

Non-invasive measurement of pulse pressure variation and systolic pressure variation using a finger cuff corresponds with intra-arterial measurement

B. Lansdorp^{1,2*}, D. Ouweneel¹, A. de Keijzer¹, J. G. van der Hoeven², J. Lemson² and P. Pickkers²

¹MIRA—Institute for Biomedical Technology and Technical Medicine, University of Twente, PO Box 217, 7500 AE Enschede, The Netherlands

²Department of Intensive Care, Radboud University Nijmegen Medical Centre, PO Box 9101, 6500 HB Nijmegen, The Netherlands

* Corresponding author. E-mail: b.lansdorp@utwente.nl

Editor's key points

- The Nexfin™ monitor is a new method for measuring pulse pressure variability and systolic pressure variation using a non-invasive finger cuff.
- Overall correlation between a finger cuff and direct arterial measurements was close.
- Fluid responsiveness was misclassified in a small proportion of patients.
- Further studies are required to confirm these data.

Background. Pulse pressure variation (PPV) and systolic pressure variation (SPV) are reliable predictors of fluid responsiveness in patients undergoing controlled mechanical ventilation. Currently, PPV and SPV are measured invasively and it is unknown if an arterial pressure (AP) signal obtained with a finger cuff can be used as an alternative. The aim of this study was to validate PPV and SPV measured using a finger cuff.

Methods. Patients receiving mechanical ventilation under sedation after cardiac artery bypass graft (CABG) surgery were included after arrival on the intensive care unit. AP was measured invasively in the radial artery and non-invasively using the finger cuff of the Nexfin™ monitor. I.V. fluid challenges were administered according to clinical need. The mean value of PPV and SVV was calculated before and after administration of a fluid challenge. Agreement of the calculated PPV and SPV from both methods was assessed using the Bland–Altman analysis.

Results. Nineteen patients were included and 28 volume challenges were analysed. Correlation between the two methods for PPV and SPV [mean (SD)=6.9 (4.3)% and 5.3 (2.6)%, respectively] was $r=0.96$ ($P<0.0001$) and $r=0.95$ ($P<0.0001$), respectively. The mean bias was -0.95% for PPV and -0.22% for SPV. Limits of agreement were -4.3% and 2.4% for PPV and -2.2% and 1.7% for SPV. The correlation between changes in PPV and SPV as a result of volume expansion measured by the two different methods was $r=0.88$ ($P<0.0001$) and $r=0.87$ ($P<0.0001$), respectively.

Conclusions. In patients receiving controlled mechanical ventilation after CABG, PPV and SPV can be measured reliably non-invasively using the inflatable finger cuff of the Nexfin™ monitor.

Keywords: blood pressure determination; diagnostic techniques and procedures; fluid therapy; haemodynamics; pulse pressure; systolic pressure

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I.V. volume expansion is frequently used in critically ill patients to improve tissue perfusion, but overzealous fluid administration may also be detrimental.^{1–4} Several predictors of fluid responsiveness are available to identify patients who may benefit from i.v. volume expansion indicated by an increase in cardiac stroke volume (responders) and to prevent hypervolaemia in patients who do not (non-responders). Among these, several studies have shown that dynamic indices are more reliable than traditional measures (e.g. central venous pressure and pulmonary capillary wedge pressure) to guide volume resuscitation in patients undergoing controlled mechanical ventilation.^{5–7} Dynamic indices quantify the cyclic changes in left and right ventricular preload and afterload⁸ by measuring, for example, the variation in pulse pressure (pulse pressure variation, PPV) or

systolic pressure (systolic pressure variation, SPV). Patients whose cardiac function is operating on the steep portion of the Frank–Starling curve are more likely to show an increase in these arterial pressure (AP) variations and benefit from i.v. fluid administration.⁹

Although dynamic indices such as PPV and SPV have proven their predictive value, they depended on direct intra-AP monitoring, which is a relative drawback. The ability to monitor PPV and SPV non-invasively may increase their clinical usefulness in patients without an arterial catheter, for example, in acute situations in the emergency room.

