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# Stroke volume optimization in elective bowel surgery: a comparison between pulse power wave analysis (LiDCOrapid) and oesophageal Doppler (CardioQ)

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# **Editor's key points**

- LIDCOrapid was compared with CardioQ in predicting responsiveness to fluid challenges.
- Twenty patients undergoing elective bowel surgery were studied.
- The ability of LIDCOrapid to track changes in stroke volume as assessed by CardioQ was weak.
- Importantly, the authors conclude that LIDCOrapid and CardioQ are not interchangeable for stroke volume optimization.

**Background.** Goal-directed fluid therapy improves outcome in major surgery. We evaluated a new device (LiDCOrapid) against our standard oesophageal Doppler method (ODM) for stroke volume (SV) optimization during colorectal surgery.

**Methods.** This was an observational study in 20 patients undergoing major colorectal surgery within a fast-track protocol. We compared SV values measured simultaneously by LiDCOrapid and ODM before and after 86 fluid challenges. We also evaluated the LiDCOrapid dynamic indices SV variation (SVV) and pulse pressure variation (PPV) as predictors for volume responsiveness, defined as an increase in SV  $\geq$  10% after 200 ml of colloid.

**Results.** SV increased  $\geq$ 10% after 27 out of 86 fluid challenges. For 172 paired SV values, the overall correlation was r=0.39, and bias (limits of agreement) -28 (-91-35) ml, percentage error 70%. The ability of LiDCOrapid to track changes in SV was weak with a concordance rate of 80%, and a sensitivity and specificity of 48% and 81%, respectively, to detect a positive fluid challenge. The area under the curve values (with 95% confidence intervals) for SVV and PPV were 0.72 (0.60–0.83) and 0.66 (0.52–0.79), respectively, indicating low predictive capacity in these setting.

**Conclusions.** LiDCOrapid and ODM devices are <u>not interchangeable</u>. We <u>cannot recommend</u> that the <u>LiDCOrapid replace</u> the standard <u>Doppler</u> method until further device-specific outcome studies on volume optimization are available. The dynamic indices SVV and PPV add little value to a fluid optimization protocol, and should not replace SV measurements with a validated technique.

**Keywords:** fluid therapy; measurement techniques, cardiac output; stroke volume; surgery, abdominal

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Perioperative fluid management in colorectal surgery is challenging. Hypovolaemia and fluid overload are associated with an increased risk of complications.<sup>1</sup>

Standard haemodynamic parameters such as heart rate (HR), arterial pressure (AP), and central venous pressure are poor markers of hypovolaemia and cardiac output (CO), and are not reliable in detecting volume responsiveness.<sup>2</sup>

The use of oesophageal Doppler method (ODM) for SV optimization is validated in clinical practice and has been shown to reduce postoperative morbidity and hospital length of stay in colorectal surgery.<sup>3-6</sup> However, interference from electric cautery and poor tolerance in awake patients limit its use.

LiDCOrapid (LiDCO Ltd, Cambridge, UK) is a new, minimally invasive monitor for estimating beat-by-beat CO and volume responsiveness from the arterial waveform. Dynamic parameters such as pulse pressure variation (PPV) and stroke volume (SV) variation (SVV) have been shown to be good predictors of volume responsiveness in critically ill patients receiving mechanical ventilation.<sup>7</sup>

The aims of this study were first to compare SV measurements obtained using LiDCOrapid (SV<sub>Li</sub>) with those using ODM (SV<sub>ODM</sub>) in elective colorectal patients within a fast-track programme, secondly to evaluate the ability of LiDCOrapid to track changes after fluid challenges, and finally to determine the predictive value of SVV and PPV in these patients.

# Methods

This observational single-centre study was conducted at a large Scandinavian University Hospital. Data were collected prospectively from 20 patients undergoing major colorectal surgery over a 5 month period. The study was approved by

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Patients were managed in accordance with established clinical guidelines and no additional invasive procedures, blood samples, or treatments were necessary. For this reason, informed consent was waived by the Ethics Committee. Patients were excluded if under 18 yr of age or if they presented with a history of heart failure, valvular disease, arrhythmias, or any contraindications to ODM such as coagulopathy, oesophageal varices, or known aortic aneurysm.

