zero-zones as defined by the AAMI (20 mmHg for sBP and 12 mmHg for dBP)[3] results in the benchmarks being extended by 10 to 15 ± 18 mmHg for sBP and by 6 to 11 ± 14 mmHg for dBP. Would that still be a clinically acceptable bias?

None of the studies cited by Kim *et al.* applied this zero-zone, but simply calculated accuracy as the average (more or less beat-to-beat) difference between CNBP and IBP (for this example −9 mmHg for sBP and −3 mmHg for dBP). It is obvious that this omission has a profound negative impact on the reported accuracy and precision. In our view, the data should be, where possible, reanalyzed in the manner outlined in the AAMI standard. Comparison of the data with the AAMI benchmark standard without such "zero-zone" analysis is not appropriate.

Secondly, the original AAMI approach requires patients to be hemodynamically stable, so that the sphygmomanometer is able to deliver plausible values. Maximum allowable ranges of the zero-zones are exactly defined by AAMI and all data from a subject shall be excluded if the reference zero-zone is greater than the maximum ranges.[3] Establishing the accuracy of CNBP in hemodynamically unstable situations like induction of anesthesia[5,6] or even transfemoral aortic valve implantation procedures[7] provokes additional and challenging questions as to what is the appropriate methodology and what statistics to use? Including studies in the meta-analysis with data gained from unstable patients or patients' episodes may help explain the high variation in accuracy and precision results reported. As stated by Kim *et al.*, their inclusion criteria may limit the collective comparison of all studies in a single meta-analysis.

The need to continue to explore methodologies for the testing and evaluation of all BP monitoring devices under real-life clinical conditions is emphasized by the results reported by Wax *et al.*[8] They analyzed the difference between sphygmomanometer and IBP readings from 24,225 patients in daily clinical routine. The "real-world" average bias (SD) was −1 mmHg (16 mmHg) for sBP and 5 mmHg (11 mmHg) for dBP—without applying a zero-zone.

In conclusion, there is a growing clinical requirement for the noninvasive monitoring of continuous BP, fluid, and stroke volume. Such devices are now available to clinicians and are being used in increasing numbers. It is therefore of major importance to further discuss acceptable and reasonable continuous BP evaluation standards. A new evaluation standard should be defined taking into consideration the inherent beat-to-beat nature and trending capability of these new devices.

Competing Interests

CNSystems Medizintechnik AG (Graz, Austria) develops, manufactures, and markets the continuous noninvasive arterial pressure technology. LiDCO Ltd. (London, United Kingdom) has integrated the continuous noninvasive arterial pressure technology into their LiDCOrapid products. The authors are inventors and named on one or more patents of continuous noninvasive technology.

Drs. Fortin and O'Brien are CEOs and founders of their companies, receive salary, and have equity interests. Ms. Lerche and Dr. Flotzinger are employees of CNSystems AG.

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In Reply:

We thank Fortin *et al.* for the letter to the editor related to our recently published article.[1] We fully agree with their statements and we would like to thank them for seconding our main message: continuous noninvasive blood pressure monitoring systems are generating a lot of interest in our community and there is currently no accepted standard way to evaluate the clinical performance of these systems. We, in our meta-analysis, used the Association for the Advancement of Medical Instrumentation standards[2] only because it was cited by 15 of the 28 articles included. We fully acknowledged that this is probably a misleading way to analyze these systems but we wanted to stress this point to generate discussions and provoke some changes/improvements. Even more interesting to us is the fact that studies citing the Association for the Advancement of Medical Instrumentation standards did not subsequently follow them. Here again, we agree with Fortin *et al.*

We believe that the next actions should be undertaken to move the field forward:

1. Standards are needed for the evaluation of continuous noninvasive blood pressure monitoring systems.
2. These standards should probably define separate benchmarks for systolic, diastolic, and mean arterial pressure. Because systolic, diastolic, and mean arterial pressure are inherently different by nature, different acceptability threshold should be applied.
3. These standards should probably develop a methodology for assessing the trending ability of these systems. Because these systems will be used as continuous monitors in the clinical setting, their trending ability is as important as their instantaneous accuracy.
4. When such standards exist, clinician scientists should follow them carefully when conducting clinical studies testing these systems.

In conclusion, we would like to thank Fortin *et al.* for echoing our main message and reinforcing it. We truly believe that the development and validation of this next generation of blood pressure monitoring systems is promising, but will require close collaboration between industry, clinician scientist, and regulatory agencies to make them beneficial to our patients.

Competing Interests

Maxime Cannesson is a consultant for Edwards Lifesciences (Irvine, California), Covidien (Boulder, Colorado), Masimo Corp. (Irvine, California), ConMed (Irvine, California), and Philips Medical System (Suresnes, France). A Nexfin monitor (BMEYE B.V., Amsterdam, The Netherlands) and a CNAP monitor (CNSystems, Graz, Austria) were loaned to Maxime Cannesson and his research team in 2010. Maxime Cannesson publicly endorsed the Nexfin technology in a BMEYE newsletter. The other authors declare no competing interests.

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Inotrope Use in Cardiac Surgery: A Cause of Worse Outcomes, or Just a Marker of Patients Who Are at Risk?

To the Editor:

Although Dr. Nielsen *et al.*[1] are to be commended for their efforts to investigate the potential detrimental effects of inotropic therapy in cardiac surgery, we believe that methodological problems significantly limit the validity of their conclusions.

1. Insufficient information about the result of the matching process is provided, but enough to indicate what appears to be a significant flaw in methodology. First, their matching algorithm discarded a large number of both treatment and control patients (n = 6,005 patients were identified to be "included" in analysis; after propensity matching, only n = 2,340 [39%] remained). This implies a considerable lack of common support (overlap between the propensity score distributions of the two cohorts), which, even in the presence of a good match, increases risk of bias through unmeasured confounders and makes the estimate of the treatment effect unreliable.[2] Second, the authors cite Donald Rubin (coinventor of propensity score matching), but use only one of the three metrics he recommends to judge the quality of a match: absolute standardized difference. Neither the variance ratios of the propensity scores between groups, nor the ratio of variance of the residuals of each covariate is reported.[3,4] These are important, because the match is vulnerable to systematic differences in how the propensity scores were assigned. Finally, greedy matching depends on the order of patients, so it should be preceded by randomizing the order of patients in the dataset, which the authors do not report.
2. These design decisions in the propensity matching algorithm leave the study open to the possibility that these unmeasured confounders—and not the effect of inotropic therapy—are responsible for the observed outcome difference. Some variables were treated as overly simplistic dichotomous variables, which fail to capture important differences between patients, such that inotropic support may continue to act as nothing more than a marker for sicker patients with less well-functioning ventricles. Left ventricular ejection fraction was treated as a binary variable: less than or equal to 30% or greater than 30%. Therefore, their propensity matching would not differentiate between a patient with a baseline left ventricular ejection fraction of 35% and one with a baseline left ventricular ejection fraction of 65%. Duration of myocardial insult was captured only by cardiopulmonary bypass (CPB) time, again treated as a dichotomous variable (>120 min or ≤120 min). There are two problems with this decision: first, the need for inotropic support is more closely related to the duration of myocardial ischemia, *i.e.*, the aortic cross-clamp time, than the time on bypass. Although CPB time is correlated with cross-clamp time, different surgeons may adopt different temporal approaches to weaning from bypass such that two surgeons with the same cross-clamp time will have very different CPB times. Indeed, the use of CPB time without cross-clamp time would prevent differentiation of a patient who had no aortic cross-clamp and no myocardial ischemia (*e.g.*, a