The Nexfin™ monitor (BMEYE, Amsterdam, The Netherlands) provides a continuous AP measurement using a finger cuff, based on the principle introduced by Penaz and colleagues.¹⁰ The method is based on the development of

the dynamic (pulsatile) unloading of the finger arterial walls using an inflatable finger cuff with a built-in photo-electric plethysmograph.^{11–13} In addition, the Nexfin monitor reconstructs the finger AP wave to a brachial artery wave by application of a filter¹⁴ which increases reliability in reflecting true AP.¹⁵

The aim of this study was to evaluate the reliability of PPV and SPV, calculated from the finger AP and the reconstructed brachial pressure in comparison with the gold standard of direct intra-AP measurement.

Methods

Patients

Because of the observational and non-invasive nature of this study, the local medical ethics board waived the need for informed consent. Twenty patients undergoing controlled mechanical ventilation after cardiac artery bypass graft (CABG) surgery were prospectively studied from the time of admission to the intensive care unit (ICU). Fluid challenges were administered by the attending physician based upon the presence of at least one clinical sign of inadequate tissue perfusion [low mean AP (MAP), low urine production, cold and clammy extremities, increased lactate level, or low central venous oxygen saturation]. We excluded patients who did not receive at least one fluid challenge, were showing spontaneous respiratory efforts, and those with an intra-aortic balloon pump.

Haemodynamic monitoring

In all patients, a central venous catheter was inserted into the internal jugular vein. Mechanical ventilation of the patients' lungs was performed using a Servo 300 ventilator (Maquet, Rasstat, Germany). Administration of vasoactive medications was guided by a standard clinical protocol.

AP was monitored invasively (AP_{IA}) using a 20 G radial artery catheter connected via standard low compliant tubing to a disposable pressure transducer (Edwards

Lifesciences, Irvine, CA, USA). The intra-arterial signal was registered using a HP monitor (Merlin M1046A, Hewlett Packard, USA). The non-invasive arterial signal was obtained using a finger cuff adjusted to the size of the index finger of the patient according to the guidelines of the manufacturer and connected to the Nexfin™ monitor [BMEYE Nexfin™ Monitor (BMEYE, Amsterdam, the Netherlands)]. This non-invasive measurement provides the AP in the finger arteries (AP_{FING}) and from this signal, the reconstructed AP in the brachial artery (AP_{BRACH}) is calculated. All three signals were recorded simultaneously using a sample rate of 200 Hz and stored on a hard disk. Figure 1 shows an example of the simultaneous recordings of the AP, together with a representation of the PPV and SPV.

From all the recorded waveforms, PPV and SPV were calculated offline using the mathematical computer program Matlab (Matlab R2009b, MathWorks Inc., MA, USA) using the following formula:

$$PPV = \frac{PP_{\max} - PP_{\min}}{PP_{\text{mean}}} \quad \text{and} \quad SPV = \frac{SP_{\max} - SP_{\min}}{SP_{\text{mean}}}$$

where PP and SP are the pulse pressure (systolic minus diastolic pressure) and systolic pressure, respectively. The subscripts max, min, and mean indicate, respectively, the average values of the four maximum, the four minimum, and all pulse pressures or systolic pressures during 30 s. This technique is also used by Pulsion (Pulsion Medical Systems, Munich, Germany) and Dräger (Dräger Medical, Lübeck, Germany) to calculate dynamic indices in the absence of respiratory data. The indices were detected automatically by an algorithm written in Matlab and were visually inspected offline for errors.

Design

To compare the calculation of the PPV and SPV from the non-invasive signal (PPV_{FING}/PPV_{BRACH} and SPV_{FING}/SPV_{BRACH}) with the signal from the intra-arterial catheter (PPV_{IA} and SPV_{IA}), measurements of AP were performed before and after each fluid challenge (130/0.4 6% HES solution—Volumen, Fresenius Kabi, 's-Hertogenbosch, the Netherlands) administered according to instructions of the attending physician. Infusion time and volume were registered.

The baseline measurement was performed over 30 s within the last minute before the start of the fluid challenge. The second measurement ('after VE') was performed within 3 min after the end of the infusion. To investigate the accuracy of the non-invasive method to monitor changes of the haemodynamic parameters over time, the change in PPV and SPV as a result of the fluid challenge (ΔPPV , ΔSPV) measured non-invasively was compared with the response calculated from the intra-arterial measurement.