Patients were prepared according to an ERAS (Early Recovery after Surgery) protocol.<sup>8</sup> Only patients having a low anterior rectal resection were given a preoperative bowel preparation. All but four patients received a carbohydraterich beverage before operation, typically 800 ml the night before and 400 ml 2 h before surgery.

#### Anaesthesia

All patients had a low thoracic epidural catheter inserted, and anaesthesia was then induced to the discretion of the attending physician. Typically, patients received a short-acting opioid in combination with pentothal (4–6 mg kg<sup>-1</sup>) or propofol (2–3 mg kg<sup>-1</sup>) and a non-depolarizing neuromuscular blocking agent such as rocuronium or atracurium (0.5–0.6 mg kg<sup>-1</sup>) before orotracheal intubation. Anaesthesia was maintained with sevoflurane at an age-corrected MAC (value) of 0.8– 1.2. The epidural was activated after the first SV optimization but before surgery. Additional short-acting opioids were administered as needed. A buffered glucose solution (25 mg ml<sup>-1</sup>) at a rate of 2–3 ml kg<sup>-1</sup> h<sup>-1</sup> was administered during anaesthesia to replace insensible loss. After volume optimization, norepinephrine was administered if necessary to achieve a mean AP (MAP) of above 60–70 mm Hg.

Patients were ventilated using tidal volumes of 6–8 ml kg<sup>-1</sup>, PEEP levels of 4–7 cm  $H_2O$ , and a respiratory rate of 10–15 bpm to maintain normoventilation, using a volume-controlled ventilation mode.

Routine perioperative monitoring included ECG, capnography, pulse oximetry, core temperature, airway pressure, and invasive AP obtained from a radial arterial catheter. Patients were kept normothermic using a forced-air warming mattress.

#### **Oesophageal Doppler**

The oesophageal Doppler (CardioQ-ODM<sup>TM</sup>; Deltex Medical, Chichester, UK) uses an ultrasound probe inserted into the oesophagus to measure blood flow in the descending thoracic aorta. Total left ventricular SV is calculated as the product of the velocity-time integral (representing the distance travelled down the descending thoracic aorta with each ventricular stroke) and a calibration factor derived from a nomogram based on the patient's age, height, and weight.<sup>9</sup>

#### LiDCOrapid

The LiDCO system (LiDCO Ltd) is based on a PulseCO algorithm<sup>10</sup> for calculating nominal SV from AP waveform

characteristics. In the LiDCOplus system, the nominal SV is calibrated using a lithium dilution technique to generate a true SV, whereas the recently developed LiDCOrapid studied here makes use of a nomogram-based estimate (scaling factor) that incorporates patient age, height, and weight to calibrate the nominal SV. This scaling factor was derived from calibration data in post-surgical patients *in vivo*. The LiDCOrapid measures SV on a beat-by-beat basis and can therefore display respiratory-induced changes, presented as the dynamic indices SVV and PPV.

#### **Data collection**

Simultaneous haemodynamic data from the two monitors were recorded independently throughout the study period. An oesophageal Doppler probe (DP24; Deltex Medical) was lubricated and inserted after the induction of anaesthesia. The probe was connected to the CardioQ monitor, advanced 35–40 cm, and manipulated by slight rotation until an optimal Doppler signal was obtained. SV values were calculated as the average of 10 consecutive heart cycles to minimize possible respiratory variability. Haemodynamic variables were registered manually and in addition saved on the ODM software.

All measurements were performed by the authors or a consultant anaesthetist well experienced in ODM.

The LiDCOrapid was connected to the Datex monitor to extract data from the AP line. Values for AP and HR were compared with those on the Datex monitor and were in all patients within 5% of the primary monitor's displayed values.

The LiDCOrapid was turned away from the attending anaesthetist and used only for monitoring. Values were calculated by the LiDCO monitor as an average from the pressure waveform over a 20 s period. The quality of the AP waveform was regularly checked for under- and overdamping. Values for SVV and PPV were excluded if HR variation exceeded 10%, as measured by the LiDCO monitor.

