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SPECIAL ARTICLE

CCCS-SSAI WikiRecs Clinical Practice Guideline: vasopressor blood pressure targets in critically ill adults with hypotension

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PICO[A] Question: In adult critically ill patients with hypotension and requiring vasopressor support, should we be prescribing a higher blood pressure target (MAP 75-85) when compared with a lower blood pressure target (MAP 60-70)?

Recommendation: We suggest against the use of a higher blood pressure (BP) target (MAP 75-85) when compared with a lower BP target (MAP 60-70) in adult critically ill patients with hypotension and requiring vasopressors. (Conditional recommendation)

This is a recommendation developed by the Canadian Critical Care Society and the Scandinavian Society of Anaesthesiology and Intensive Care Medicine (CCCS-SSAI) according to standards for trustworthy guidelines in collaboration with the MAGIC WikiRecs project. The WikiRecs project is an ongoing collaborative effort by a network of expert clinicians and methodologists whose aim is to produce trustworthy evidence summaries and clinical practice recommendations within 90 days of identifying potentially practice-changing evidence. See www.magicapp.org/public/guideline/OLwWKL *for more details about methods and processes, full evidence summary (GRADE SoF-table), and practical information presented in multilayered formats—available on all digital devices. The electronic supplemental material also contains similar information expanding on the WikiRecs methods and processes.*

This is a recommendation developed by the *Canadian Critical Care Society* and the *Scandinavian Society of Anaesthesiology and Intensive Care Medicine* according to standards for trustworthy guidelines in collaboration with the MAGIC WikiRecs project. An abridged version of the guideline is published in *Intensive Care Medicine* (10.1007/s00134-016-4539-5).

This article is accompanied by an editorial. Please see Can J Anesth 2017; 64: this issue.

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[A] PICO is defined as: Population, Intervention, Comparator, Outcome.

Table Evidence profile outcomes studied, pooled relative and absolute estimates of effect, GRADE certainty rating, and summary statement

Outcome	Study results and measurements	Absolute effect estimates Lower MAP target (60-70 mmHg)	Higher MAP target (75-85 mmHg)	Certainty in effect estimates (Quality of evidence)	Summary
Short-term Mortality (90 days)	Relative risk: 1.05 (95% CI 0.9 to 1.23) Based on data from 894 patients in 2 studies	411 per 1,000	433 per 1,000 Difference: 21 more deaths per 1,000 (95% CI, - 41 to 94)	Low Due to serious imprecision and serious risk of bias	Higher MAP target (75-85 mmHg) probably made little or no difference on short-term mortality
Long-term Mortality > 90 days (6 months)	Relative risk: 1.13 (95% CI 0.72 to 1.77) Based on data from 118 patients in 1 study	367 per 1,000	414 per 1,000 Difference: 47 more deaths per 1,000 (95% CI, - 103 to 282)	Low Due to serious risk of bias and serious imprecision	Higher MAP target (75-85 mmHg) probably made little or no difference on long-term mortality > 90 days
Use of Renal Replacement Therapy (RRT) (28 days)	Relative risk: 0.96 (95% CI 0.80 to 1.14) Based on data from 894 patients in 2 studies	357 per 1,000	343 per 1,000 Difference: 25 fewer patients needing RRT per 1,000 (95% CI, - 71 to 50)	Low Due to serious risk of bias and serious imprecision	Higher MAP target (75-85 mmHg) probably made little or no difference on use of renal replacement therapy
Digit, Limb or Skin Ischemia	Relative risk: 0.95 (95% CI 0.41 to 2.16) Based on data from 894 patients in 2 studies	27 per 1,000	25 per 1,000 Difference: 1 less episode of ischemia per 1,000 (95% CI, - 16 to 31)	Very Low Due to serious risk of bias and very serious imprecision	We are uncertain whether a higher MAP target (75-85 mmHg) increases or decreases digit, limb, or skin ischemia
Myocardial Ischemia (MI)	Relative risk: 1.46 (95% CI 0.38 to 5.64) Based on data from 894 patients in 2 studies	29 per 1,000	36 per 1,000 Difference: 13 more MIs per 1,000 (95% CI, -18 to 135)	Very Low Due to serious risk of bias and very serious imprecision	We are uncertain whether a higher MAP target (75-85 mmHg) increases or decreases myocardial ischemia
Ventilator-free Days (VFD) (28 days)	Based on data from 894 patients in 2 studies	15.9 (Mean)	15.1 (Mean) Mean Difference: 0.84 fewer VFDs (95% CI, - 2.28 to 0.6)	Low Due to serious risk of bias and serious imprecision	A higher MAP target (75-85 mmHg) probably made little or no difference on ventilator-free days

MAP = mean arterial pressure; CI = confidence interval

Justification: We developed this recommendation according to the standards for trustworthy guidelines, including a systematic review that identified two randomized-controlled trials (894 patients) relevant to our clinical question.[1,2] The larger trial included only patients with hypotension secondary to sepsis,[1] whereas the other trial enrolled patients with distributive shock due to any etiology.[2]

Our weak recommendation against higher BP targets takes into consideration the absence of a demonstrated benefit and high resource demands associated with higher dose or longer duration vasopressor infusions (see Table). Additionally, it may be that the prescription of higher thresholds, and a subsequent need for higher doses of vasopressors to achieve these thresholds, leads to increased harm via increased myocardial ischemia and tachyarrhythmias. Nevertheless, this signal is limited by imprecision and risk of bias. This signal for harm may be more substantive in the elderly population based on subgroup analysis; however, the panel did not consider the evidence robust enough for a stronger recommendation in this population.

All outcome data were based on low or very low certainty evidence and, as such, the panel refrained from making a more definitive recommendation. The residual uncertainty was a result of lack of blinding of group allocation in the individual studies and imprecision of the

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pooled results. The guideline panel had significant internal debate as regards lowering the overall certainty for lack of blinding (risk of bias) in view of the objective nature of mortality as an outcome and the impracticalities of blinding an intervention such as BP targets. Other than lack of blinding, both trials had a low risk of bias for all other domains included in the Cochrane randomized-controlled trials tool.[3] Ultimately, as intensive care unit mortality is often the result of end-of-life decision-making[4] and in order to remain conservative in our overall certainty judgement, we decided to lower for risk of bias due to lack of blinding.

The guideline panel also acknowledged the difficulty in making recommendations without quality of life particulars, morbidity indices, or long-term outcome data. Prescribing higher BP targets may have had a different impact on these outcomes than on mortality, and therefore, may have affected our overall recommendation. Our patient representative identified this factor as a significant limitation, and this represents an important consideration for future research in this area.

Conflict of interest None declared.

Editorial responsibility This submission was handled by Dr. Hilary P. Grocott, Editor-in-Chief, *Canadian Journal of Anesthesia.*

Author contributions *Bram Rochwerg* contributed by chairing the guideline panel, helping to employ GRADE methodology and certainty of evidence assessments, and drafting the manuscript. *Mathieu Hylands* and *Francois Lamontagne* coordinated the evidence search and synthesis and were guideline panel members. Annette Kristiansen was the methods chair for the guideline panel. *Morten Møller, Pierre Asfar*, *Dian Cohen*, *Rachel Khadaroo*, *Jon Laake*, *Anders Perner*, *Teddie Tanguay*, *Sandy Widder,* and *Per Vandvik* were panel members, contributed significantly to formulating the recommendation, and provided edits to the manuscript.

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