

# Haemodynamic effects of cold versus warm fluid bolus in healthy volunteers: a randomised crossover trial

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The use of intravenous fluid bolus (FB) therapy is common in patients during anaesthesia and in the perioperative, emergency and critical care setting.<sup>1-3</sup> The most frequent reasons to administer an FB are hypotension and low urine output.<sup>4</sup> The rationale is to increase cardiac index, mean arterial pressure (MAP) or both in order to ultimately increase oxygen delivery to vital organs.<sup>5</sup> The haemodynamic effects of FB therapy, however, may be small and short-lived in both major surgery and critical illness.<sup>6,7</sup> For example, in a study of patients with circulatory shock there was a significant increase in MAP of 8 mmHg at 30 minutes, which was absent after 60 minutes.<sup>8</sup> Despite such short-lived effects, clinicians still use FB therapy as the mainstay in resuscitation of critically ill and surgical patients.<sup>9-11</sup>

In clinical practice, the effects seen are usually on blood pressure (BP) because cardiac index is only measured in a small proportion of patients and, when such effects occur, they are ascribed to the volume expansion achieved by the FB. However, an important feature of FB therapy is that it is given at room temperature. Thus, its rapid delivery may cause a decrease in core temperature with an associated pressor effect and changes in venous return — effects that are independent of volume.<sup>12,13</sup> In contrast, if the same amount of fluid was given at near body temperature, such effects might be altered in favour of vasodilation, decreased afterload and diminished pressor effect. However, no studies have addressed this possible differential effect and mechanism of action.

We hypothesised that changes in both cardiac index and MAP during the infusion of a bolus of 500 mL of crystalloid would be significantly altered by the temperature of the fluid given (either room temperature or near body temperature).

## Methods

Ethics approval was obtained from the Ethical Review Board of Stockholm, Sweden, (EPN 2016/986-31/1) and the Swedish Medical Products Agency as a clinical drug trial. The trial was registered on EudraCT (no. 2016-002548-18) and on Clinicaltrials.gov (identification no. NCT03209271).

## ABSTRACT

**Objective:** To test the hypothesis that changes in cardiac index and mean arterial pressure (MAP) during and after a fluid bolus (FB) are altered by fluid temperature.

**Design:** Randomised, controlled, crossover trial.

**Setting:** Research laboratory at Swedish teaching hospital.

**Participants:** Twenty-one healthy adult volunteers.

**Interventions:** Subjects were randomly allocated to 500 mL of Ringer's acetate at room temperature (22°C; cold) or body temperature (38°C; warm).

**Main outcome measures:** For 2 hours after starting the FB, we measured cardiac index, MAP, systolic blood pressure, diastolic blood pressure and pulse rate (PR) continuously. We recorded temperature and O<sub>2</sub> saturation every 5 minutes during infusion and every 15 minutes thereafter. In a second session, volunteers crossed over.

**Results:** During the first 15 minutes, mean cardiac index increased more with warm FB (0.09 L/min/m<sup>2</sup> [95% CI, 0.06–0.11] v 0.03 L/min/m<sup>2</sup> [95% CI, 0.01–0.06]; *P* < 0.001). This effect was mediated by a significant difference in mean PR (+0.80 beats/min [95% CI, 0.47–1.13] v –1.33 beats/min [95% CI, –1.66 to –1.01]; *P* < 0.010). In contrast, MAP increased more with cold FB (4.02 mmHg [95% CI, 3.63–4.41] v 0.60 mmHg [95% CI, 0.26–0.95]; *P* < 0.001). Cardiac index and MAP returned to baseline after a median of 45.3 min (interquartile range [IQR], 10.7–60.7 min) and 27.7 min (IQR, 5.3–105.0 min), respectively, after cold FB, and by 15.8 min (IQR, 3.8–64.3 min) and 22.7 min (IQR, 3.3–105.0 min), respectively, after warm FB.

**Conclusion:** Intravenous FB at body temperature leads to a greater increase in cardiac index compared with room temperature, while the reverse applies to MAP. These findings imply that in healthy volunteers, when a room temperature FB is given, the temperature of the fluid rather than its volume accounts for most of the MAP increase.

**Trial registration:** EudraCT no. 2016-002548-18 and Clinicaltrials.gov NCT03209271.

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**Table 1. Baseline characteristics of subjects\***

Groups	Warm	Cold	P
Total number of patients	20	20	
Cardiac index, L/min/m <sup>2</sup>	3.5 (3.2–3.8)	3.5 (3.1–3.8)	0.54
MAP, mmHg	89.5 (85.9–93.0)	90.5 (86.3–94.7)	0.38
SBP, mmHg	119.1 (114.3–123.9)	119.3(112.8–125.7)	0.91
DBP, mmHg	72.2 (69.4–75.0)	72.9 (69.5–76.3)	0.56
PR, beats/min	65.6 (61.3–69.9)	65.4 (60.2–70.6)	0.91
Temperature, °Celsius	36.6 (36.4–36.8)	36.7 (36.5–36.8)	0.68
Pulse oximetry oxygen saturation, (%)	99.6 (99.2–99.9)	99.2 (98.8–99.6)	0.10

DBP = diastolic blood pressure. MAP = mean arterial pressure. PR = pulse rate. SBP = systolic blood pressure. \* Values are mean with 95% CI.

The study was conducted at the research facilities of the Department of Clinical Science and Research at Södersjukhuset, Karolinska Institutet, Stockholm, Sweden, from January to April 2017.

Informed consent was obtained from each volunteer.

Twenty-one healthy volunteers were recruited for this study.

### Study design

The inclusion criteria were participants aged 18 years or older and with no significant health problems.

The exclusion criteria were a grade of II or higher as per ASA (American Society of Anesthesiologists Physical Status Classification System) grading system and known pregnancy.

The volunteers fasted for at least 6 hours and were encouraged to void before the experiment. The volunteers were supine during the study session. Randomisation was provided by allocation from sequentially numbered opaque envelopes before study commencement, prepared by members of the research group not involved in randomisation or performing the study. At the first session of each volunteer, an envelope was opened randomly allocating them to receive either 500 mL of acetated Ringer's solution at room temperature ("cold") or warmed to body temperature ("warm") (22°C v 38°C)

After a period of at least one day, the volunteers returned for their second session in a crossover fashion.

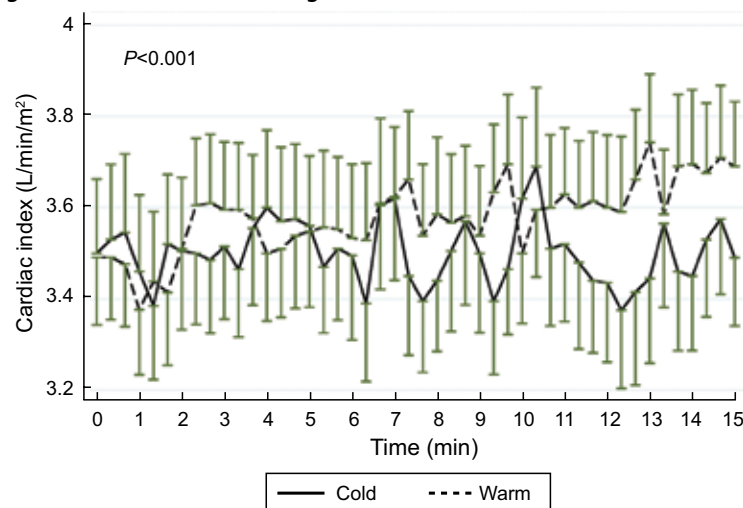
### Monitoring

We used a bedside monitor (Philips Healthcare, Amsterdam, The Netherlands) for oxygen saturation measured by

pulse oximetry (Sp<sub>o</sub><sub>2</sub>) and electrocardiogram for heart rate. In all participants, cardiac index, MAP, systolic blood pressure (SBP), diastolic blood pressure (DBP) and pulse rate (PR) were measured continuously by a non-invasive device using the arterial clamp method by having an inflatable ClearSight (Edwards Lifesciences, Irvine, CA, USA) cuff around the middle phalanx.