Statistical analysis

Haemodynamic measurements are reported as mean [standard deviation (SD)]. Agreement between the two methods was assessed using the method described by Bland and

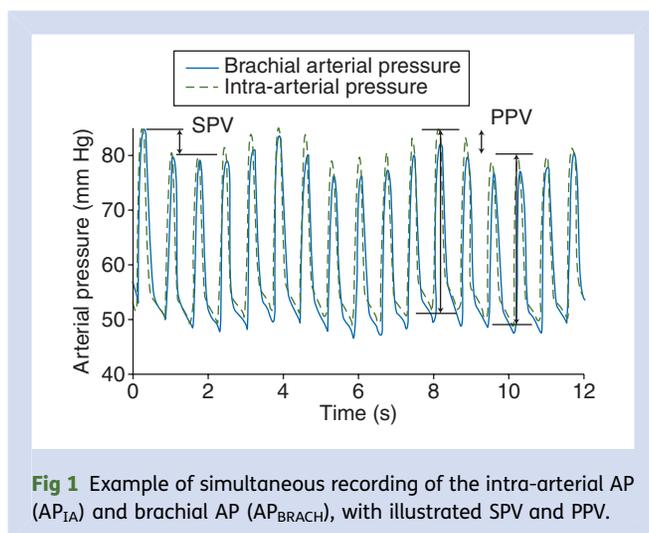


Fig 1 Example of simultaneous recording of the intra-arterial AP (AP_{IA}) and brachial AP (AP_{BRACH}), with illustrated SPV and PPV.

Altman.¹⁶ The correlation between PPV_{FING}/PPV_{BRACH} and PPV_{IA} and between SPV_{FING}/SPV_{BRACH} and SPV_{IA} was calculated using the Pearson correlation coefficient (r) after normality was checked and corrected for repeated measurements.¹⁷ To detect a correlation of at least 0.7 with a power of 90% and a P -value of 0.05, at least 18 individual measurements were needed. We therefore included 20 patients with the possibility of multiple measurements per patient. In addition, the bias (the difference between the two methods given by $PPV_{FING}/PPV_{BRACH} - PPV_{IA}$ and $SPV_{FING}/SPV_{BRACH} - SPV_{IA}$) was calculated and plotted against the average of the two different methods. Limits of agreement were calculated using the standard deviation of the differences (s) ($d - 1.96 s$ and $d + 1.96 s$), also corrected for multiple observations per individual.¹⁶ Finally, the standard errors and confidence intervals were calculated. Statistical analysis was done using SPSS Statistics 18.0 for windows (SPSS Inc., Chicago, IL, USA).

Results

A total of 30 fluid challenges were administered. Two fluid challenges were excluded because AP variations could not reliably be calculated, one because of arrhythmias and one because of a distorted signal due to incorrect placement of the finger cuff. Table 1 shows the characteristics of the remaining 19 patients and 28 fluid challenges. A total of 56 simultaneous PPV and SPV measurements were available for final analysis. A strong correlation was found between the dynamic indices derived from the intra-arterial waveform and those from the finger and reconstructed brachial waveform, for both the PPV and the SPV (Fig. 2). Figure 2 also shows that both SPV_{BRACH} and PPV_{BRACH} have only a few false positives and false negatives taking into account the previously published cut-off values regarding their predictive value for fluid responsiveness: 7% and 12% for SPV and PPV,⁶

Table 1 Patients characteristics and baseline haemodynamic and respiratory variables, presented as mean (range), mean (sd) or number

| | |
|---|-------------|
| Patients (#) | 19 |
| Male/Female (#) | 14/5 |
| Age (yr) | 66 (58–79) |
| Weight (kg) | 78.9 (15.0) |
| Heart rate (beats min^{-1}) | 66.0 (14.8) |
| Mean arterial pressure (mm Hg) | 70.0 (5.9) |
| Central venous pressure (mm Hg) | 10.1 (2.8) |
| Tidal volume (ml kg^{-1} IBW) | 7.6 (1.0) |
| Ventilatory frequency (bpm) | 12.1 (1.4) |
| PEEP (cm H_2O) | 5.7 (2.0) |
| Plateau pressure (cm H_2O) | 16.9 (2.7) |
| Intervention | |
| Number of fluid challenges (#) | 28 |
| Infusion volume (ml) | 390 (130) |
| Infusion duration (min) | 7.6 (6.5) |

respectively. This results in a sensitivity and specificity of 92% and 96% for SPV and 100% and 94% for PPV.