#### Statistical analysis

The distributions were tested for normality using the Kolmogorov-Smirnov test. Data are presented as mean (sD), median (range), or number (%) as appropriate. Patients were divided into two groups according to the percentage increase in SV after a fluid bolus. Responders were defined as patients with an increase of 10% or more in SV, and nonresponders as patients with <10% increase. Changes in SV induced by fluid boluses, and comparisons of means between the groups were analysed using a two-sided paired and unpaired Student's *t*-test, respectively.

Several methods were used to determine the agreement between  $SV_{ODM}$  and  $SV_{Li}$ . First, the Pearson correlation coefficient (*r*) was calculated for absolute SV values and for SV changes after a fluid challenge. The Bland – Altman analysis<sup>11</sup> was used to assess the bias (mean difference) and precision (95% CI of the bias) of  $SV_{ODM}$  and  $SV_{Li}$ , and also the percentage error (2 sp of the difference divided by the mean SV).<sup>12</sup> There was no correction for repeated measurements. To further assess the trending ability of SV<sub>Li</sub>, we used fourquadrant plots for analysis of concordance (the percentage of the total number of data points plotted in one of the two quadrants of agreement).<sup>13</sup> Central data points correspond to small changes in SV and reflect random measurement errors rather than trending ability. Therefore, an exclusion zone of 10% was used.<sup>13</sup> A contingency table was constructed to determine the specificity and sensitivity for the LiDCO device to detect a positive fluid response. The relationship between changes in SV and MAP after a fluid challenge was determined using linear regression.

To assess the predictive capacity of SVV and PPV, receiver operating characteristic analyses were performed and the area under the curve (AUC) was calculated. The optimal threshold values were calculated from the highest sum of the sensitivity and specificity. We also used an alternative approach suggested by Cannesson and collegues<sup>14</sup> that defines three classes of response: negative, inconclusive, and positive. Inconclusive responses were defined as values with a sensitivity or specificity lower than 90%, thus forming a grey zone where strict conclusions could not be drawn.

GraphPad Prism version 4.00 for Windows, GraphPad Software, San Diego, CA, USA, was used for statistical calculations.

#### Study protocol

After induction of anaesthesia but before start of surgery, a standardized optimization manoeuvre was conducted when haemodynamic stability was achieved. Haemodynamic stability was defined as a <10% variation in SV and AP over a period of 5 min. During the observation period, anaesthesia and ventilator settings were unchanged, no vasoactive drugs were administered and no postural changes were made.

Fluid loading was done using 200 ml of 6% hydroxyethyl starch solution (HES 130/04; Volulyte<sup>®</sup>; Fresenius Kabi, Uppsala, Sweden), or a dextran 60 solution (Plasmodex<sup>®</sup>; Meda, Solna, Sweden), administered over 3–5 min. Haemo-dynamic data were registered independently before and 1–2 min after volume administration. If SV<sub>ODM</sub> increased  $\geq$ 10%, the fluid challenge was considered positive and an additional fluid bolus was given.

After SV optimization was achieved, the epidural was activated and surgery subsequently commenced. During the course of surgery, optimization manoeuvres were repeated at the discretion of the anaesthetist.

## Results

A total of 20 patients were studied and their characteristics and intraoperative data are listed in Table 1.

In these patients, a total of 57 optimization manoeuvres (1–4 per patient) were performed. Each manoeuvre consisted of 1–3 fluid boluses, resulting in 86 fluid challenges and a total of 172 paired observations. Data from the initial optimization manoeuvre were omitted in one patient due to technical problems with the AP signal.

#### Stroke volume

Initial median (range)  $SV_{ODM}$  and  $SV_{Li}$  values were 80 (37–191) and 58 (29–102) ml, respectively, increasing to 88 (44–199) and 70 (31–103) ml during the course of surgery (*P*<0.02). Paired SV measurements showed a poor correlation *r*=0.39 (*P*<0.01, Fig. 1). The bias (limits of agreement) was -28 ml (-91 to +35 ml) and the percentage error was 70%.

There were also substantial differences between patients in the relationship between the two devices (Supplementary Fig. S1).

