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Original Article

Mean arterial pressure targets in intensive care unit patients receiving noradrenaline: An international survey

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ABSTRACT

Objective: This study aimed to evaluate intensive care doctors' views about a large-scale pragmatic minimum mean arterial pressure (MAP) targets trial and their attitudes and beliefs about minimum MAP targets in different clinical scenarios.
Design: An online survey was conducted.

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Setting and participants: An online survey was distributed to intensive care doctors in sites participating in a large-scale international randomised clinical trial evaluating oxygen therapy targets in 15 countries and to additional intensive care clinicians from Canada.
Main outcome measures: Outcomes included the expressed level of support for a large pragmatic trial to evaluate minimum MAP targets in critically ill adults and stated current practice and acceptability of minimum MAP for specific scenarios.
Results: The response rate to our survey for respondents who work in sites participating in the mega randomised registry trial research program was 265 out of 701 (37.8%), with an additional 56 out of 256 (21.8%) responses obtained from a direct email containing a link to the survey sent to intensive care clinicians in Canada. A total of 309 of 321 respondents (96.3%) were supportive, in principle, of conducting a very large pragmatic trial to evaluate MAP targets in intensive care unit patients receiving noradrenaline. The commonest response in all scenarios was to agree that the optimal minimum MAP target was uncertain. In all scenarios, except for active bleeding, the most common reported minimum MAP target was 65 mmHg; for patients who were actively bleeding, the most common reported target was 60 mmHg.
Conclusions: Our data suggest that intensive care clinicians are broadly supportive of a large-scale pragmatic minimum MAP targets in intensive care unit patients receiving noradrenaline.

1. Introduction

Millions of patients receive treatment in intensive care units (ICUs) each year,[1] and a key component of this treatment is supportive care with the titration of specific therapies in response to prescribed physiological targets. One of the commonest examples of such supportive care is the titration of vasopressor drugs to avoid undesirably low blood pressure.[2] Thresholds for initiation and targets guiding administration of vasopressors reflect a balance between the benefits of maintaining blood pressure above specific thresholds[3–5] and the risks associated with vasopressor use. Such risks include excessive vasoconstriction, organ ischaemia, and tachyarrhythmia,[6] all of which have the potential to influence patient-important outcomes such as mortality.

Lower vs. higher minimum mean arterial pressure (MAP) targets in critically ill patients have been investigated in randomised clinical trials in the post-cardiac-arrest setting[7–9] and in critically ill patients with distributive shock.[10–13] A recent meta-analysis of randomised clinical trials including postsurgical and critically ill patients raises the possibility that allocation to lower blood pressure targets than higher targets might reduce mortality.[14] However, in the trials included in this analysis, minimum MAP targets ranged from 45 to 70 mmHg in the low blood pressure group and from 65 to 100 mmHg in the high blood pressure group.[14] The wide range of targets evaluated, combined with the variety of types of patients included, means that available evidence to define the *optimal* minimum MAP for critically ill patients either overall, or for particular subgroups, remains of very low certainty. Importantly, the possibility that there are clinically important mortality reductions attributable to prescription of specific minimum MAP targets has not been excluded.[14]

Accordingly, we undertook a survey to evaluate intensive care clinicians' views about a large-scale pragmatic minimum MAP targets trial and their attitudes and beliefs about minimum MAP targets in different clinical scenarios.

2. Methods

2.1. Sampling frame

Intensive care clinicians caring for critically ill patients were the population of interest for this survey. We were particularly interested in the views of clinicians from sites that are participating in a series of large trials involving oxygen targets[15–19] because these sites would potentially be able to participate in a large-scale pragmatic minimum MAP targets trial in the future. We sought to include additional participants from Canada as we are hoping to include a large number of Canadian sites in future trials.

2.2. Ethical approval

This low-risk survey of clinicians was outside the scope for requiring review by the New Zealand Health and Disability Ethics Committees. Consent to participate in the survey was not specifically sought from respondents but was inferred by completion of the survey.

2.3. Survey development

Our survey was developed by PY with input from RB and FL. Previous similar surveys were reviewed,[20,21] and a particular focus on feasibility aspects related to a possible future large-scale pragmatic clinical trial was incorporated. We explicitly focussed on clinical scenarios for adults receiving vasopressor infusions.

