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RESEARCH ARTICLE

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Preferences and attitudes on acetate- versus lactate-buffered crystalloid solutions for intravenous fluid therapy—An international survey

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Abstract

Background: Clinical practice guidelines recommend use of buffered crystalloid solutions in critically ill patients but do not distinguish between solutions based on different buffering anions, that is, acetate- versus lactate-buffered solutions. We therefore surveyed relevant physicians about their preferences and attitudes toward each solution.

Methods: We conducted an international online survey of anesthesiologists (within perioperative care) and intensive care unit (ICU) physicians. The survey comprised 13 questions on respondents' attitudes and preferences regarding the use of acetate- and/or lactate-buffered crystalloid solutions, including their opinions on a potential clinical trial comparing these solutions and the clinical importance of such a trial.

Results: A total of 1321 respondents participated, with a response rate of 34%, ranging from 14% to 96% across 18 countries. Most surveyed physicians reported using buffered crystalloid solutions "*very often*" (76%) or "*often*" (16%). Availability of acetate- and lactate-buffered solutions varied, as 35% of respondents reported having both types available, 35% reported having only acetate-, and 24% reported having only lactate-buffered solutions available.

Most respondents (87%) would support a randomized trial in adult emergency surgical patients and ICU patients comparing an acetate- versus lactate-buffered crystalloid solution. The median rating of the clinical importance of this question was 5 (interquartile range 4–6) on a scale from 1 to 9.

Conclusions: In this international survey, the reported use of buffered crystalloid solutions was high. Availability of the different solutions varied widely. The support

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for a potential randomized trial was high, with the clinical importance rated important but not critical by most respondents.

KEYWORDS
acetate, crystalloid, fluid therapy, intravenous fluid, lactate

Editorial Comment

In this international survey of anesthesiologists and intensivists, the vast majority of respondents reported frequent use of buffered crystalloids but there was a large variability for which buffer was available to clinicians. There was overall support for performing a trial of different buffered solutions and survival, although the clinical importance was only graded as moderate, and the vast majority of answers were from a single country.

1 | BACKGROUND

Administration of intravenous (IV) fluids is a routine practice in many medical settings.[1] IV fluids are used for resuscitation in acute circulatory failure and for replacement or maintenance therapy.[1]

The most frequently used IV fluids are isotonic crystalloid solutions, which fall into two main categories: saline (0.9%) and buffered crystalloid solutions (i.e., Ringer's solutions, Hartmann's solution, Plasmalyte).

Buffered crystalloid solutions are often perceived as more physiological than 0.9% saline, owing to their chemical composition more closely resembling that of extracellular fluid.[2–4] However, buffered solutions are in fact often relatively hypotonic compared to plasma. In addition, alternative anions have been added as a substitute to the naturally occurring buffer bicarbonate, which cannot be used due to its instability in soft plastic containers.[2–5] Despite being grouped together, buffered crystalloid solutions vary in composition, with some containing primarily acetate and others lactate as the buffering agent.[2–4]

Recent studies suggest a negative impact from 0.9% saline compared with buffered crystalloid solutions on acid–base balance, renal physiology, and mortality.[6,7] As a result, clinical practice guidelines increasingly recommend the use of buffered solutions over 0.9% saline.[8–10] Notably, these guidelines do not distinguish between the different types of buffered solutions based on the buffering anion, that is, acetate- versus lactate-buffered solutions.[8–10]

Lactate-buffered solutions, such as Ringer's Lactate or Hartmann's solution, have a long history of use, dating back to their introduction as the first marketed buffered solutions.[11] However, concerns about the potential for hyperlactatemia, particularly in patients with impaired liver functions exist.[2,12,13] Acetate-buffered solutions, such as Ringer's Acetate, PlasmaLyte, or Sterofundin, were introduced later,[11] and concerns, primarily from animal studies, about potential negative cardiovascular effects have been proposed.[14–17] These concerns, despite being primarily based on theoretical conceptions and animal studies, have already warranted changes in clinical practice, as the use of acetate as the buffer in dialysis fluids has declined, prompting a shift toward more costly bicarbonate-based solutions in contemporary clinical practice.[18] Importantly, the evidence base supporting the use of acetate- versus lactate-buffered solutions is sparse and of very low certainty.[19–21]

The preferences and attitudes toward IV use of different buffered crystalloid solutions among physicians are poorly described. Hence, we aimed to describe preferences and attitudes towards the use of different buffered crystalloid solutions (acetate- and lactate-buffered solutions) among anesthesiologists working within perioperative care and intensive care unit (ICU) physicians.