The pulsating artery is clamped by applying equivalent counter pressure by an inflatable bladder cuff, adjusted 1000 times per second to keep the artery at a constant volume. The volumes are measured via a plethysmograph and the finger artery waveform is used to calculate BP and cardiac output from the pulse contour with proprietary algorithms. The device is approved by the United States Food and Drug Administration for the continuous measurement of cardiac index and BP, with a good agreement with invasive BP monitoring.<sup>14–16</sup> Body temperature was measured by a forehead zero heat flux sensor 3M SpotOn (3M Health Care, Maplewood, MN, USA).<sup>17–19</sup>

Cardiac index, MAP, SBP, DBP and PR were measured every 20 seconds for 2 hours. Temperature and Sp<sub>o</sub><sub>2</sub> were continuously recorded every 5 minutes during infusion, and then every 15 minutes thereafter until the end of the experiment at 120 minutes.

**Figure 1. Cardiac index during the 15 minutes of fluid bolus administration**

Mean (standard error of the mean) cardiac index during the 15 minutes of fluid bolus administration in subjects receiving a warm (dotted line) and cold (solid line) fluid bolus, respectively. *P* value represents the interaction between time and group on repeated measures analysis of variance.

**Table 2. Average change in haemodynamic variables from baseline during the fluid bolus\***

Parameter	Warm, average change <sup>†</sup>	Cold, average change <sup>†</sup>	Average difference <sup>†</sup>	P <sup>†</sup>
Total number of patients	20	20		
Cardiac index, L/min/m <sup>2</sup>	0.09 (0.06–0.11)	0.03 (0.01–0.06)	–0.05 (–0.09 to –0.02)	0.001
MAP, mmHg	0.60 (0.26–0.95)	4.02 (3.63–4.41)	3.42 (2.86–3.97)	0.001
SBP, mmHg	1.94 (1.39–2.49)	5.55 (5.01–6.09)	3.61 (2.81–4.40)	0.760
DBP, mmHg	0.17 (–0.01 to 0.44)	2.90 (2.56–3.24)	2.73 (2.25–3.20)	0.001
PR, beats/min	0.80 (0.47–1.13)	–1.33 (–1.66 to –1.01)	–2.13 (–2.61 to –1.65)	0.010

DBP = diastolic blood pressure. MAP = mean arterial pressure. PR = pulse rate. SBP = systolic blood pressure. \* Values are mean with 95% CI. † Average difference and change calculated with the paired *t* test, while the *P* values were calculated with repeated measures analysis of variance for the same period.

### Fluid bolus

An 18-20-gauge intravenous line (BD Venflon, BD, Franklin Lakes, NJ, USA) was inserted in the upper extremity for fluid infusion. The fluid was acetated Ringer's solution (Baxter International, Deerfield, IL, USA). The infusion time was set to 15 minutes via Braun infusion pumps (B Braun Melsungen, Melsungen, Germany). The fluid in the "cold" group was kept to a standardised room temperature of 22°C using a laboratory cooler. The fluid in the "warm" group was administered via a Fluido (The 37Company, Amersfoort, The Netherlands) fluid warming system at a set temperature of 38°C, as the warming system only allows settings of full degrees.

### Outcomes

The primary outcome of the study was the change in cardiac index during the 15-minute infusion. The secondary outcomes were changes in MAP, SBP, DBP, PR, SpO<sub>2</sub> and body temperature during the 15-minute infusion as well as changes in all these variables during 120 minutes. We also calculated time for return to baseline values after the end of the FB for cardiac index, MAP, SBP, DBP and PR.

Baseline was defined as the mean of the three measurements before the FB.

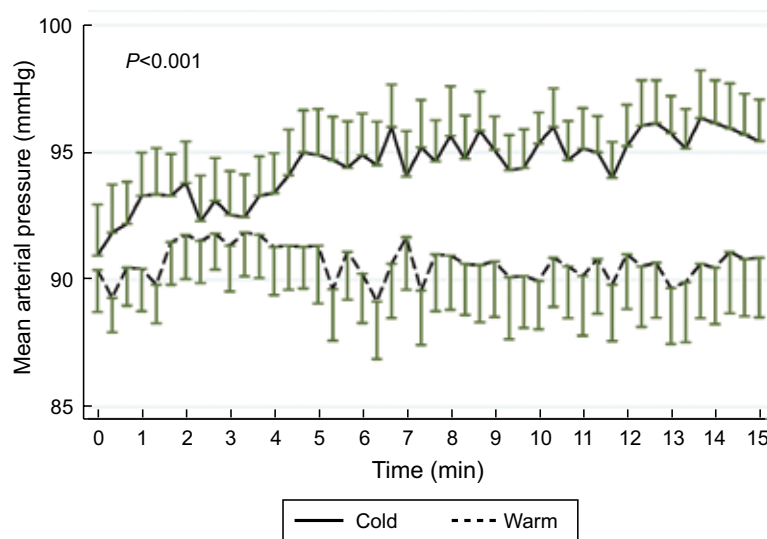
A response was defined as any rise above baseline after the termination of the FB for all variables except PR, for which a response was defined as a decrease below this level.

The time to return to baseline was defined as three consecutive measurements at or below baseline, except for PR, for which it was defined as three consecutive measurements at or above baseline.

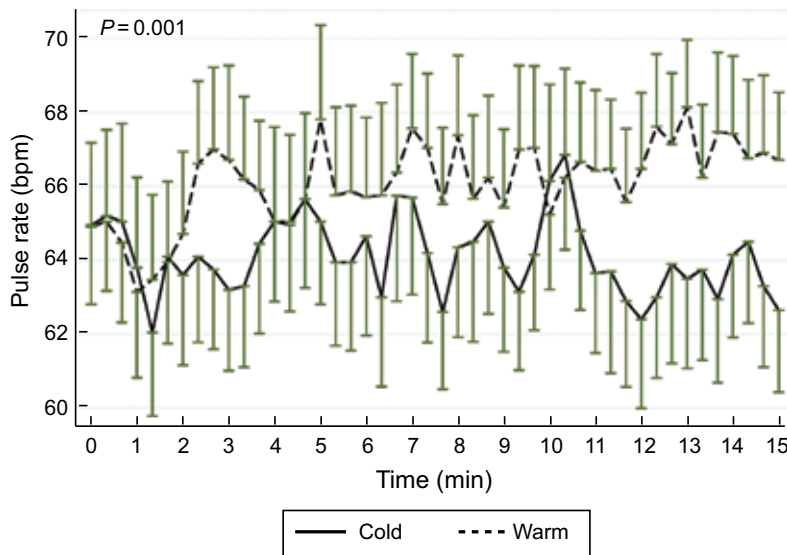
### Statistics

Descriptive statistics were used when appropriate. Normality was tested using the Shapiro–Wilk test. Comparisons were made using paired *t* test and analysis of variance for repeated measures for the change over 15 and 120 minutes for all variables. Fisher exact test was used to test the difference in fluid response and return to baseline was tested with Wilcoxon signed rank test.

A sample size of 21 subjects was calculated to detect a difference of 0.36 L/min/m<sup>2</sup> cardiac index between the different treatments, standard deviation of 0.55 L/min/m<sup>2</sup> (due to lack of previous data) for the difference within pairs given a power of 80%, and a two-sided level of significance

**Figure 2. Mean arterial pressure (MAP) during the 15 minutes of fluid bolus administration**

Mean (standard error of the mean) MAP during the 15 minutes of fluid bolus administration in subjects receiving a warm (dotted line) and cold (solid line) fluid bolus, respectively. *P* value represents the interaction between time and group on repeated measures analysis of variance.

**Figure 3. Pulse rate during the 15 minutes of fluid bolus administration**

Mean (standard error of the mean) pulse rate during the 15 minutes of fluid bolus administration in subjects receiving a warm (dotted line) and cold (solid line) fluid bolus, respectively. *P* value represents the interaction between time and group on repeated measures analysis of variance.

of 5% with a paired *t* test. As the study was conducted, we found the monitoring gave access to data points every 20 seconds. Having more data points for analysis made a more advanced and robust statistical analysis possible. Since the original power analysis was made for only one time point, while the study measured the outcome variable repeatedly, this significantly heightens the power using a repeated measures analysis of variance.