2.4. Survey testing

Prior to distribution of the survey, it was tested by 13 intensive care specialists from Wellington Hospital ICU to improve clarity. Minor changes were made after this testing.

2.5. Survey content

Respondents were asked about their support for a large pragmatic trial to evaluate minimum MAP targets in critically ill adults (Fig. 1). We also asked about clinician views on minimum MAP targets for specific patient groups and reported current practice for minimum MAP targets and acceptability of minimum MAP targets in a clinical trial. Finally, we asked open questions about additional clinical scenarios where minimum MAP targets might be of particular interest. Our full survey is available online (Appendix 1, electronic supplemental material).

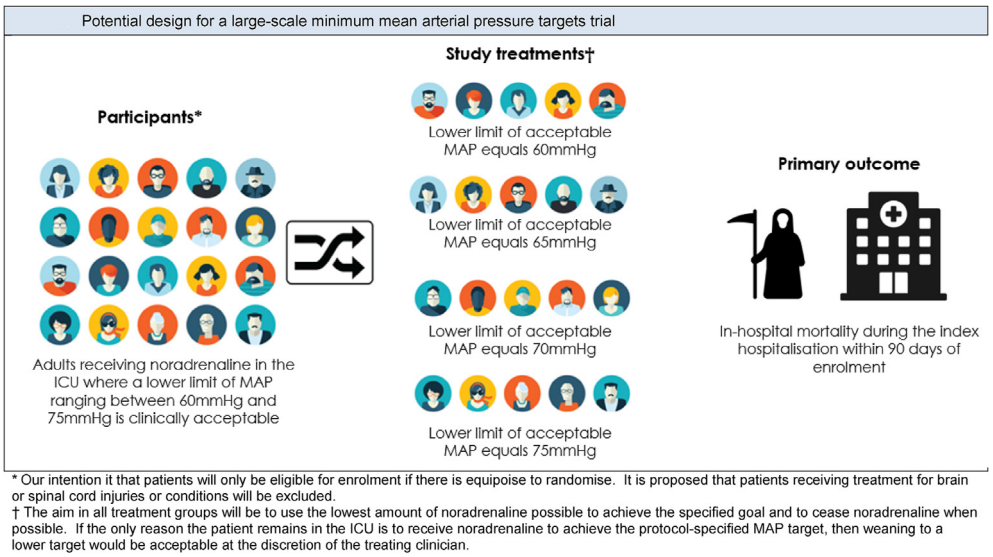

Figure 1. Potential design for a large-scale minimum mean arterial pressure targets trial. ICU, intensive care unit; MAP, mean arterial pressure.

2.6. Survey distribution

Our sample was obtained by directly emailing principal investigators at sites participating in the mega randomised registry trial research program (Mega-ROX) and asking them to forward the survey to clinicians at their site. In addition, a direct email invitation was sent to 256 clinicians in Canada who were not participating in Mega-ROX. The email provided a link to an online survey prepared using Google Forms. The survey was open from 11th June 2024 until 17 September 2024. No incentives were provided to complete the survey, and no reminders were sent. No specific measures prevented multiple responses being provided by a single respondent; however, no duplicated responses were received.

2.7. Analysis of survey data

Descriptive data obtained from our survey are summarised as counts and percentages for categorical variables. Recruitment rate estimates for a proposed trial are described as median interquartile range and the average estimate per site per week and per site per year. Where an individual did not complete the entire survey, we used data that were available for each question and specified the number of responses received for each question. Analyses were conducted using Microsoft Excel, 2016.

3. Results

3.1. Responses

The response rate to our survey from respondents who work at sites participating in Mega-ROX was 265 out of 701 (37.8%), with responses obtained from clinicians in 57 ICUs in 12 countries. The response rate from Canadian respondents who were contacted by a separate direct email was 56 out of 256 (21.8%). The number and proportion of responses by country are shown in Table 1. A list of ICUs where clinicians who responded worked is provided in Table S1 (see online supplementary material).

Table 1
Responses by country.