2 | METHODS

2.1 | Study design and approvals

We conducted an international online survey of anesthesiologists working within perioperative care and ICU physicians on their preferences and attitudes towards the use of different buffered crystalloid solutions (i.e., acetate- versus lactate-buffered solutions). We used the secure web application Research Electronic Data Capture (REDCap) hosted by the Capital Region of Denmark.[22] The survey was approved by the Legal Department of Scientific Research in the Capital Region of Denmark (Approval number: p-2022-499). Ethical approvals were waived as no patient-attributable data were collected. We report the findings of this survey according to the Consensus-Based Checklist for Reporting of Survey Studies (CROSS) checklist (Electronic Supplementary Material (ESM, suppl. 1)).[23]

2.2 | Survey content

The survey was designed and drafted by the managing committee (KLE, PS, AP, and MHM) and pilot-tested by three ICU physicians and six researchers working at the coordinating site (Rigshospitalet,

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Denmark), who were not members of the management committee. The pilot test focused on content validity, ease of completion, response time, functionality, and clarity. All revisions were implemented prior to survey distribution. The survey was developed in English, and no translations were made.

Overall, the survey consisted of 13 main questions that explored the characteristics of respondents including their professional setting, access to and preferred use of different buffered crystalloid solutions, and lastly, their attitudes toward a future randomized trial comparing an acetate- versus lactate-buffered crystalloid solution. All 13 main questions were mandatory to increase completeness of the survey. The survey employed branching logic functions and non-mandatory open-ended fields allowing respondents to elaborate on their answers provided within the 13 main questions. Lastly, respondents were asked to provide their work e-mail address (non-mandatory) to verify the uniqueness of responses. The distributed survey is presented in the ESM suppl. 2.

2.3 | Survey distribution and data collection

Distribution of the survey internationally was based on the recruitment of a national investigator within each country. National investigators were invited through an established international network for ICU researchers, the Collaboration for Research in Intensive Care (CRIC, www.cric.nu) and through contacts established in previous research collaborations.

National investigators were responsible for coordinating the distribution of the survey within their country. The survey could be distributed either personally by the national investigator or through designated local investigators. Each national investigator was responsible for reporting the total number of physicians to whom a survey invitation was sent within their country, representing the total national denominator.

The survey was distributed between April 29, 2024 and May 31, 2024, via email or WhatsApp message containing an online survey link. Participation in the survey was voluntary, and no financial compensation was provided. Activation and completion of the survey link were considered informed consent.

All national investigators were encouraged to send out two reminders to potential respondents prior to survey closure. In case of duplicate responses by the same e-mail, we used the most recently provided form. In case of missing data, we did not reach out to respondents for additional information or clarification.

2.4 | Statistics

We present data descriptively with categorical variables as numbers and percentages. We report the proportion of missing data without imputation. We conducted no sample size estimation, and the results are based on a convenience sample. Statistical analyses were performed using R (version 4.3.2).

3 | RESULTS

A total of 1336 responses were received from anesthesiologists and ICU physicians across 18 countries (Figures 1 and 2). Fifteen responses were removed from the analysis (4 were not anesthesiologists /ICU physicians, and 11 were duplicates), yielding a total number of 1321 responses (Figure 1). The overall response rate was 34%, with response rates per country ranging from 14% to 96% (ESM, suppl. 3). Respondents were mainly specialist physicians (85%) from public hospitals (87%), working in ICU (45%), perioperative care (22%), or both (32%) (Table 1). Less than 2% of responses were missing for any of the 13 main questions (ESM, suppl. 4).

