

Serum Calcium Dynamics and Respiratory Support Trajectories in Critically Ill Children with Lower Respiratory Tract Infections

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Abstract

Purpose: Lower respiratory tract infections (LRTIs) are a major cause of pediatric intensive care unit (PICU) admission, where respiratory support requirements change dynamically during critical illness. We investigated whether longitudinal serum electrolyte levels are associated with day-to-day respiratory support transitions in critically ill children with LRTIs.

Materials and Methods: This retrospective longitudinal study included previously healthy children (1 month–18 years) admitted to a tertiary PICU with LRTIs between 2021 and 2026. Previous-day serum electrolyte levels were evaluated in relation to next-day respiratory support escalation and de-escalation using generalized estimating equation models adjusted for illness severity and relevant clinical covariates. Secondary analyses assessed the robustness and temporal characteristics of significant associations.

Results: A total of 344 children contributing 1,993 patient-days were included. Respiratory support escalated on 3.6% and de-escalated on 16.7% of patient-days. No electrolyte was associated with next-day respiratory support escalation after multiple-testing correction. Higher previous-day calcium was the only electrolyte independently associated with next-day respiratory support de-escalation (adjusted OR 1.27 per SD, 95% CI 1.13–1.44; $p < 0.001$). The association remained robust across sensitivity analyses and was primarily driven by within-patient variation.

Conclusion: Higher previous-day serum calcium was independently associated with subsequent respiratory support de-escalation. Its temporal pattern and within-patient nature suggest that calcium reflects the physiological recovery process accompanying respiratory improvement rather than a causal determinant of de-escalation. Prospective studies are needed to validate these findings.

What is Known?

- Electrolyte disturbances are common in critically ill children and may influence respiratory and neuromuscular function.
- Previous studies have primarily evaluated single-time-point electrolyte measurements in relation to mechanical ventilation, weaning, or adverse outcomes.

What is New?

- Longitudinal analysis showed that higher previous-day serum calcium was independently associated with next-day respiratory support de-escalation, whereas no electrolyte predicted escalation.
- The predominantly within-patient and temporally concentrated association suggests that serum calcium may reflect the physiological recovery process accompanying respiratory improvement.

1. Introduction

Lower respiratory tract infections (LRTIs), including bronchiolitis and pneumonia, affect the airways below the larynx and the pulmonary parenchyma and represent an important cause of respiratory morbidity in children [1, 2]. In severe cases, admission to the pediatric intensive care unit (PICU) is generally driven not by the infectious diagnosis itself but by the degree of associated respiratory and systemic compromise, including hypoxemia, hypercapnia, increased work of breathing, apnea, altered consciousness, shock, and other organ dysfunctions [1–4]. Accordingly, respiratory support may need to be progressively escalated from conventional oxygen therapy to high-flow nasal cannula, non-invasive ventilation, and, when necessary, invasive mechanical ventilation. Thus, the requirement for intensive care in children with LRTIs is largely determined by the severity of respiratory failure and overall hemodynamic deterioration rather than by the specific type of infection alone [1, 2, 4].

Electrolyte disturbances may influence respiratory function through their essential roles in neuromuscular transmission, cellular energy metabolism, and muscle contraction [5–7]. Hypophosphatemia has been associated with impaired diaphragmatic contractility, respiratory muscle weakness, prolonged mechanical ventilation, and weaning failure [6, 8–10], while potassium abnormalities may similarly compromise respiratory muscle function [5, 7]. Calcium is essential for excitation–contraction coupling and neuromuscular signaling, and lower calcium levels have been associated with greater illness severity and adverse outcomes in critically ill children [11, 12]. Magnesium disturbances may impair respiratory muscle function, but evidence linking them to ventilatory support and successful liberation from mechanical ventilation has been inconsistent [13, 20, 21]. In addition, hyponatremia has been reported in children with severe pneumonia, although its relation to respiratory-support intensity remains uncertain [14].

Respiratory support in critically ill children represents a dynamic process that evolves according to changes in clinical status. Depending on the severity and progression of respiratory failure, support may be escalated from conventional oxygen therapy to high-flow nasal cannula (HFNC), non-invasive ventilation (NIV), and invasive mechanical ventilation (IMV), whereas clinical recovery allows progressive de-escalation toward less intensive modalities [15, 16]. Although several clinical and laboratory factors have been investigated in relation to mechanical ventilation requirements, duration of ventilation, and successful liberation from ventilatory support, most studies examining electrolyte-related outcomes have focused on measurements obtained at a single time point or on specific outcomes such as invasive ventilation and weaning [9, 17, 20]. Consequently, little is known about how longitudinal electrolyte levels relate to day-to-day transitions in respiratory support intensity, particularly across the broader spectrum of both escalation and de-escalation.

Therefore, this study aimed to explore the relationship between electrolyte status and the dynamic course of respiratory support in critically ill children with LRTIs. We sought to determine whether longitudinal electrolyte levels are associated with respiratory support escalation or de-escalation and to identify potential biochemical markers reflecting respiratory recovery.