Country, n (%)	Responses (N = 321)
Australia	107 (33.3)
Brazil	9 (2.8)
Canada	64 (19.9)
India	13 (4.0)
Ireland	4 (1.2)
Japan	5 (1.6)
Kuwait	20 (6.2)
Malaysia	35 (10.9)
Nepal	5 (1.6)
New Zealand	32 (10.0)
Pakistan	8 (2.5)
Saudi Arabia	15 (4.7)
United Kingdom	1 (0.3)
Unknown	3 (0.9)

3.2. Support for a large pragmatic trial to evaluate MAP targets

A total of 309 of 321 respondents (96.3%) were supportive, in principle, of conducting a very large pragmatic trial to evaluate MAP targets in ICU patients receiving noradrenaline; eight of 321 (2.5%) were not supportive, and four of 321 (1.2%) indicated they did not know. Rates of support were similar in a question about specific support for a trial that included a broad cohort of patients receiving noradrenaline in the ICU, with four treatment arms including minimum MAP targets of 60 mmHg, 65 mmHg, 70 mmHg, and 75 mmHg and a primary outcome of in-hospital mortality. Here, 283 of 321 (88.2%) were "supportive", 25 of 321 (7.8%) responded "*don't know or maybe*", and 13 of 321 (4.0%) were "*not supportive*". Respondents estimated that a median of eight patients per week (interquartile range, 4.5 to 10) would be eligible for inclusion in this specific trial in their ICU. This equated to an average of 8.4 patients per site per week or 436.8 patients per site per year. Among 265 respondents from sites participating in the Mega-ROX trial, a total of 209 (78.9%) believed that the number of eligible participants for the specific pragmatic MAP targets trial proposed would equal or exceed the number eligible for Mega-ROX.

3.3. Views about MAP targets for specific patient groups

The extent to which respondents agreed that the optimal minimum MAP target is uncertain for specific scenarios in adults in the ICU receiving a noradrenaline infusion is shown in Fig. 2. The commonest response in all scenarios was to agree that the optimal minimum MAP target was uncertain. In each scenario, well over