3.1 | Use of buffered crystalloid solutions

Among the surveyed physicians, most reported using buffered crystalloid solutions "*very often*" (76%, 95% confidence interval [CI] 73%–78%) or "*often*" (16%, 95% CI 14%–18%) in daily clinical practice (Table 2). Regarding indications for use, 90% (95% CI 89%–92%) of respondents reported use of buffered crystalloid solutions as "*resuscitation fluid*," 79% (95% CI 76%–81%) as "*maintenance fluid*," 76% (95% CI 74%–78%) as "*replacement fluid*" and 35% (95% CI 32%–37%) as "*carrier fluid*" for medication (Table 2).

When distinguishing between acetate- and lactate-buffered crystalloid solutions, 35% (95% CI 33%–38%) of respondents reported having both solutions readily available within their department, while 59% (95% CI 56%–61%) had only one or the other available (Table 2). The most used buffered crystalloid solution was Ringers Lactate (35%; 95% CI 32%–37%) followed by Ringers Acetate (33%; 95% CI 31%–36%), Plasmalyte (19%; 95% CI 17%–21%) and Hartmann's solution (5%; 95% CI 4%–6%) (Figure 3). The use and availability of specific products varied across countries (ESM, suppl. 5, Table 5a). All countries had both acetate- and lactate-buffered solutions available to different extents, except for Sweden, where all seven respondents (representing seven individual institutions) reported only having an acetate-buffered solution available (ESM, suppl. 5, Table 5b).

Among respondents who had both acetate- and lactate-buffered solutions available ($n = 468$), 42% (95% CI 38%–47%) mostly used acetate-, 35% (95% CI 31%–39%) mostly used lactate- buffered solutions while 23% (95% CI 19%–26%) reported using the solutions interchangeably. When choosing to prescribe a specific type of buffered crystalloid solution, 70% (95% CI 66%–74%) of respondents reported doing so based on "*clinical considerations, including safety*" and 23% (95% CI 19%–27%) based on "*adherence to local guidelines*" while 30% (95% CI 26%–34%) of respondents base their choice on "*habit*," 10% (95% CI 8%–13%) on "*opinions of colleagues*" and 11% (95% CI 8%–14%) on "*cost*" (ESM, suppl. 6).

Among respondents who had only one type of solution available ($n = 851$), 28% (95% CI 25%–31%) reported having a personal preference for either acetate- or lactate-buffered solutions. Of these respondents, 44% (95% CI 38%–50%) reported their preference being based on "*clinical considerations, including safety*," 31% (95% CI 26%–

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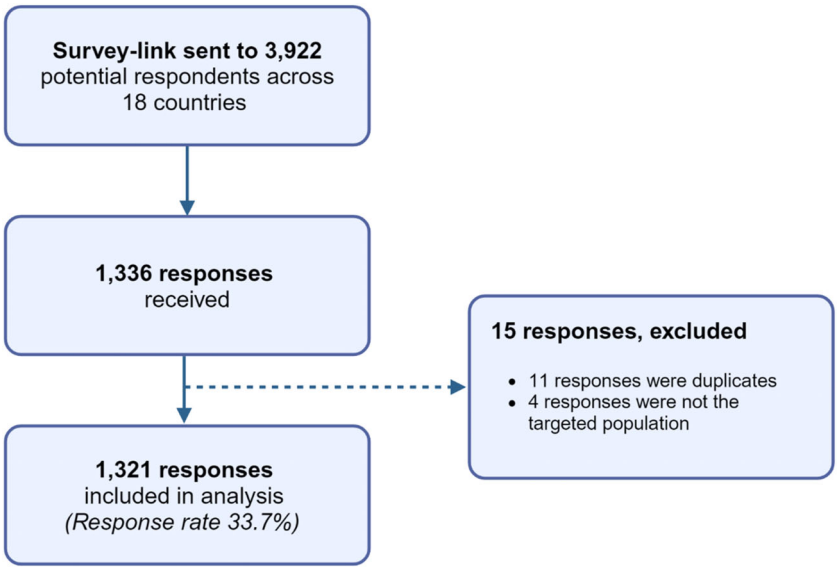


FIGURE 1 Flow chart for inclusion of survey responses.