The mean (absolute) bias compared with the intra-arterial measurement was -0.95% and -0.22% for PPV_{BRACH} and SPV_{BRACH} , respectively. For PPV_{FING} and SPV_{FING} , the mean bias was -0.74% and -0.11% , respectively. The mean bias, including the relative bias, and the related limits of agreement are also shown in Table 2. The Bland–Altman plot of the absolute values of PPV_{IA} and PPV_{BRACH} and SPV_{IA} and SPV_{BRACH} is shown in Figure 3. There was no relationship between the difference and the mean value of the two measurement methods.

To study the ability of the non-invasive method to monitor changes of PPV and SPV over time, the change in PPV and SPV (ΔPPV and ΔSPV) caused by volume expansion was calculated for the measurement with the arterial catheter and the finger cuff. Correlation between ΔPPV and ΔSPV

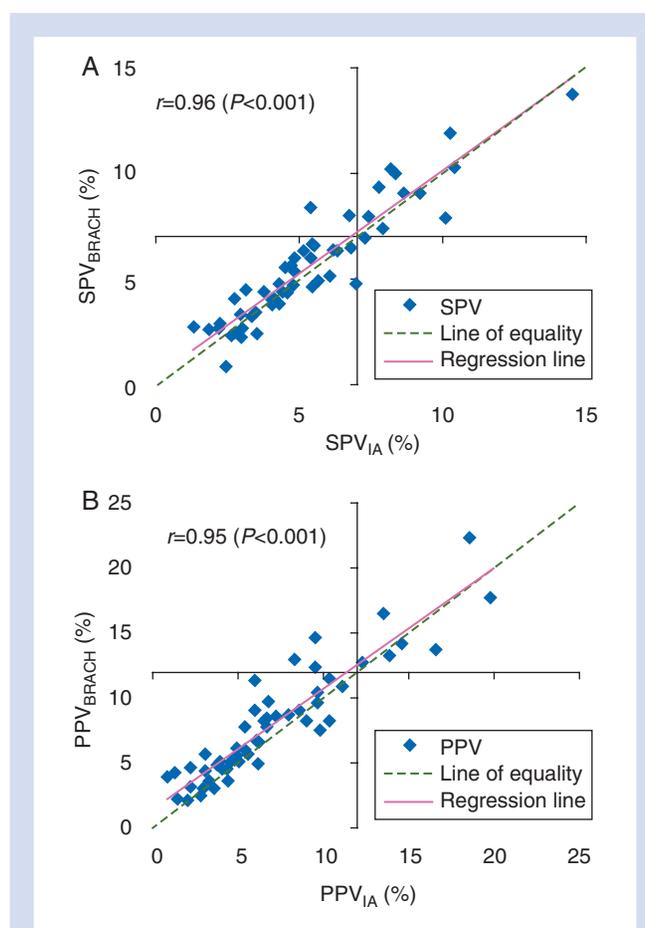


Fig 2 Correlation between SPV (A) and PPV (B) measured from the intra-arterial signal (SPV_{IA} and PPV_{IA}) and from the non-invasively measured reconstructed brachial pressure (SPV_{BRACH} and PPV_{BRACH}). Taking into account the previously published cut-off values for SPV and PPV regarding their predictive value for fluid responsiveness (7 and 12%, respectively, see axes), both SPV_{BRACH} and PPV_{BRACH} have only a few false positives and false negatives. This results in a sensitivity and specificity of 92% and 96% for SPV and 100% and 94% for PPV, respectively.

Table 2 Correlation coefficients and the Bland–Altman variables for the SPV and PPV measured from the non-invasively measured reconstructed brachial pressure (SPV_{BRACH} and PPV_{BRACH}) and the non-invasively measured finger pressure (SPV_{FING} and PPV_{FING}), both compared with the SPV and PPV measured from the intra-arterial signal (SPV_{IA} and PPV_{IA}). Correlation coefficients were significant (**P*<0.001). No significant differences were observed while comparing the correlation coefficients of SPV_{FING} and SPV_{BRACH} or PPV_{FING} and PPV_{BRACH}