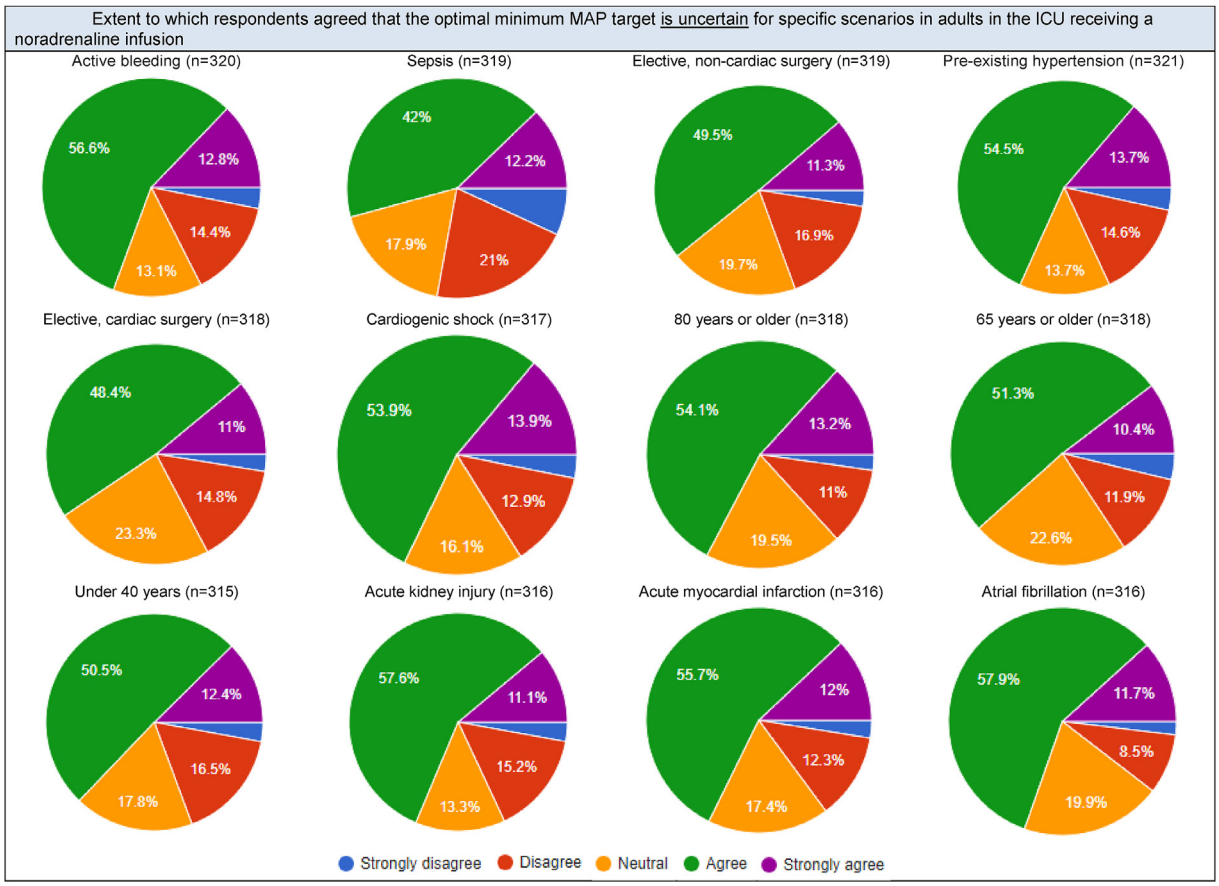

Figure 2. Extent to which respondents agreed that the optimal minimum MAP target is uncertain for specific scenarios in adults in the ICU receiving a noradrenaline infusion. ICU, intensive care unit; MAP, mean arterial pressure.

Table 2
Reported practice for lower-limit MAP targets for specific scenarios in adults in the ICU receiving a noradrenaline infusion.

Scenario	Reported current practice for minimum MAP target,[a] n/N (%)				
	60 mmHg	65 mmHg	70 mmHg	75 mmHg	Other
Active bleeding (N = 321)	**196 (61.1)**	92 (28.7)	4 (1.2)	2 (0.6)	27 (8.4)
Sepsis (N = 317)	58 (18.3)	**235 (74.1)**	9 (2.8)	3 (0.9)	12 (3.8)
Pre-existing hypertension (N = 317)	25 (7.9)	**161 (50.8)**	95 (30.0)	18 (5.7)	18 (5.6)
Elective, noncardiac surgery (N = 319)	61 (19.1)	**235 (73.7)**	14 (4.4)	3 (0.9)	6 (1.9)
Elective, cardiac surgery (N = 315)	58 (18.4)	**207 (65.7)**	33 (10.5)	3 (1.0)	14 (4.4)
Cardiogenic shock (N = 317)	126 (39.7)	**157 (49.5)**	19 (6.0)	3 (0.9)	12 (3.8)
80 years or older (N = 318)	78 (24.5)	**183 (57.5)**	48 (15.1)	2 (0.6)	7 (2.2)
65 years or older (N = 317)	53 (16.7)	**240 (75.7)**	18 (5.7)	1 (0.3)	5 (1.6)
Under 40 years (N = 316)	81 (25.6)	**214 (67.7)**	12 (3.8)	2 (0.6)	7 (2.2)
Under 65 years (N = 312)	55 (17.6)	**243 (77.9)**	9 (2.9)	0 (0)	5 (1.6)
Acute kidney injury (N = 317)	27 (8.5)	**189 (59.6)**	83 (26.2)	12 (3.8)	6 (1.9)
Acute myocardial infarction (N = 316)	57 (18.0)	**220 (69.6)**	32 (10.1)	2 (0.6)	5 (1.6)
Atrial fibrillation (N = 317)	64 (20.2)	**227 (71.6)**	21 (6.6)	0 (0)	5 (1.6)

ICU, intensive care unit; MAP, mean arterial pressure.
[a] The commonest target selected is shown in bold for each scenario.

half the respondents indicated agreement or strong agreement that the optimal target was uncertain (Fig. 2).

3.4. Reported current practice for minimum MAP targets

In all scenarios, except for active bleeding, the most common reported minimum MAP target was 65 mmHg; for patients who were actively bleeding, the most common reported target was 60 mmHg (Table 2).