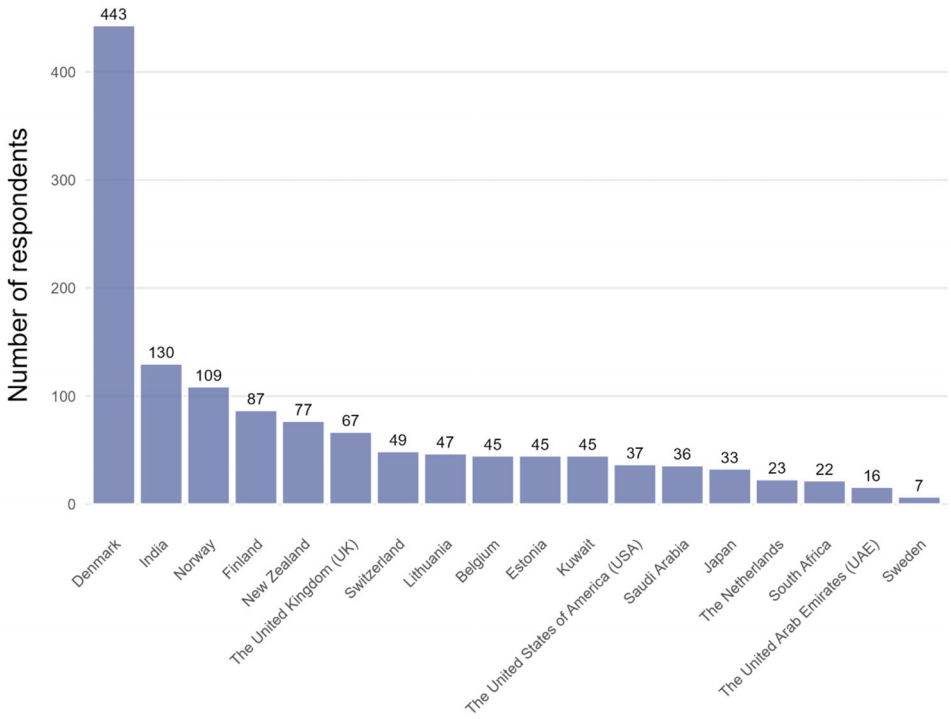


FIGURE 2 Number of respondents per country. The United Kingdom included responses from both England and Northern Ireland.

*The United Kingdom included responses from both England and Northern Ireland.

37%) on "*habit*," 8% (95% CI 5%–12%) on "*opinions of colleagues*" and 2% (95% CI 0%–3%) on "*cost*" (ESM, suppl. 6).

3.2 | Preferences for a future cluster randomized trial

A total of 1146 (87%; 95% CI 85%–89%) respondents reported willingness to participate in a cluster randomized trial assessing the effects of acetate- versus lactate-buffered crystalloid solutions on patient-important outcomes in acutely admitted adult emergency surgical patients (perioperative use) and ICU patients (ESM, suppl. 7). The most common reasons for not wanting to participate (reported in optional free-text fields) were "*expected low effect size*," "*not aware of physiological rationale*," "*lack of clinical importance*," and "*unwanted workload*" (ESM, suppl. 8). A total of 283 respondents (21.%; 95% CI 19%–24%) reported presence of potential barriers for a trial within their setting (ESM, suppl. 8). The most common barriers included lack of fluid availability, difficulty in changing habit of staff, poor documentation of fluid use, and limited logistical and financial resources.

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TABLE 1 Characteristics of respondents.