| | PPV _{BRACH} | PPV _{FING} | SPV _{BRACH} | SPV _{FING} |
|--------------------------------------|----------------------|---------------------|----------------------|---------------------|
| Absolute value of PPV/SPV | | | | |
| Correlation coefficient (<i>r</i>) | 0.96* | 0.94* | 0.95* | 0.93* |
| Absolute mean bias (%) | -0.95 | -0.74 | -0.22 | -0.11 |
| Relative mean bias (%) | -12.9 | -10.1 | -4.1 | -2.0 |
| Limits of agreement (%) | ± 3.36 | ± 3.99 | ± 1.96 | ± 2.47 |
| Change in PPV/SPV | | | | |
| Correlation coefficient (<i>r</i>) | 0.88* | 0.82* | 0.87* | 0.78* |
| Absolute mean bias (%) | -0.33 | -0.21 | 0.07 | 0.31 |
| Limits of agreement (%) | ± 4.35 | ± 5.03 | ± 2.32 | ± 3.04 |

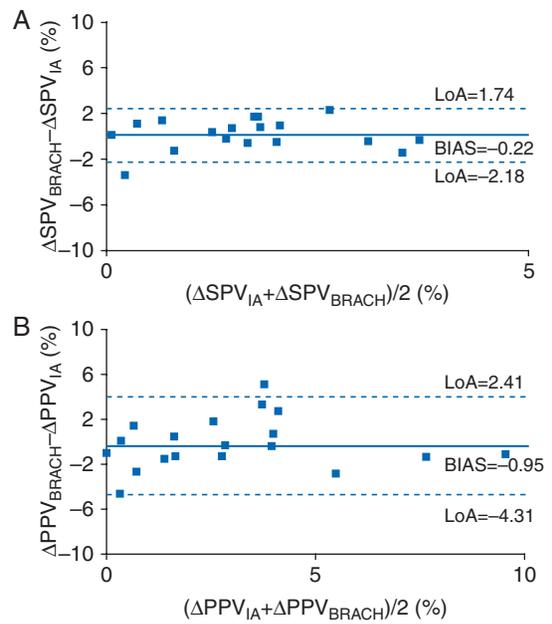


Fig 4 Mean bias [BIAS (%), solid line] and limits of agreement [LoA (%), dashed line] according to the Bland–Altman analyses. Comparison of the change in SPV (A) and PPV (B) as a result of the fluid challenge, measured from the intra-arterial signal (%SPV_{IA} and %PPV_{IA}) and from the non-invasively measured reconstructed brachial pressure (%SPV_{BRACH} and %PPV_{BRACH}).

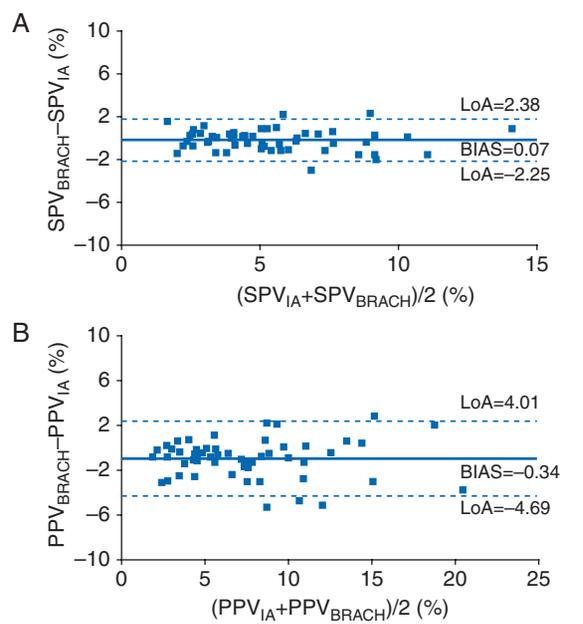


Fig 3 Mean bias [BIAS (%), solid line] and limits of agreement [LoA (%), dashed line] according to the Bland–Altman analyses. Comparison of the SPV (A) and PPV (B) measured from the intra-arterial signal (SPV_{IA} and PPV_{IA}) and from the non-invasively measured reconstructed brachial pressure (SPV_{BRACH} and PPV_{BRACH}).

measured from the intra-arterial signal (ΔPPV_{IA} and ΔSPV_{IA}) and from the non-invasively measured reconstructed brachial pressure (ΔPPV_{BRACH} and ΔSPV_{BRACH}) was 0.88 and 0.87 for PPV and SPV, respectively (both *P*<0.001). The corresponding Bland–Altman plots are shown in Figure 4. Correlation coefficients, including the mean bias and limits of agreement, are all displayed in Table 2. No significant differences were observed while comparing the correlation coefficients of SPV_{FING} and SPV_{BRACH} or PPV_{FING} and PPV_{BRACH}.

