommended by the fourth-report guidelines. Given the advent of new AAP thresholds, the reinterpretation of OBP measurements by the AAP thresholds is a strength of our study that makes our observations relevant to current practice. The ABP interpretation based on the ABPM references proposed by Wuhl et al. has been endorsed by the fourth-report and AAP recommendations. A homogenous study sample selection, with the exclusion of those individuals with secondary hypertension and those on antihypertensive medications, minimized the confounding effect arising from patient selection, therefore enhancing the validity of our observations for those with essential hypertension.

There were also multiple limitations of our study. The most important limitation was the lack of a comparative assessment of hypertension-induced target-organ damage as per the 2 ABP thresholds, which is not known at this point. Other limitations include a relatively small sample size, the retrospective nature of the study, and the fact that most of the study subjects were Caucasian, which may affect the generalizability of our observations to other ethnicities. The patient population, however, consisted of referrals to a tertiary care academic center for the assessment of hypertension. Therefore, the results should be generalized to a primary care population with caution. The exclusion of individuals on antihypertensive medications, to restrict the confounding effect of antihypertensive medications limits the applicability of our findings to those who are already on treatment. Similarly, the exclusion of those with secondary hypertension, to limit selection heterogeneity, restricts the generalizability of our findings to individuals with secondary hypertension.

We conclude that the AHA and ESH thresholds have a very good agreement for classifying OBP into normotension, WCH, MH, and hypertension, especially in children younger than 13 years. However, the ESH thresholds classify more subjects as having hypertension and MH, and the AHA threshold diagnoses more subjects with normotension. Future outcome-based studies are needed to establish the usefulness of the AHA and ESH thresholds for predicting hypertension-induced target-organ damage.

**DISCLOSURE**

All the authors declared no competing interests.

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