Variable	No. respondents	Percentages % (95% confidence intervals[CIs])
Country (%)[a]		
Belgium	45	3 (2–4)
Denmark	443	36 (31–36)
Estonia	45	3 (2–4)
Finland	87	7 (5–8)
India	130	10 (8–11)
Japan	33	3 (2–3)
Kuwait	45	3 (2–4)
Lithuania	47	4 (3–5)
New Zealand	77	6 (5–7)
Norway	109	8 (7–10)
Saudi Arabia	36	3 (2–4)
South Africa	22	2 (1–2)
Sweden	7	1 (0–1)
Switzerland	49	4 (3–5)
The Netherlands	23	2 (1–2)
The United Arab Emirates (UAE)	16	1 (1–2)
The United Kingdom (UK)	67	5 (4–6)
The United States of America (USA)	37	3 (2–4)
Hospital (%)		
Public general hospital	600	45 (43–48)
Public specialist hospital	555	42 (39–45)
Private general hospital	54	4 (3–5)
Private specialist hospital	112	8 (7–10)
Physician (%)[b]		
Intensive care medicine	600	45 (43–48)
Perioperative care (anesthesia)	296	22 (20–25)
Both	423	32 (30–35)
Type of intensive care unit (ICU) ($n = 1023$[c])		
Mixed ICU	822	80 (78–83)
Cardio-thoracic ICU	80	8 (6–10)
Neurological/ neurosurgical ICU	41	4 (3–5)
Medical ICU	40	4 (3–5)
Surgical ICU	34	3 (2–4)
Other	2	0 (0–1)
Level of training[d]		
Specialist (yes)	1125	85 (83–87)

[a]Data on country missing for 3 respondents.
[b]Data on type of physician missing for 2 respondents.
[c]Number of respondents equals the no. of respondents who replied work setting as "ICU" or "Both."
[d]Data on level of training missing for 2 respondents.

TABLE 2 Fluid characteristics.

	No. respondents	Percentages % (95% CIs)
Q How often do you prescribe/use any buffered crystalloid solution?[a]		
Very often	997	76 (73–78)
Often	217	16 (14–18)
Sometimes	73	5.5 (4–7)
Rarely	25	2 (1–3)
Very rarely	7	1 (0–1)
Q For which indication(s) do you use buffered crystalloid solutions?[b]		
Resuscitation fluid	1192	90 (89–92)
Maintenance fluid	1039	79 (76–81)
Replacement fluid	1004	76 (74–78)
Carrier fluid	459	35 (32–37)
Q Do you currently have both acetate- and lactate-buffered crystalloid solutions readily available within your department?[a]		
Yes, we have both options available	468	35 (33–38)
No, we only have an acetate-buffered solution	458	35 (32–37)
No, we only have a lactate-buffered solution	315	24 (22–26)
I am not aware	78	6 (5–7)

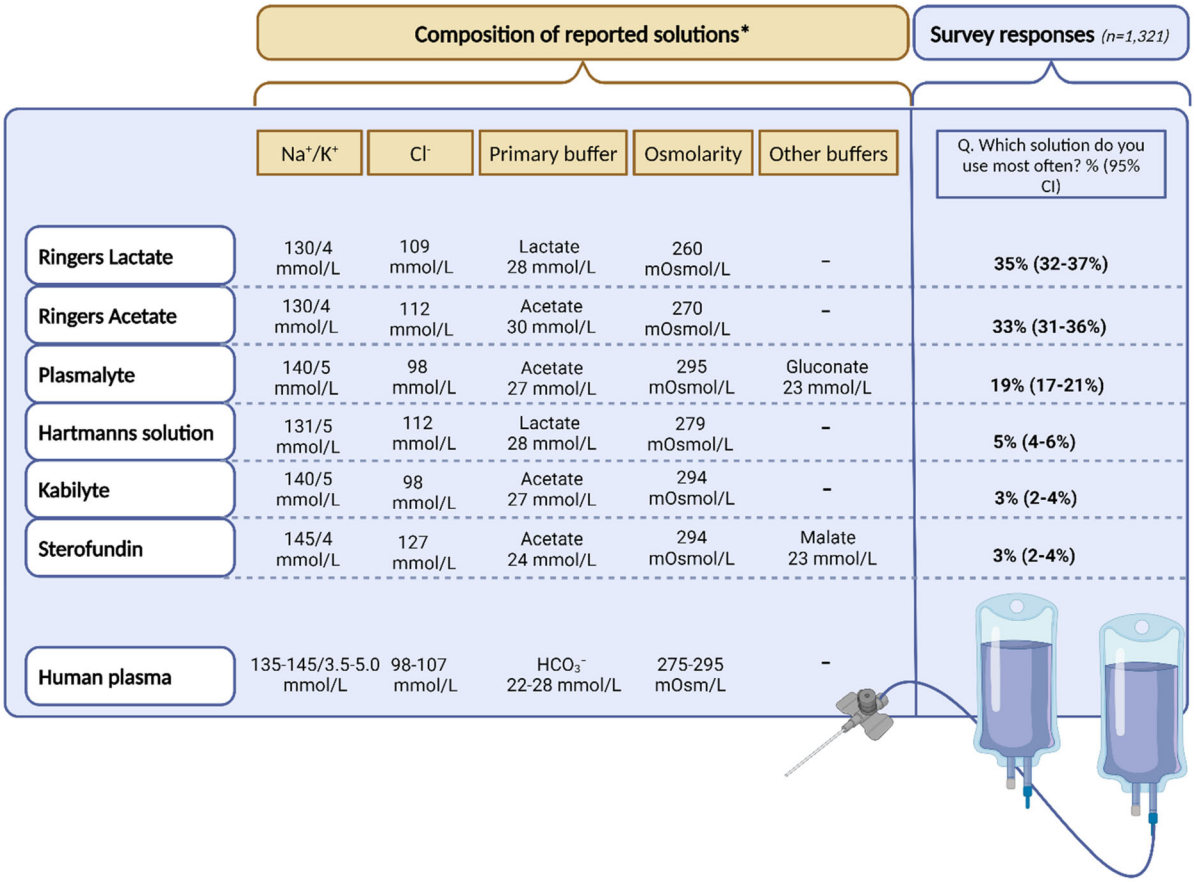
[a]Data missing for 2 respondents.
[b]Data missing for 3 respondents.