Statistical analysis was performed using IBM SPSS Statistics, version 23 for Windows (IBM, Armonk, NY, USA) and Stata version 11.2 (StataCorp, College Station, TX, USA). *P* < 0.05 was considered significant.

## Results

We included 21 healthy volunteers, 14 men and seven women with a mean age of 28 years (95% CI, 24.8–32.0). Their baseline characteristics are presented in Table 1. Mean height was 177 cm (95% CI, 171.8–182.8), mean weight was 74 kg (95% CI, 67–80.6), mean body mass index was 23.2 kg/m<sup>2</sup> (95% CI, 22.1–24.4), and mean body surface area 1.91 m<sup>2</sup> (95% CI, 1.79–2.02).

While 21 volunteers were recruited for two sessions each, only 41 sessions were available for analysis (21 warm and 20 cold) due to a malfunction in the retrieval of the study data. Since the cold session was excluded, no data for volunteer no. 19 were included in the analysis. Due to a technical issue with the monitoring noticed during the fluid infusion, one study session had to be terminated and the participant returned later to complete a second session. The mean time between study sessions was 10 days.

## Cardiac index

Baseline cardiac index was similar in the two groups (Table 1). There was a small but statistically significant increase in cardiac index during the 15 minutes of FB infusion with warm fluid compared with cold fluid (*P* = 0.001) (Figure 1) (Table 2). There was no statistically significant difference in the increase of cardiac index during the overall 120-minute period (online Appendix, Figure 4; available at [cicm.org.au/Resources/Publications/Journal](http://cicm.org.au/Resources/Publications/Journal)). There were 16 responders (80%) in the warm group and 13 (65%) in the cold group (Table 3). There was no statistically significant difference in the median (interquartile range [IQR]) time for cardiac index to return to baseline for these participants (Table 3).

## Blood pressure

Baseline MAP was similar in the two groups (Table 1). During FB infusion, MAP increased significantly more in the cold fluid group (Figure 2) (Table 2). A similar effect was seen for DBP (*P* = 0.001) (online Appendix, Figure 5) but not SBP (online Appendix, Figure 6). There was no statistically significant difference in the increase of MAP during the full 120 minutes of observation (online Appendix, Figure 7). There were 12 responders in the warm group and 18 in the cold group (*P* = 0.06) (Table 3). The median (IQR) time for MAP to return to baseline for these participants was similar in both groups at between 20 and 30 minutes (Table 3). The mean increases for each variable and group over 120 minutes are presented in the online Appendix, Figures 7–9.

## Pulse rate

The baseline PR was similar in the two groups (Table 1). Warm FB administration significantly increased PR more than cold FB (*P* = 0.01) (Figure 3). There was no statistically significant difference in the PR during the overall 120 minutes (online Appendix, Figure 10). Significantly more patients in the cold group had a decrease in PR (Table 3). The median (IQR) time for PR to return to baseline for these participants was similar and less than a few minutes in both groups (Table 3).

## Pulse oximetry and temperature

There were no instances of desaturation (oxygen saturation < 95%).

Baseline temperature was similar in both groups (Table 1). At 15 minutes, body temperature was significantly lower in the cold FB group (*P* = 0.046) (online Appendix, Figure 11). There

**Table 3. Time to return to baseline for haemodynamic values\***

Parameter	Warm	Cold	P
Total number of patients	20	20	
Cardiac index, L/min/m <sup>2</sup>			
Response	16/20 (80.0%)	13/20 (65.0%)	0.48
Return to baseline	14/16 (87.5%)	13/13 (100%)	0.49
Time to baseline (min), median (IQR)	15.8 (3.8–64.3)	45.3 (10.7–60.7)	0.89
MAP, mmHg			
Response	12/20 (60.0%)	18/20 (90.0%)	0.06
Return to baseline	9/12 (75%)	13/18 (72.2%)	1.00
Time to baseline (min), median (IQR)	22.7 (3.3–105.0)	27.7 (5.3–105.0)	0.89
SBP, mmHg			
Response	14/20 (70.0%)	17/20 (85.0%)	0.45
Return to baseline	9/14 (64.3%)	9/17 (52.9%)	0.72
Time to baseline (min), median (IQR)	37.3 (9.3–105.0)	72.7 (3.7–105.0)	0.75
DBP, mmHg			
Response	10/20 (50.0%)	15/20 (75.0%)	0.19
Return to baseline	9/10 (90.0%)	9/15 (60.0%)	0.18
Time to baseline (min), median (IQR)	11.3 (3.0–38.0)	40.3 (10.3–105.0)	0.08
PR, beats/min			
Response	7/20 (35.0%)	16/20 (80.0%)	0.01
Return to baseline	7/7 (100%)	14/16 (87.5%)	1.00
Time to baseline (min), median (IQR)	2.5 (1.3–5.7)	6.2 (2.0–13.0)	0.05

DBP = diastolic blood pressure. IQR = interquartile range. MAP = mean arterial pressure. PR = pulse rate. SBP = systolic blood pressure. \* Baseline was defined as the mean of the three values before fluid infusion. Response was defined as any rise above this level after the termination of the fluid bolus except for PR, for which a response was defined as a decrease below this level. Subjects returned to baseline when three consecutive values were back at or below baseline (above in the case of PR).

was no significant difference in body temperature between groups at 120 minutes ( $P = 0.26$ ) (online Appendix, Figure 12). None of the participants had any instances of shivering.

## Discussion

### Key findings

We conducted a randomised, controlled, crossover study to test the hypothesis that varying the temperature of the FB given would significantly change the cardiac index and MAP response to such FB. During FB infusion, we found a statistically significant greater increase in cardiac index with warm fluid. In contrast, we observed that a room temperature FB significantly decreased body temperature and induced a statistically significant increase in MAP and DBP and decrease in PR. Since the difference in cardiac index was small, and there was a corresponding difference

in PR, it is plausible that the difference in cardiac index was due to this change in PR rather than a change in SV. Moreover, we found that all of the above effects were short lived.

### Relationship with previous studies

This is the first study to compare changes in cardiac index and MAP in humans after an FB at room temperature or at body temperature with a clinically relevant fluid volume. However, our findings are consistent with the study by Tølløfsrud and colleagues<sup>20</sup> who found similar differences in BP with larger fluid volumes of similar temperatures. The FB temperature effect on cardiac index was divergent from the MAP effect. This study together with studies by Frank and colleagues<sup>12,13</sup> have previously explored that more severe lowering of core temperature by infusion of cold fluids can have haemodynamic effects, with a release of catecholamines and pressor response. This observation concurs with other data that increases in MAP do not reliably reflect increases in cardiac output.<sup>21</sup> The volunteers showed a response to fluids, both regarding MAP and cardiac index. This is in accordance with other studies that have shown fluid responsiveness in most healthy volunteers without volume depletion,<sup>22</sup> whereas fluid

responsiveness perioperatively has been found to be anywhere from 28% to 51%, and around 50% in the intensive care unit.<sup>23–26</sup> The effects of the FB dissipated at a faster rate than in than previous studies;<sup>6,8,27</sup> however, several of these studies did not measure the response continuously but only at set intervals.

### Study implications

Our findings imply that much of the MAP increase seen in clinical practice when an FB is given at room temperature may be due to the cooling effect of rapidly delivered cold fluid. More specifically, by showing that only 15% (0.6 mmHg v 4 mmHg) of the MAP increase with room temperature was achieved when the same volume was given at body temperature, our observations imply that about 85% of the

MAP increase seen when a 500 mL crystalloid FB is given to humans is not due to the fluid itself but simply to the fact that such fluid is much colder than core temperature. The findings challenge the current understanding of the mechanism responsible for the effect of FB on MAP.