3.5. Acceptability of minimum MAP targets in a clinical trial

The perceived acceptability of specific MAP targets in a randomised clinical trial in some specific clinical scenarios is shown in Fig. 3. Lower minimum MAP targets (≥60 mmHg or ≥65 mmHg) were generally preferred in patients who were bleeding but appeared to be less acceptable in patients with pre-existing hypertension and acute kidney injury (Fig. 3). The acceptability of specific minimum MAP targets appeared to be broadly similar for

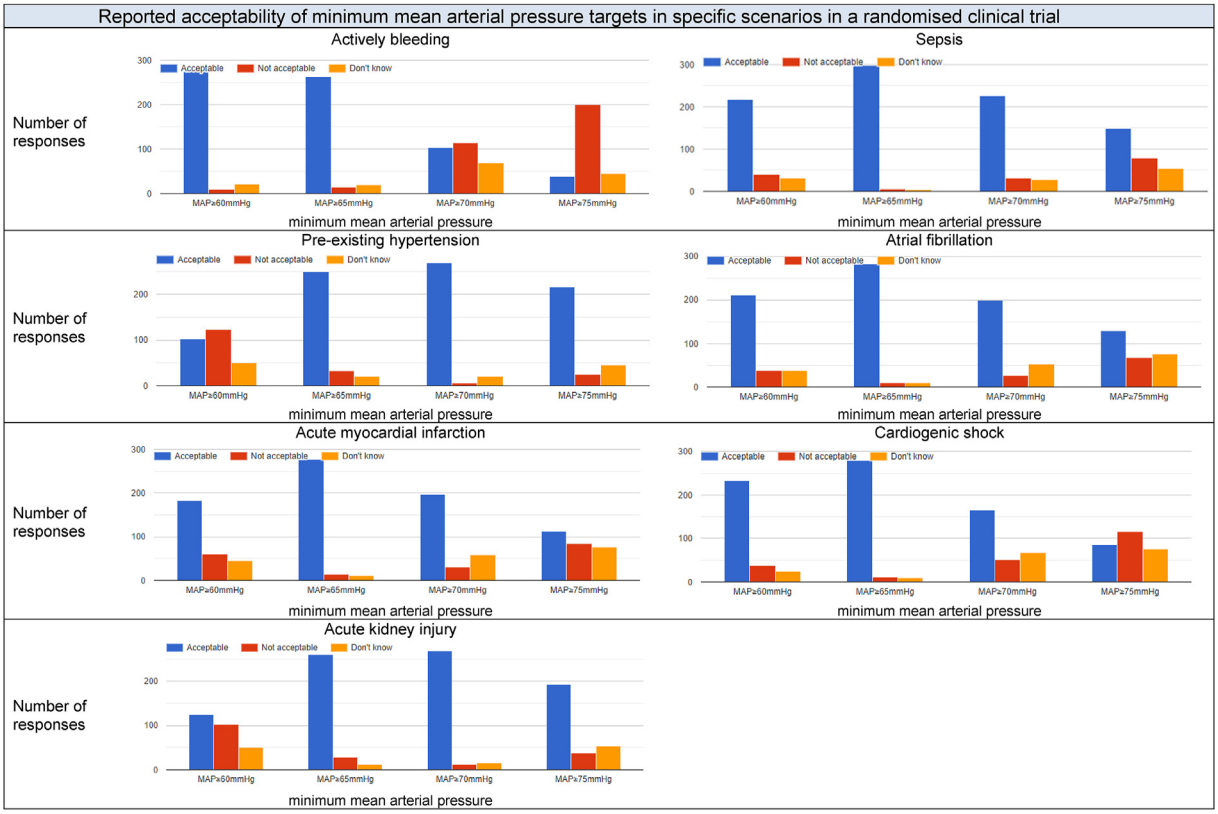

Figure 3. Reported acceptability of minimum mean arterial pressure targets in specific scenarios in a randomised clinical trial. MAP, mean arterial pressure.

elective cardiac surgery and elective non-cardiac-surgery patients and for different age groups (Fig. 4).

3.6. Responses to open questions

In response to an open free-text question, participants indicated a number of additional groups where minimum MAP targets were of potential interest (Table 3).