Overall, the median rating of the clinical importance of a clinical trial on this question (on a scale of 1–9) was 5 "important" (interquartile range 4–6) across all respondents (Figure 4). The availability of both acetate- and lactate-buffered solutions appeared to be related to higher ratings of clinical importance compared to respondents with only one type of fluid available (Table 3).

4 | DISCUSSION

This international survey has several key findings regarding the reported use of buffered crystalloid solutions among anesthesiologists and ICU

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*Composition may vary according to manufacturer

FIGURE 3 Composition and reported use of specific buffered crystalloid solutions among all respondents. Only the six most reported solutions are presented. Data were missing for 1 respondent. Data on composition was apprehended from the national resource Pro.medicin.dk which is maintained by the Danish Medicines Agency in collaboration with the Danish Medical Association. The figure was Created with Biorender.com.

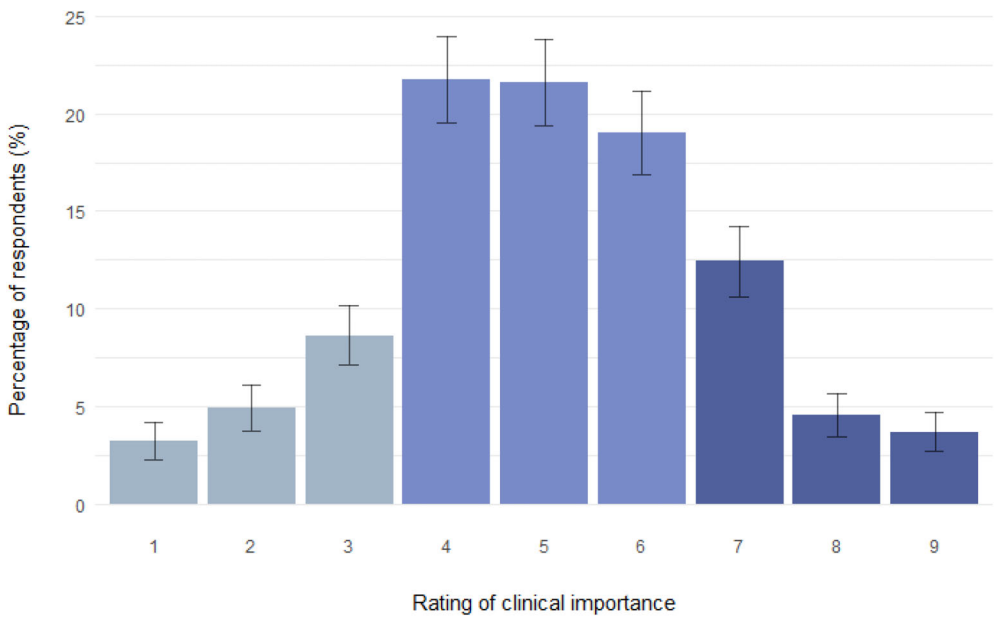


FIGURE 4 Bar plot illustrating the rating of clinical importance of the research question on a scale of 1–9 (1–3 not important, 4–6 important, 7–9 critical) among all respondents (%). The black bars represent 95% confidence intervals for each category. Data were missing for 11 respondents.