### Study strengths and limitations

The volumes and temperatures mirror what is used in clinical practice to approximate clinical settings; we monitored the haemodynamic effects for 120 minutes, while most other studies of FB therapy have limited their monitoring to 60 minutes.<sup>8,13,28</sup> Moreover, we monitored not only PR and BP but also cardiac index, which allowed us to document how these parameters diverge in their response to fluids with different temperatures. We performed continuous cardiac index and non-invasive BP measurements using a validated, evidence-supported non-invasive method.<sup>14-16,29-35</sup> We chose to use non-invasive monitoring as this device has proven accurate in measuring both cardiac index and MAP in patients without critical illness in the operation room setting. In cardiac surgery, the correlation between BP measured by arterial clamp and invasive methods has shown to be above 95% as well as a significant correlation for cardiac output.<sup>15,31</sup> Since this was a volunteer study, using invasive monitoring on the subjects was not ethically justified. Moreover, both groups used the same measurement technology, minimising measurement and ascertainment bias. Finally, given the fact that this study was performed in human subjects and given the growing interest in the epidemiology and effects of fluid therapy in critically ill patients and in those who received major surgery,<sup>36-42</sup> the findings of this study have clinical relevance.

Our study carries some limitations. It was conducted in volunteers rather than patients. Therefore, care should be taken about implications about the effect of different FB temperatures in patients with sepsis receiving FB therapy. However, volunteer studies are the first necessary step in the evaluation of the effect of fluid temperature on systemic haemodynamics. Also, patients presenting for outpatient procedures might be comparable to our healthy, fasted volunteers without circulatory impairment and respond similarly. Our study only tested acetated Ringer's solution and the results might not be the same using other fluid types. Non-core temperature was measured rather than core temperature, and a warmer fluid temperature may more accurately reflect core temperature. We did not measure other effects of the FB such as urinary output or central venous pressure. Such measurements would have required invasive procedures that would have been unjustified in volunteers and would have provided data on variables of uncertain clinical value.

### Conclusion

In healthy volunteers, warming an FB to body temperature leads to a slight increase in cardiac index and PR but not in MAP compared with administration at room temperature. A room-temperature FB decreases PR and increases MAP. The haemodynamic effects of an FB on cardiac index were most apparent during the infusion and dissipated after 15–45 minutes depending on fluid temperature. These observations imply that, in healthy volunteers, fluid temperature is a mediator of the haemodynamic effect of an FB. A randomised trial in the critically ill setting addressing this is warranted to investigate if this observation has implications for clinical practice.

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### Competing interests

None declared.

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**Appendix**

This appendix was part of the submitted manuscript and has been peer reviewed. It is posted as supplied by the authors.

**Additional figures**

Table 4. Average change in hemodynamic variables from baseline during 120 minutes

Parameter	Warm, average change (n=20)	Cold, average change (n=20)	Average difference	p-value
CI, L/min/m <sup>2</sup>	0.08 (0.07-0.09)	0.04 (0.03-0.05)	-0.04 (-0.06 - -0.02)	0.96
SBP, mmHg	4.93 (4.66-5.19)	7.71 (7.44-7.99)	2.79 (2.46-3.12)	0.99
DBP, mmHg	1.47 (1.33-1.61)	3.60 (3.44-3.76)	2.13 (1.94 – 2.32)	0.91
MAP, mmHg	2.34 (2.16-2.51)	4.81 (4.62-5.00)	2.48 (2.26 – 2.70)	0.93
PR, bpm	-0.02 (-1.81-0.14)	-1.73 (-1.90 - -1.56)	-1.71 (-1.93 - -1.49)	0.51

Values are mean with 95% confidence interval. CI= Cardiac Index. SBP= Systolic Blood Pressure.

DBP= Diastolic Blood Pressure. MAP= Mean Arterial Pressure. PR= Pulse Rate. Average difference calculated with the paired t-test, while the p-values were calculated with RMANOVA for the same period.

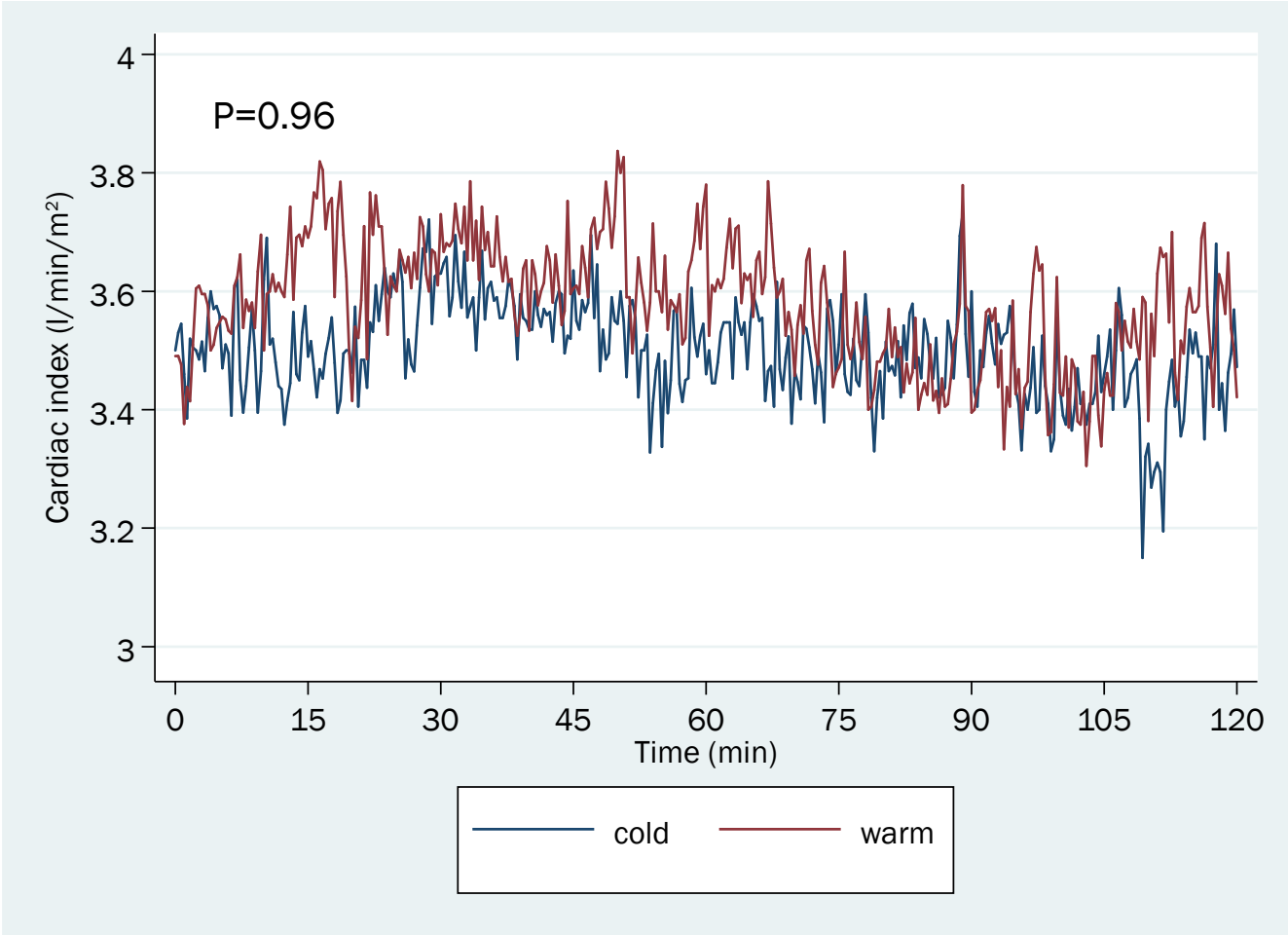


Fig. 4 Mean cardiac index during the 120 minutes of monitoring in subjects receiving a warm (red line) and cold (blue line) fluid bolus, respectively. P value represents the interaction between time and group on repeated measures analysis of variance.