Discussion

This study indicates that the respiratory variations in pulse pressure and systolic pressure can be calculated reliably using a non-invasive finger AP measurement. Therefore, an arterial line may not be necessary to assess fluid responsiveness using dynamic indices. Only one other study describes the calculation of dynamic indices from the finger AP obtained non-invasively.¹⁸ In accordance with the results of this study, we found a small mean bias with similar limits of agreement for the PPV_{FING} compared with the PPV_{IA}. In addition, we used the reconstructed brachial pressure for the calculation of PPV and SPV. The resultant waveform of this signal is more similar to the invasively measured pressure in the radial artery and the reliability was further improved when the reconstructed brachial pressure signal was used, illustrated by a slightly higher correlation coefficient and narrower limits of agreement.

Over the past few years, other non-invasively obtained dynamic indices have been suggested as predictors for volume responsiveness, including pulse oximetry wave variation and the cyclic changes derived by Doppler echocardiography. In comparison with our results, the respiratory variations in pulse oximetry plethysmographic waveform amplitude show a less strong correlation coefficient with arterial PPV^{19 20} and wider limits of agreement.^{18 19} Respiratory variations in the diameter of the inferior vena cava visualized by echocardiography predict volume responsiveness with a positive predictive value of 93% and a negative predictive value of 92%.^{21 22} Sensitivity and specificity for variation of peak aortic blood velocity were 100% and 89%, respectively.^{23 24} Although these results are comparable with PPV and SPV determined via an arterial line or non-invasively as in our study, limitations of echo(cardio)graphy include high costs, training, and workload to perform the measurements.

Measuring the PPV and SPV without the need of an intra-arterial catheter is an advantage for patients undergoing surgery or in the emergency room who are undergoing mechanical ventilation but without an intra-arterial catheter *in situ*. The intra-arterial catheter waveform and subsequent pressure calculations are considered the gold standard. However, errors may occur resulting from both the catheter and fluid-filled tubing that transfers the pressure signal, while the finger pressure cuff has a more direct relation to the finger artery. Theoretically, the finger AP measurement may be more reliable on some occasions, but clinical experience is scarce.

It may also be useful to assess AP variations in patients breathing spontaneously. Recent findings show that dynamic indices can predict volume responsiveness in spontaneous breathing patients whether or not in combination with the passive leg raising test or the Valsalva manoeuvre.^{25–27} Although we investigated the validity of PPV and SPV in patients undergoing mechanical ventilation, we hypothesize that the origin (positive or negative airway pressure) of the AP variation does not influence the accuracy of the non-invasive measurement method.

We appreciate that there are several limitations in our study. First, because of the observational character of this study, we did not measure cardiac output. As it was not the aim of this study to confirm that dynamic indices predict fluid responsiveness as determined by an increase in cardiac output, we cannot draw any conclusions from our results about the predictive value regarding fluid responsiveness using the dynamic indices derived from the finger cuff. However, the predictive value of dynamic indices has been demonstrated previously and we found that non-invasive measurement had a high sensitivity and specificity in distinguishing presumed responders and non-responders defined by indices measured invasively. However, it is important to realize that three patients would have been misclassified using the non-invasive system and further data are required for clinical validation. Secondly, the 56 measurements that we used for comparison of the various methods were derived from 28 fluid challenges in 19 patients. To overcome this issue, we corrected the statistics for repeated

measurements per individual. Another potential limitation is the use of cardiac surgery patients, since they might not be representative for standard more general ICU population. Especially, since there have been concerns about the use of the Penaz techniques in general critical care patients with poor peripheral perfusion.²⁸ Nevertheless, in recent years, this technique has significantly been improved and appears also applicable in the critically ill.²⁹

In conclusion, PPV and SPV can be measured reliably in a non-invasive manner using a non-invasive finger AP measurement in ICU patients on controlled mechanical ventilation after CABG surgery.

Conflict of interest

None declared.

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