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TABLE 3 Rating of the clinical importance of the research question among respondents depending on the availability of fluids.[a]

Availability of solutions[b]	1–3 Not important	4–6 Important	7–9 Critical
Only one type of solution available (either acetate- or lactate-buffered) ($n = 773$)	154 (20%, 95% CI 17%–23%)	498 (65%, 95% CI 61%–68%)	119 (15%, 95% CI 13%–18%)
Both acetate- and lactate-buffered solutions available ($n = 468$)	52 (11%, 95% CI 8%–14%)	274 (59%, 95% CI 54%–63%)	142 (30%, 95% CI 26%–35%)

[a]Data for the question on rating of clinical importance was missing for a total of 11 respondents.
[b]A third group of respondents replied, "I don't know" ($n = 78$) to the question on availability of one or both types of fluid. Ratings of importance for this group are as follows: 16 (21%) rated 1–3 Not important, 51 (65%) rated 4–6 Important, and 11 (14%) rated 7–9 Critical.

physicians. The reported use of these solutions in clinical practice was very common. However, substantial variation existed in the choice between acetate- and lactate-buffered solutions, influenced by both availability and individual preferences. Overall, there was support for a clinical trial comparing an acetate- versus lactate-buffered crystalloid solution in perioperative care and ICU, although most respondents rated the research question as important but not critical.

Complementary to our findings, both observational studies[24,25] and a previously published international survey on use of IV fluids in adults with septic shock (1097 critical care- and emergency department physicians) confirm a high use of buffered crystalloid solutions.[26] In addition, respondents of the latter were surveyed on their typical- versus ideal choice of fluid. Herein, the use of Plasmalyte among critical care physicians differed markedly, with 15.3% using it typically and 36.5% of respondents reporting to use it ideally (absolute difference −21.2%; 95% CI −24.9% to −17.6%).[26] These findings support that personal preferences exist among physicians and that there are differences in availability for specific buffered crystalloid solutions, as identified in our survey.

Our findings reveal significant disparities in the availability of buffered solutions, both between countries and within them, an issue highlighted by several previous studies.[24,25,27] These differences are probably influenced by various non-clinical factors such as procurement agreements, supply chain logistics, promotional strategies of pharmaceutical companies, and historical usage patterns within institutions and countries.[2] It is likely, that the availability of specific fluids can influence individual physician preferences. However, in our survey many physicians stated to base their choice of specific solution on clinical considerations including safety, highlighting that the perceived clinical benefits and limitations of acetate- versus lactate-buffered solutions are also considered.

Overall, the evidence on acetate- vs. lactate-buffered solutions on patient important outcomes is sparse and of very low certainty,[19–21] and both desirable and undesirable effects have been suggested from either solution, as previously addressed. In addition, it has been suggested that infusion of lactate-buffered solutions might impair the interpretation of arterial blood gas analysis,[28] a concern which was also raised by respondents in this survey.

In this survey, the rating of clinical importance of the research question concerning the choice between acetate- and lactate-buffered solutions varied widely. On a scale of 1–9, approximately one-fifth of respondents considered it "1–3 not important," another one-fifth rated it as "7–9 critical" and the remaining respondents rated it as "4–6 important." Importantly, our results may be affected by "central tendency bias," where respondents tend to choose a middle option on a rating scale, irrespective of their true opinions.[28] Additionally, the act of receiving a survey itself can make a topic more salient to respondents, potentially causing them to overestimate its importance.[29] However, the wide range of perceived importance reported in this survey underscores the diversity of opinions within the field. Notably, there was a difference in ratings between groups based on availability: those with access to both types of solutions rated the clinical importance higher. This finding suggests that having more options may increase physicians' awareness of the nuances and potential implications of their fluid choice.