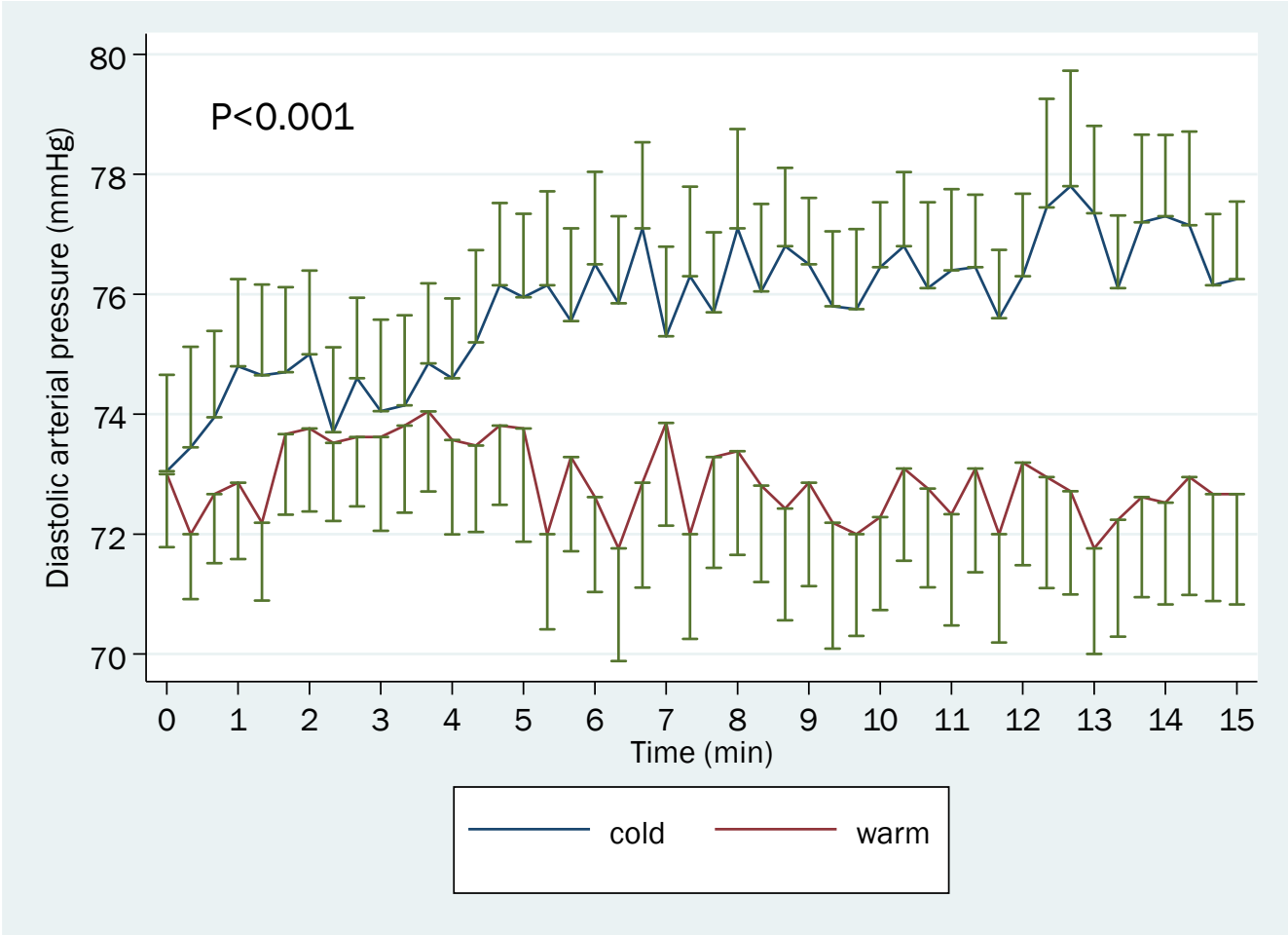


Fig. 5 Mean (SEM) diastolic arterial pressure during the 15 minutes of fluid bolus administration in subjects receiving a warm (red line) and cold (blue line) fluid bolus, respectively. P value represents the interaction between time and group on repeated measures analysis of variance.

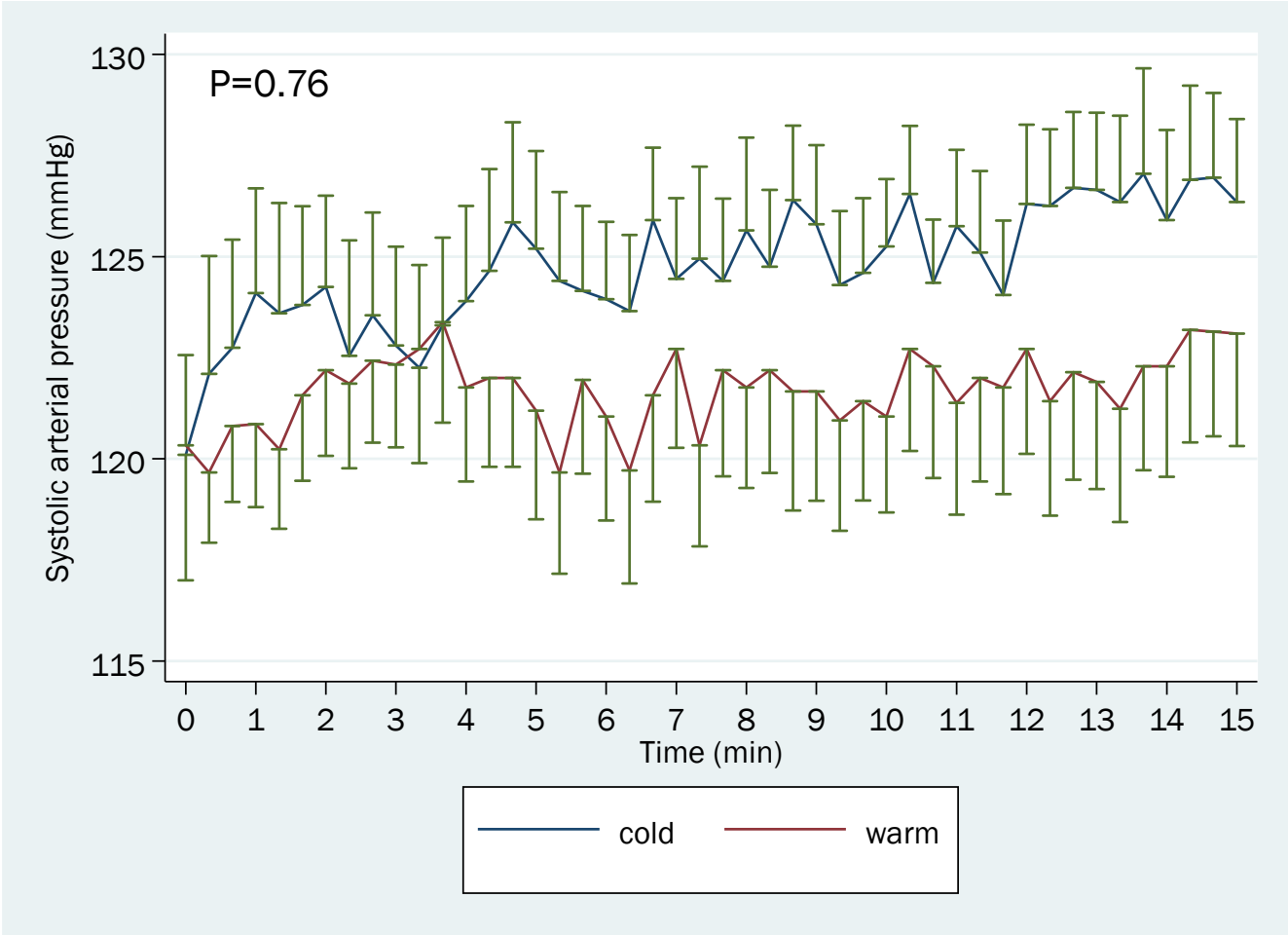


Fig.6 Mean (SEM) systolic arterial pressure during the 15 minutes of fluid bolus administration in subjects receiving a warm (red line) and cold (blue line) fluid bolus, respectively. P value represents the interaction between time and group on repeated measures analysis of variance.