Table 1Patient characteristics and intraoperative data. Valuesare given as absolute numbers or median values (range). BMI,body mass index; PEEP, positive end-expiratory pressure; Pmax,peak pressure

Male/female (n)	11/9		
Age (yr)	69 (51-82)		
Weight (kg)	72 (46–98)		
BMI (kg $m^{-2}$ )	24 (17-33)		
ASA classification (I/II/III)	4/10/6		
Surgical procedure (n)			
Anterior rectal resection	7		
Abdominoperineal resection	6		
Hemicolectomy/small intestine	7		
Duration of surgery (min)	317 (147–783)		
Blood loss (ml)	550 (100-3550)		
Blood transfusion (ml)	0 (0-1550)		
Crystalloid (ml)	1400 (620-5400)		
Colloid (ml)	1325 (750-4000)		
Norepinephrine infusion (n)	12		
Tidal volume (ml kg <sup>-1</sup> )	6.5 (4.9-8.7)		
PEEP (cm H <sub>2</sub> O)	5 (4-9)		
Pmax (cm H <sub>2</sub> O) 18 (14-25			



**Fig 1** Bland-Altman plot for 172 paired SV values obtained using oesophageal Doppler ( $SV_{ODM}$ ) and LiDCOrapid ( $SV_{Li}$ ) during elective bowel surgery in 20 patients. Black and blue dotted lines represent the mean difference (bias) and limits of agreement [bias (1.96 sD)], respectively.

**Table 2** Haemodynamic parameters (n=22-59) before and after a fluid challenge (200 ml of colloid), separated for 27 positive volume responses (increase in SV  $\geq$  10%), and 59 non-responses. Data are presented as mean (sD) or median (inter-quartile range). FTc, flow time corrected; ODM, oesophageal Doppler monitor; Li, LiDCOrapid; SVV, stroke volume variation; PPV, pulse pressure variation. \*P<0.05 vs baseline, \*P<0.05 between groups

	Responders		Non-responders	
	Before	After	Before	After
MAP (mm Hg)	62 (7)	64 (9)	62 (9)	64 (10)
HR (beats min <sup>-1</sup> )	65 (12)	64 (12)	59 (13)	60 (12)
Ftc (ms)	326 (37)	354 (40)*	331 (46)	338 (44)
SV <sub>ODM</sub> (ml)	78 (59–93)	89 (70-112)*	88 (67–103)	94 (71–105)
SV <sub>Li</sub> (ml)	58 (50–68)	64 (57–76)*	61 (50-73)	64 (49-76)
CO <sub>ODM</sub> (litre min <sup>-1</sup> )	4.7 (3.8-6.2)	5.5 (4.4–7.6)	5.2 (3.9-6.5)	5.6 (4.1-6.6)
CO <sub>Li</sub> (litre min <sup>-1</sup> )	3.6 (3.3-4.8)	4.1 (3.5-5)	3.5 (3.0-4.3)	3.7 (3-4.5)
SVV (%)	10.6 (2.9)	7.3 (2.5)	8.5 (4.2)	7.9 (5.1)
PPV (%)	12.5 (4.5)	8.5 (2.9)	10.5 (6.2)	9.8 (5.4)
$\Delta SV_{ODM}$ (ml)	12 (10-16)		3 (-1.5-6) <sup>†</sup>	
$\Delta {\sf SV}_{\sf ODM}$ (%)	16 (14–19)		3.4 ( <i>-</i> 1.4 <i>-</i> 7.6) <sup>†</sup>	
$\Delta SV_{Li}$ (ml)	6 (1.5–9)		3 (0-5) <sup>†</sup>	
$\Delta {\rm SV}_{\rm Li}$ (%)	9.7 (2.4–16)		4.1 (0-6.8) <sup>+</sup>	

#### SV optimization

Before surgery, nine out of 19 patients responded to the first fluid challenge with an increase in  $SV_{ODM} \ge 10\%$ , but none of these responded to a second fluid challenge. Initial SV tended to be lower in the group of responders, but there was no difference in CO, due to a higher HR in the same group. Twenty-seven out of 86 of all fluid challenges were positive, and 18 out of 20 patients did respond to a fluid challenge at some point. Haemodynamics before and after fluid challenges for responders and non-responders are shown in Table 2.

The relationship for percentage changes in SV after a fluid bolus for the two devices was also low (Fig. 2). The bias (limits of agreement) was -1% (-20 to +18%) and the percentage error was 260%. When studying the trending abilities of LiDCOrapid against ODM, the concordance was 62%, increasing to 80% with a 10% exclusion zone of central data.