4. Discussion

4.1. Statement of principal findings

In this survey, intensive care clinicians, most of whom are involved in another large multicentre pragmatic physiological target trial focussed on oxygen, were broadly supportive of a large-scale pragmatic minimum MAP targets trial in ICU patients receiving noradrenaline. Respondents' estimates, in relation to recruitment rates, indicate that a very large trial in this patient group is potentially feasible. Based on the recruitment rate estimates, 100 ICUs would be expected to have >40,000 eligible participants per year. Respondents expressed considerable uncertainty about optimal minimum MAP targets and showed interest in further research across various patient groups. With the exception of the scenario of active bleeding, most respondents indicated that they prescribed a minimum MAP target of ≥65 mmHg in each of the scenarios presented. This minimum MAP target may represent the usual prescribed minimum blood pressure target for nonbleeding patients[22] and could define the comparator group in a large-scale randomised clinical trial. Other alternatives include a nonprescriptive usual care group or a comparator reflecting usual MAP values during vasopressor therapy as opposed to prescribed targets.[22]

4.2. Relationship to previous literature

Titration of vasoactive drugs to avoid low blood pressure is a ubiquitous treatment in the ICU, and at a global scale, due to the large number of patients treated, very small differences in mortality attributable to the minimum MAP target chosen would have profound public health importance. We are currently enrolling around 1000 patients a month into a 40,000-participant international randomised clinical trial[16] evaluating oxygen therapy targets in critically ill adults and consider that a similar trial of minimum MAP targets may be justified. Our observation that prescribed minimum MAP targets of ≥65 mmHg appear to represent usual care in patients receiving vasopressors is consistent with a prior survey of Canadian intensivists.[20] In a more recent survey, conducted from November 2016 to April 2017 and including 839 physicians from 82 countries, 70% of respondents indicated a preferred minimum MAP target of greater than 60–65 mmHg.[21] A minimum MAP target of 65 mmHg is also the recommended initial target for adults with septic shock on vasopressors specified in the Surviving Sepsis Campaign Guidelines.[23]

It is notable that stated practice with respect to prescribed targets differs from MAP values achieved during vasopressor therapy, even when targets are prescribed in a range rather than as a minimum lower boundary. In two prior randomised clinical trials evaluating "permissive hypotension" (MAP target: 60–65 mmHg),[11,12] the observed average MAP was just over 65 mmHg. In the most recent of these trials, the 65 trial, which included adults aged 65 years or older with distributive shock,[11] allocation to permissive hypotension was associated with reduced mortality compared to usual care in patients with chronic hypertension. Given these prior findings, another notable finding of our survey is that in patients with chronic hypertension, *higher* blood pressure

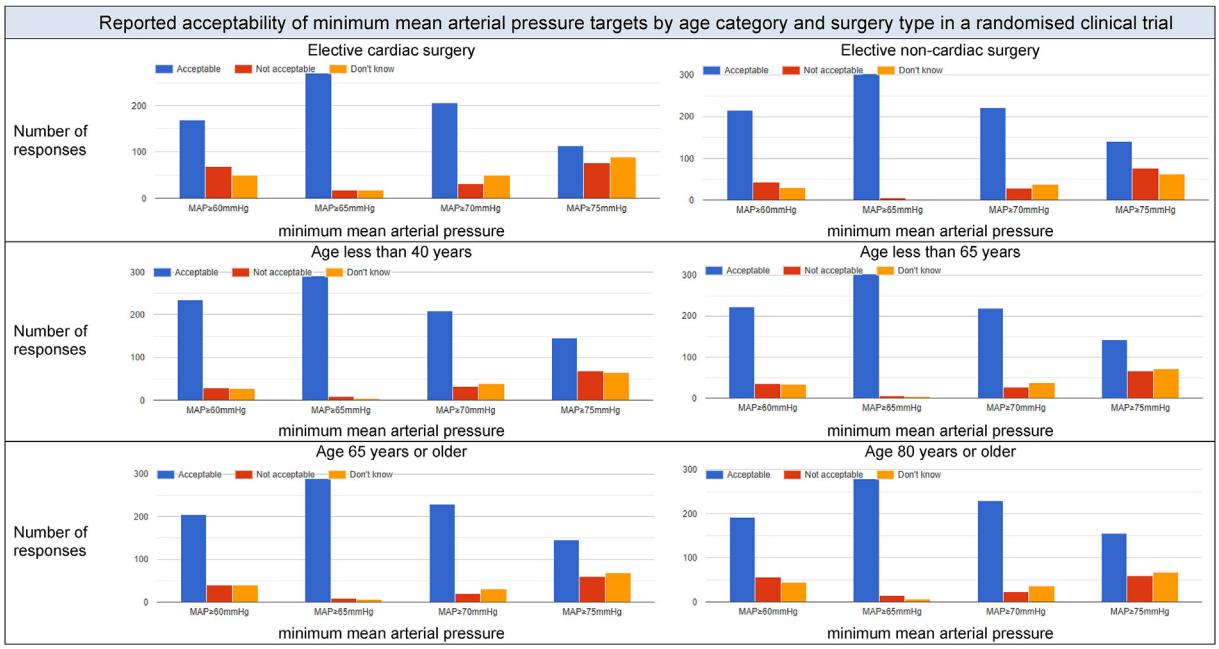

Figure 4. Reported acceptability of minimum mean arterial pressure targets by age category and surgery type in a randomised clinical trial. MAP, mean arterial pressure.