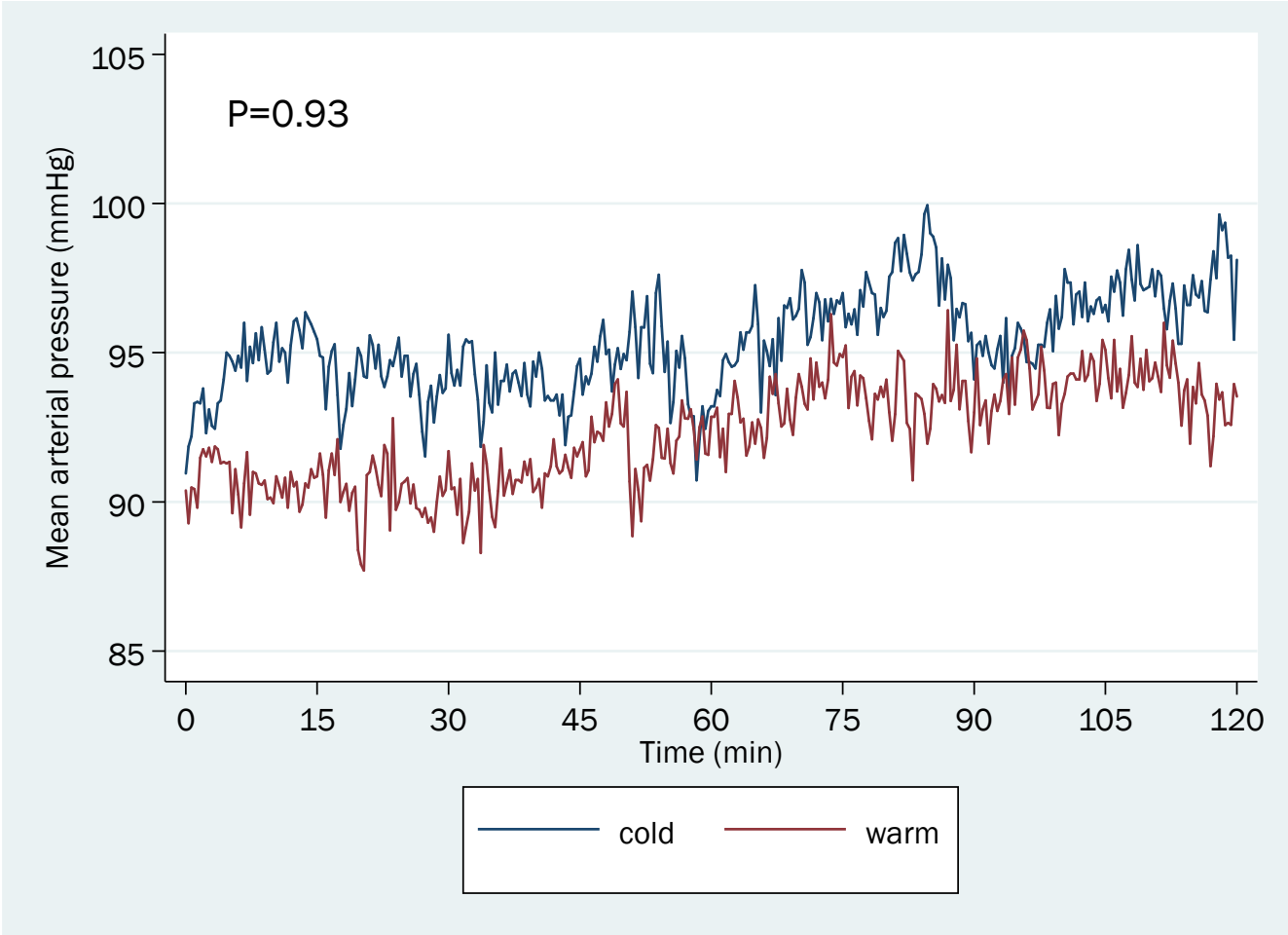


Fig. 7 Mean mean arterial pressure during the 120 minutes of monitoring in subjects receiving a warm (red line) and cold (blue line) fluid bolus, respectively. P value represents the interaction between time and group on repeated measures analysis of variance.

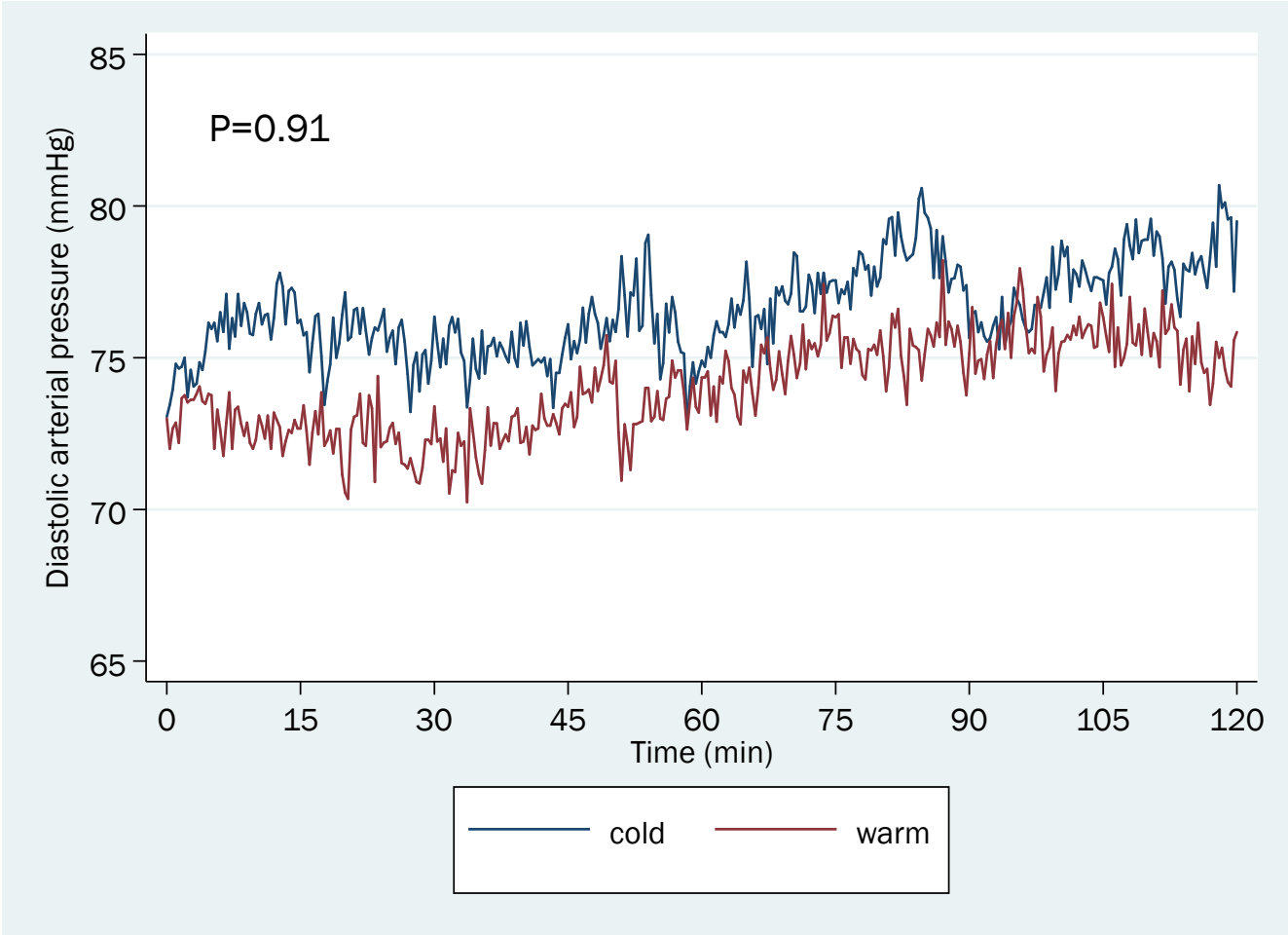


Fig.8

Mean diastolic arterial pressure during the 120 minutes of monitoring in subjects receiving a warm (red line) and cold (blue line) fluid bolus, respectively. P value represents the interaction between time and group on repeated measures analysis of variance.