It is possible that the choice of an acetate versus lactate-buffered solution does not largely affect patient-centered outcome measures,[19,20] a concern put forth by several respondents of this survey. However, considering their vast use, also confirmed by this survey, even small differences in benefit, harm, or cost per patient may impact many patients and health care systems. The reported heterogeneity in practice and the perceived importance of this topic underscore the need for more robust evidence. However, based on the rating of the clinical importance of the research question among respondents, the feasibility and timing of a potential trial may be questioned. A potential approach could be to conduct a cluster-randomized trial at the institutional level to mitigate potential barriers arising from personal preferences.

4.1 | Strengths and limitations

This survey has strengths. First, we sought to include responses worldwide including countries from most continents, increasing external validity. Second, we were successful in including a large sample of anesthesiologists and ICU physicians, with a limited amount of missing data for all mandatory questions.

This survey also has limitations. First, the overall response rate was not high; however, it is consistent with similar surveys conducted in our research network.[30–32] Second, the proportion of respondents per country varied considerably, as it relied on the discretion of national investigators, potentially introducing selection bias. Notably, one-third of respondents were Danish, while other countries, had fewer respondents and/or lower response rates. This may reflect

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varying levels of interest in acetate- versus lactate-buffered crystalloids, potentially introducing bias and affecting the generalizability of the results. To ensure that a future randomized controlled trial (RCT) is relevant across diverse settings, addressing this variation and engaging stakeholders in countries with lower response rates will be essential to better understand regional differences in responses. Third, this survey is subject to limitations inherent to the study design including a risk of response bias, in which respondents consciously or unconsciously provide answers they perceive as more favorable or aligned with expectations. Fourth, some technical features of the survey design might also have introduced bias. In total, 29% of responses did not include email addresses, raising the possibility of duplicate entries within this subset. In addition, as the applied secure web application, REDCap, allowed for submission of uncompleted forms, the extent of missing data may have been higher than otherwise.

5 | CONCLUSIONS

In this international survey of anesthesiologists and ICU physicians, the reported use of buffered crystalloid solutions was high. Availability and preferences for acetate and/or lactate-buffered crystalloid solutions varied within- and across countries. The support for a potential randomized trial was high; however, the clinical importance was rated as important, but not critical, by most respondents.

AUTHOR CONTRIBUTIONS

K. L. E.: Survey design and development; acquisition of data; data analysis; drafting of article; final approval of article. **P. S.**, **A. P.**, **M. H. M.**: Survey design and development; interpretation of data; critical revision for important intellectual content; final approval of article. **S. N. M.**, **L. G.**, **J. H.**, **P. J. Y.**, **A. J. B.**, **M. O.**, **C. A. P.**, **I. J.**, **J. D. W.**, **A. R. B.**, **A. A.**, **A. K. K.**, **Y. M. A.**, **T. F.**, **E. K.**, **M. C.**: Acquisition of data; critical revision for important intellectual content; final approval of article.

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CONFLICT OF INTEREST STATEMENT

P. S., K. L. E., A. P., and M. H. M. are affiliated with the Department of Intensive Care at Rigshospitalet, which has received funding for other projects from the Novo Nordisk Foundation. A. P. has received an honorarium from Novartis for participation in an advisory board. J. D. W. has consulted for Menarini, MSD, Pfizer, ThermoFisher, and Viatris with fees and honoraria paid to institution. J. H. has received an honorarium from Paion for participation in an advisory board. A. R. B. received speaker or consultancy fees from Nutricia Danone and VIPUN Medical and she is holding a grant from the Estonian Research Council (PRG1255). A. K. consults for Medtronic, Edwards Life Sciences, Philips Research North America, Baxter, GE Healthcare, Potrero Medical, Retia Medical, and Caretaker Medical. P. Y. reports that this research was completed during the tenure of a Clinical Practitioner Fellowship awarded by the Health Research Council of New Zealand. The remaining authors declare no conflict of interests. No external organizations had influence on the design, conduct, or the decision to publish the results of this article.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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