Table 3
Other subgroups of potential interest.

Abdominal compartment syndrome
Aortic syndromes
Bowel anastomosis
Carotid stenosis
Congestive cardiac failure
Dialysis dependent
Hepatorenal syndrome
Limb ischaemia
Liver failure
Obesity
Overdose
Peripheral vascular disease
Plastic surgery (e.g., free flaps)
Renal transplant
Vascular anastomosis
Visceral ischaemia
Young age (e.g., <20 years)

targets were often preferred and a target of >60 mmHg was considered *unacceptable* to a substantial proportion of respondents. This observation suggests that clinical practice in relation to minimum MAP targets in patients with chronic hypertension may be at variance with existing evidence. Data from the 65 trial indicate the possibility that the optimal MAP target might differ in different clinical circumstances.[24] The interest in exploring optimal minimum MAP targets in a range of clinical scenarios expressed by respondents in our survey indicates that clinicians consider the notion that a need for such individualisation of therapy is plausible.

4.3. Limitations

We acknowledge certain limitations. First, we took a pragmatic approach to survey development and did not use focus groups or other methods to develop survey questions. Second, our questions focussed on the default minimum MAP targets prescribed rather than considering modifications to such targets incorporating additional clinical assessments of central venous pressure, organ perfusion, or skin perfusion.[25] Third, we asked about specific minimum MAP targets between 60 mmHg and 75 mmHg; in all scenarios, some respondents checked "other" and indicated a preference for more extreme values than we had prespecified. Fourth, we specifically asked about blood pressure targets for patients receiving noradrenaline. We did not account for the dose of noradrenaline required or for scenarios where a patient was receiving an alternative vasopressor. Fifth, although the response rate was not high, it was typical for surveys of this nature.[26–28] Sixth, despite receiving responses from clinicians in more than 50 ICUs in 13 countries, our findings may not be generalisable to other ICUs, particularly those in different regions or health systems. The responses received may also not be representative of the views of clinicians in the ICUs where respondents work. Because our sampling method focussed on Mega-ROX principal investigators, we may have inadvertently enriched our sample with clinicians who are open to practice change through clinical trial participation. Seventh, as we did not collect information on the characteristics of respondents, we cannot be certain of the clinical experience of respondents who may have included residents, registrars, and consultants. Eighth, we did not provide detailed definitions of clinical scenarios that defined subgroups of potential interest. Accordingly, different respondents may not have interpreted scenarios such as "active bleeding" consistently. Finally, we did not specifically follow the Checklist for Reporting Results of Internet E-Surveys[29] or the Consensus-Based Checklist for Reporting of Survey Studies[30]; however, where we deviated from these checklists, we have acknowledged this as a limitation.

5. Conclusion

Our data suggest that intensive care clinicians are broadly supportive of a large-scale pragmatic minimum MAP targets in ICU patients receiving noradrenaline.

CRediT authorship contribution statement

Young: conceptualisation, methodology, data collection, data curation, analysis, writing—original draft preparation. **Bellomo and La Montagne:** methodology, data collection,

writing—reviewing and editing. **All other authors:** data collection, writing—reviewing and editing.

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No specific funding was provided for this study.

Conflict of interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: Paul Young reports financial support was provided by Health Research Council of New Zealand. Nai An Lai reports a relationship with Edwards Lifesciences Corporation that includes funding grants. Mahesh Ramanan reports a relationship with Metro North Hospital and Health Services that includes funding grants. Francois Lamontagne has patent pending to the University of Sherbrooke. Rinaldo Bellomo and Paul Young declare that they are members of the Editorial Board for *Critical Care and Resuscitation*. If there are other authors, they declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ccrj.2024.12.001.

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