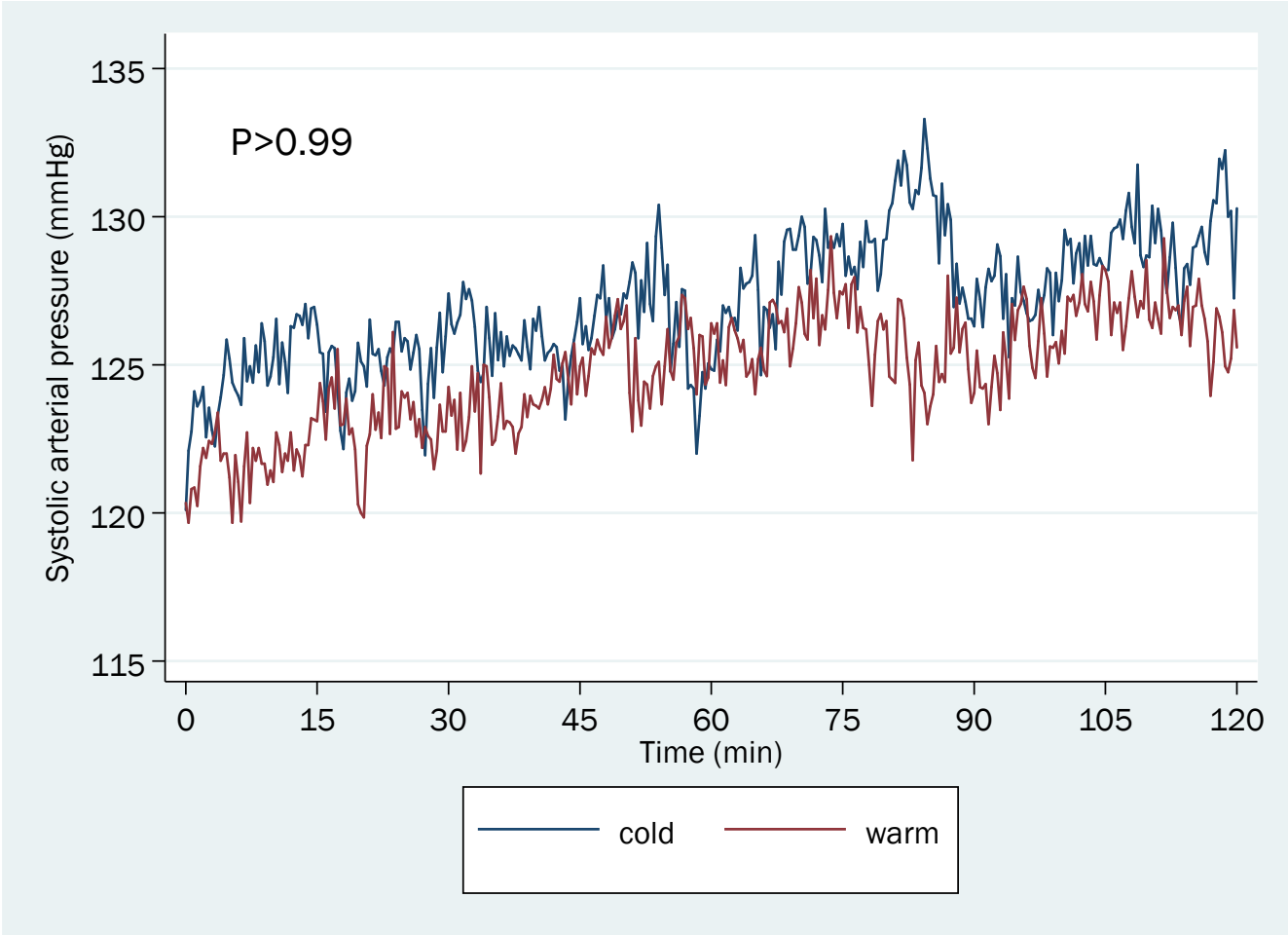


Fig.9  
Mean systolic arterial pressure during the 120 minutes of monitoring in subjects receiving a warm (red line) and cold (blue line) fluid bolus, respectively. P value represents the interaction between time and group on repeated measures analysis of variance.

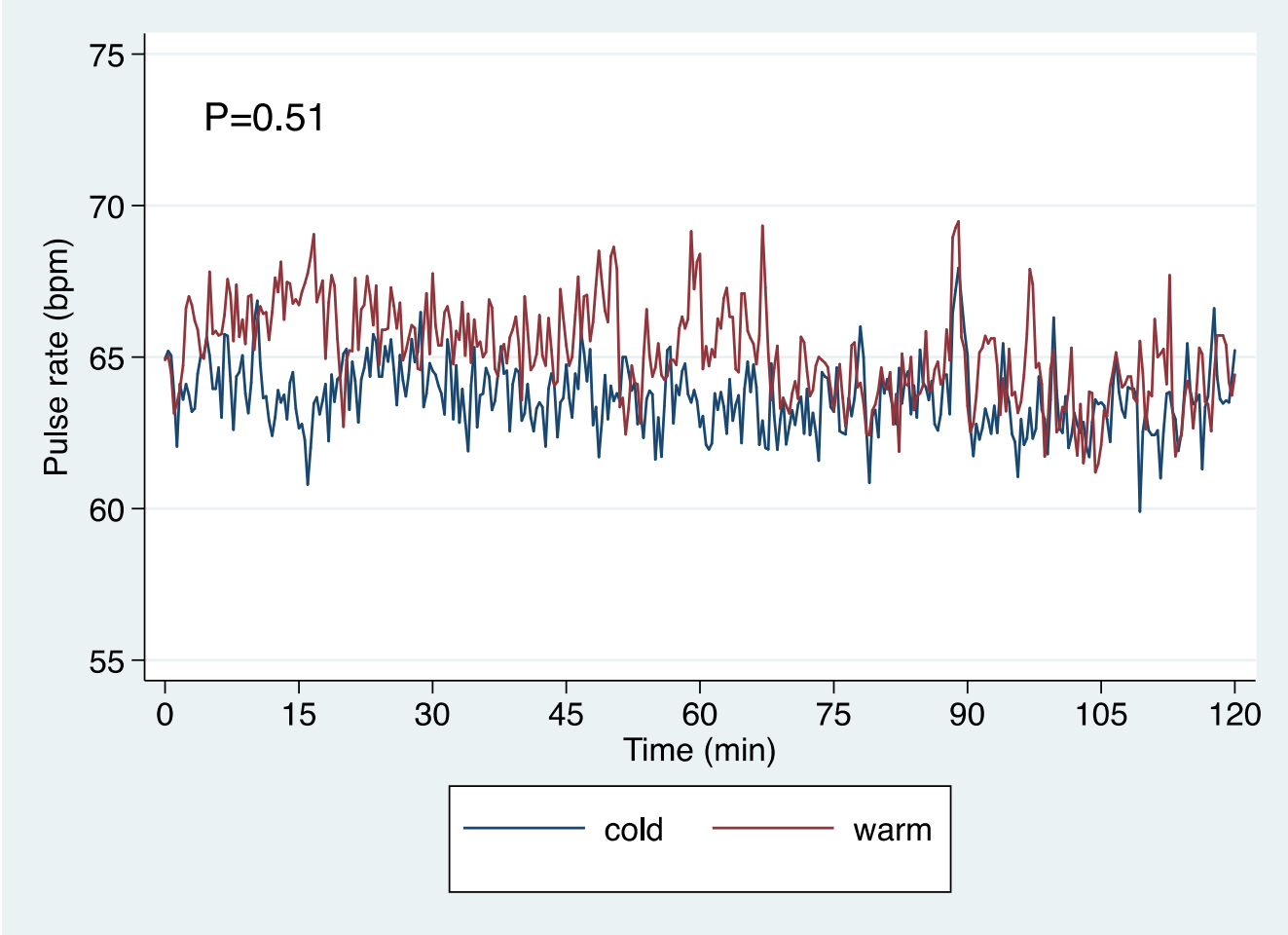


Fig. 10

Mean pulse rate during the 120 minutes of monitoring in subjects receiving a warm (red line) and cold (blue line) fluid bolus, respectively. P value represents the interaction between time and group on repeated measures analysis of variance.