#### Specificity and sensitivity

The sensitivity of the LiDCOrapid device was 48% and the specificity 81% to accurately detect a positive volume response ( $\Delta SV_{ODM} \ge 10\%$ ).

There was a positive relationship for changes in SV<sub>Li</sub> and MAP ( $r^2$ =0.45, P<0.001), but not for SV<sub>ODM</sub>, (Fig. 3). A corresponding increase in MAP after a fluid bolus increased the sensitivity of LiDCOrapid to 67% with a concomitant decrease in the specificity to 74%. An unchanged or decreased MAP decreased the sensitivity to 11%, while increasing the specificity to 95%.

#### Prediction of volume responsiveness

Initial SVV and PPV values were higher in the group of responders, when compared with the group of non-responders, and decreased after a fluid challenge (Table 2).

The AUC values (with 95% confidence intervals) for SVV and PPV were 0.72 (0.60-0.83) and 0.66 (0.52-0.79),



**Fig 2** Four-quadrant plot showing the trending ability for LiDCOrapid SV measurements (SV<sub>Li</sub>) in 86 fluid challenges (200 ml of colloid) in 20 patients. A 10% exclusion zone of central data was applied. SV<sub>ODM</sub>, SV values according to the oesophageal Doppler monitor.

respectively. The optimal cut-off value was 8.5% for both SVV (sensitivity 0.79, specificity 0.63) and PPV (sensitivity 0.79, specificity 0.45). The grey zones, according to the definition by Cannesson and colleagues, were 6.5-13.5% for SVV and 6-17.5% for PPV.

## **Discussion**

To our knowledge, this is the first study to evaluate the noncalibrated, pulseCO algorithm used by the LiDCOrapid within



**Fig 3** Graphs showing the relationship between changes in SV and MAP after a fluid challenge (200 ml of colloid), for the oesophageal Doppler monitor (A) and LiDCOrapid (B), during elective bowel surgery (86 fluid challenges in 20 patients).

an ODM-guided SV optimization protocol. The overall agreement for absolute SV values was low, and varied considerably between patients. Furthermore, the trending ability of SV changes after fluid challenges was poor, and dependent on concomitant changes in MAP. Finally, the dynamic indices SVV and PPV suffered low predictive values to detect volume responders in this setting.

In high-risk surgery, such as major colorectal procedures, it is of great importance to maintain intravascular volume and CO in order to provide the body with sufficient oxygen. Moreover, detrimental effects from hypovolaemia and fluid overload need to be avoided. Unfortunately, standard peroperative haemodynamic monitoring is insufficient in guiding the anaesthetist, and there is a need for minimally invasive CO monitoring devices that are able to track changes after interventions such as fluid challenges. Studies on goal-directed fluid therapy guided by the calibrated LiDCO PulseCO algorithm show improved<sup>15</sup> or unchanged<sup>16</sup> outcome after major surgery. Calibration with lithium limits its use, and recently, a non-calibrated system based on the same pulseCO algorithm has been marketed. The ODM is a reliable tool for trending changes in SV after haemodynamic alterations.<sup>13</sup> Furthermore, SV optimization guided by ODM has consistently been shown to improve outcome in major surgery,<sup>3 5 6 17 18</sup> although recently questioned,<sup>19</sup> and this evidence base has led the UK health body NICE to issue a recommendation that CardioQ-ODM should be considered for use in patients undergoing major or highrisk surgery or other surgical patients in whom a clinician would consider using invasive cardiovascular monitoring.<sup>20</sup>

For that reason and also because the ODM has been used for SV optimization in our department for several years, it was chosen as the reference method in this study.

The intravascular deficit in our patients was lower than that reported for other groups of patients.<sup>21</sup> <sup>22</sup> This is hardly surprising since the ERAS concept promotes normovolaemia by prescription of carbohydrate-rich fluids up to 2 h before induction of anaesthesia and restrictive use of preoperative bowel preparation.

Overall,  $SV_{Li}$  values were lower and with a more narrow range, compared with  $SV_{ODM}$  values. It has been previously shown that pulse power signals tend to underestimate SV at higher SV values.<sup>23</sup>

Absolute values for SV were poorly correlated between the two devices and the percentage error of 70% was much higher than acceptable as suggested by Critchley and Critchley.<sup>12</sup> This is well in line with results from comparisons of the LiDCO system with transpulmonary thermodilution techniques performed in cardiothoracic patients and during liver transplantation.<sup>24-26</sup> Furthermore, the recorded data from the two devices differed substantially between individual patients. This could partly be explained by the fact that each device uses a different method in relation to the vascular system. Methods based on arterial waveform analysis are sensitive to changes in peripheral vasomotor tone,<sup>27</sup> whereas the accuracy (but not trending ability) of Doppler readings is dependent on changes in the ratio of blood flow to the upper or lower part of the body, that is, because of the activation of epidural anaesthesia.

The calibrated LIDCO algorithm has been shown to detect SV changes after venous occlusion in cardiac patients.<sup>23</sup> However, the haemodynamic changes in that study were more pronounced than in the present study, and one cannot rule out that the non-calibrated algorithm is less accurate than the calibrated, also for tracking changes.

One of the aims of this study was to evaluate the ability of LiDCOrapid to trend changes in SV after fluid challenges within our optimization protocol. In general, the correlation regarding changes in SV between the two devices was very low and with unacceptably high percentage error. Good trending capability is associated with concordance rates of above 95%, whereas poor capability is seen for rates below 90%.<sup>28</sup> In comparison, the LiDCOrapid was only 80% concordant with an exclusion zone of 10%. Furthermore, LiDCOrapid only managed to track less than half of the positive volume responses after a fluid challenge. The sensitivity increased when there was a concomitant increase in MAP, while decreasing to only 11% when MAP decreased or

remained unchanged. This is not surprising, however, since all arterial waveform analysis is sensitive to changes in peripheral resistance.<sup>29</sup>

Dynamic indices have been shown to reliably predict fluid responsiveness in mechanically ventilated patients, especially when strict conditions regarding tidal volumes (>8 ml kg<sup>-1</sup>), no arrhythmias, normal respiratory rate, and breath-by-breath calculations were applied.<sup>30-33</sup> However. in a recent study, only 23% of surgical patients met the criteria for invasive monitoring of fluid responsiveness.<sup>34</sup> The poor predictive value of the dynamic indices in our study is probably due to the tidal volumes of 6-8 ml kg<sup>-1</sup> used, and the relatively small changes in SV seen after 200 ml fluid boluses, in line with findings in cardiac and major abdominal surgery patients, and in a mixed intensive care unit population.<sup>31 35 36</sup> This could also explain why the grey zones for SVV (6.5-17.5%) and PPV (6-13.5%) were larger than previously reported.<sup>14</sup> Increasing our cut-off value to define a positive volume response from 10% to 15% did not improve the predictive value of neither SVV nor PPV (data not shown).

There are weaknesses to our study. The accuracy of ODM is dependent on a signal well focused on the midstream of aortic flow. To ensure this, the probe was refocused before each measurement. A limitation of  $SV_{Li}$  estimation is the quality of the arterial waveform. Different damping, air bubbles, or blood clots may profoundly alter CO measurements. Thus, the arterial waveform signal was regularly checked for quality and adjusted if needed. During the perioperative period, marked dynamic variations occurred over time due to patient positioning, significant changes in afterload from vasopressor administration, activation of epidurals, and bleeding. However, these alterations were kept to a minimum during the time of fluid optimizations.

Although this protocol has been used in most randomized studies,<sup>37</sup> the volume given was only 200 ml for each bolus and the cut-off for a positive response was 10%, resulting in many data points within the exclusion zone. Another limitation is that the perioperative management was not strictly protocolized, but to the physician's discretion. However, this corresponds to the clinical reality and again, during SV readings anaesthetic interventions were kept to a minimum.

From the present study, we conclude that the LiDCOrapid and ODM devices are not interchangeable. We cannot recommend that the LiDCOrapid replace the standard Doppler method until further device-specific outcome studies on volume optimization are available.

The dynamic indices SVV and PPV add little value to a fluid optimization protocol during conventional ventilation parameters, and should not replace SV measurements with a validated technique.

# Supplementary material

Supplementary material is available at British Journal of Anaesthesia online.

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# **Declaration of interest**

None declared.

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