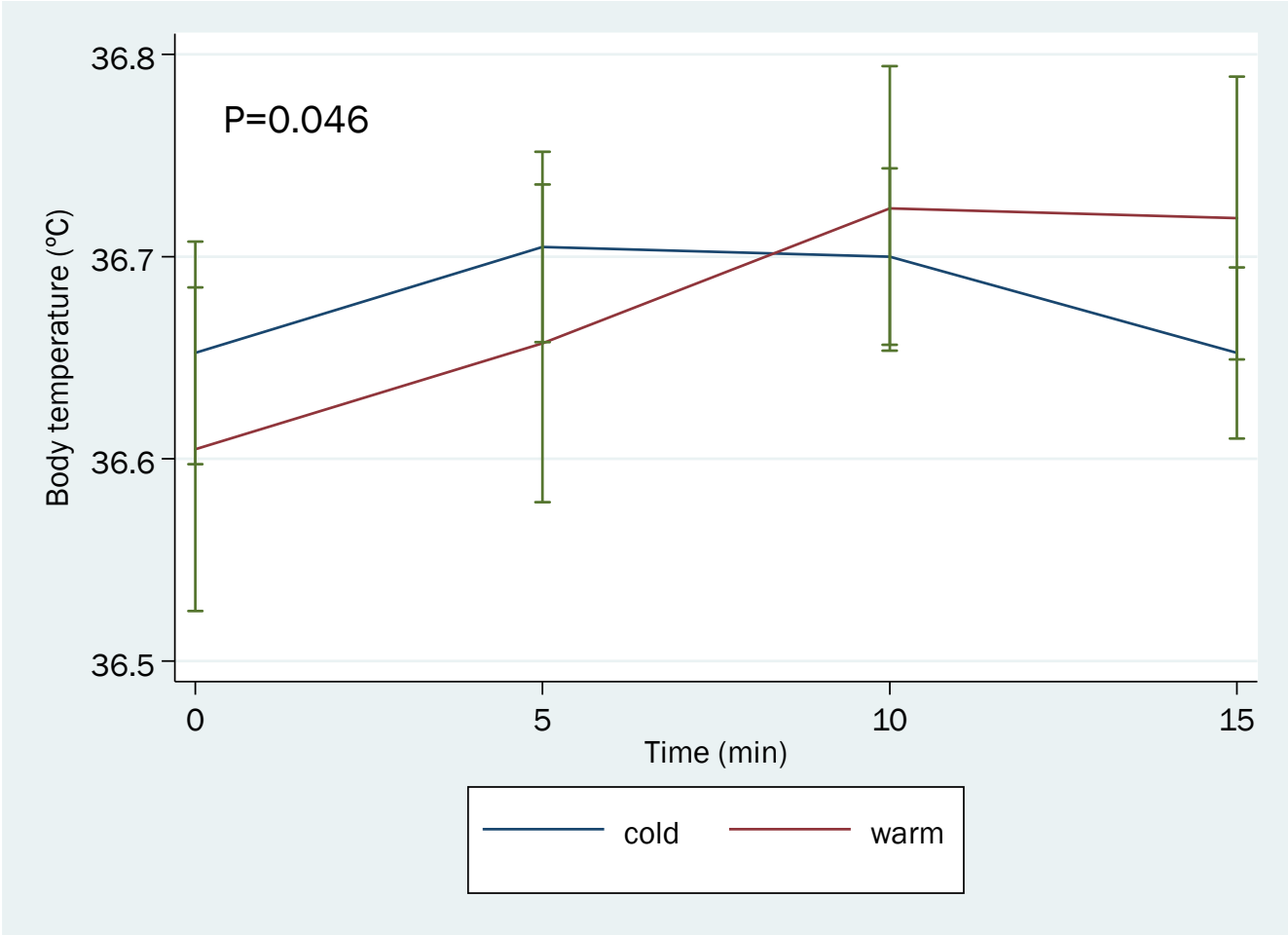


Fig. 11  
Mean (SEM) body temperature during the 15 minutes of fluid bolus administration in subjects receiving a warm (red line) and cold (blue line) fluid bolus, respectively. P value represents the interaction between time and group on repeated measures analysis of variance.

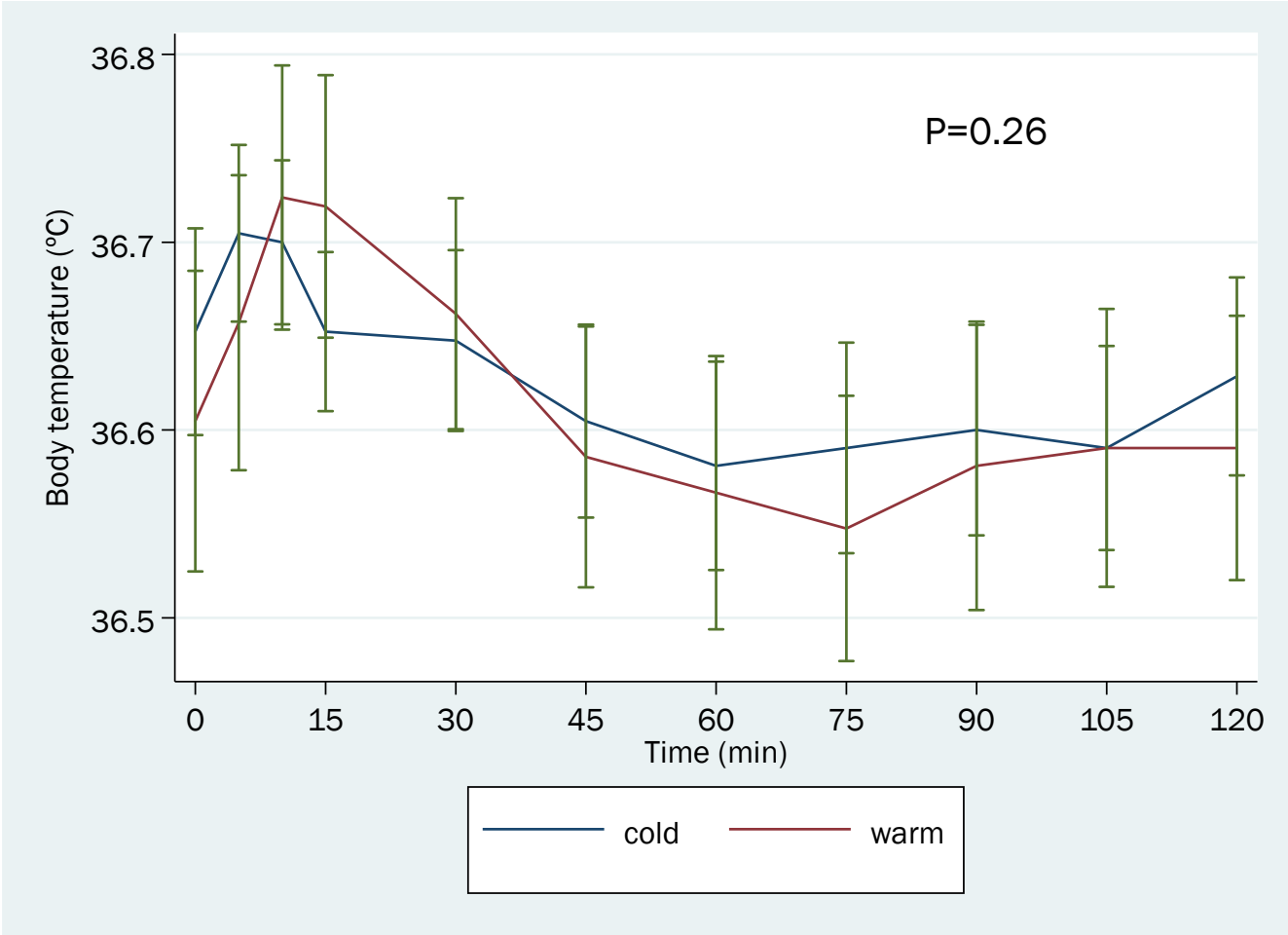


Fig. 12  
Mean (SEM) body temperature during the 120 minutes of monitoring in subjects receiving a warm (red line) and cold (blue line) fluid bolus, respectively. P value represents the interaction between time and group on repeated measures analysis of variance.