2. Materials and Methods

2.1 Ethical Approval

This retrospective study was conducted in a tertiary-level PICU from 2021 to 2026. The study was conducted in accordance with the ethical principles of the Declaration of Helsinki. Ethical approval was obtained from the Bahçeşehir University Non-Interventional Research Ethics Committee prior to the initiation of the study (13 March 2026, approval number E-78097791-020-5355).

2.2 Inclusion and Exclusion Criteria

The inclusion criteria were age between 1 month and 18 years, admission to the PICU with a diagnosis of lower respiratory tract infection (LRTI), including pneumonia, bronchopneumonia, or bronchiolitis, previously healthy status without underlying chronic comorbidities, requirement for PICU admission and respiratory monitoring or support, and availability of serial clinical and laboratory data, including electrolyte measurements and daily respiratory support records, during the observed PICU stay. LRTI diagnoses were established by the attending pediatric intensivist according to the patient's clinical presentation and available radiological findings when clinically indicated and were identified through retrospective review of the electronic medical records. Previously healthy was defined as the absence of chronic cardiopulmonary, neurological, metabolic, genetic, immunological, renal, hepatic, or oncological diseases requiring regular medical follow-up or long-term treatment. The exclusion criteria included incomplete longitudinal electrolyte measurements or missing key clinical data, a PICU length of stay of less than 24 hours, the presence of underlying chronic comorbidities, transfer from another intensive care unit after initiation of intensive care, and receipt of respiratory support for reasons other than LRTIs.

Clinical and laboratory data were retrospectively obtained from electronic medical records. Demographic characteristics, admission diagnoses, disease severity scores, daily respiratory support modalities, serum electrolyte levels, blood gas parameters, relevant treatments, PICU length of stay, and clinical outcomes were recorded during the observed PICU window. **For each PICU day, the first serum electrolyte measurement obtained as part of routine daily biochemical testing was used to represent that day's electrolyte status for the longitudinal analyses.** Patients admitted directly from the emergency department or hospital wards were eligible, whereas those transferred from another intensive care unit after initiation of intensive care were excluded. No patient had more than one eligible PICU admission during the study period. Respiratory support and laboratory data were evaluated on a daily basis to assess their longitudinal relationship during the clinical course. Electrolyte values outside prespecified plausibility bounds were set to missing before lagging. Previous-day values were recomputed within each child only across consecutive observed days, and analyses were limited to the first 30 observed PICU days. **Patient-days without an available routine electrolyte measurement were excluded only from analyses involving the corresponding electrolyte, and no imputation of missing values was performed.**

2.3 Respiratory Support Escalation and De-escalation Strategy

Respiratory support was managed stepwise according to institutional PICU practice and the clinical judgment of the attending intensivist. The respiratory support hierarchy was defined as room air, low-flow oxygen, HFNC, NIV, IMV, and extracorporeal membrane oxygenation (ECMO). Escalation to a higher level of support was based on clinical deterioration, including worsening respiratory distress, hypoxemia, hypercapnia, apnea, or hemodynamic instability, whereas de-escalation to a lower level was performed following sustained improvement in respiratory status and reduced support requirements. For each PICU day, the highest respiratory support level reached, and source-recorded binary indicators of within-day step-up and step-down were available. The primary longitudinal outcomes were the recorded step-up and step-down indicators on day t . They were not reconstructed from consecutive-day maximum levels. Previous-day maximum support level was used as an adjustment covariate, whereas between-day changes in daily maximum support are summarized in Supplementary Figure S1 and modeled separately in the exploratory ordinal analysis reported in Supplementary Table S2.

2.4 Statistical Analysis

Continuous variables were summarized as median with interquartile range or mean with standard deviation, and categorical variables as number and percentage. The primary analysis evaluated the population-averaged association between previous-day serum electrolyte levels and source-recorded within-day step-up or step-down on the following PICU day. Separate generalized estimating equation logistic regression models were fitted for sodium, potassium, chloride, calcium, magnesium, and phosphorus, using an independence working correlation and patient-cluster sandwich standard errors. All models were adjusted for log-transformed PICU day, previous-day respiratory support level, age, sex, and admission PRISM score. Each electrolyte was standardized once using its nonmissing values in the verified analysis cohort, and odds ratios were reported per empirical standard-deviation increase. Continuous covariates were also standardized. The primary analyses followed a complete-case approach at the patient-day level. Patient-days without an available measurement for the corresponding electrolyte or with missing covariates were excluded only from analyses involving that electrolyte, and no imputation of missing values was performed. Two-sided p -values and 95% confidence intervals were reported, with Benjamini–Hochberg false-discovery-rate correction applied separately to escalation and de-escalation analyses. Values of $q < 0.05$ were considered statistically significant after correction for multiple testing. **Secondary analyses assessed the robustness and temporal characteristics of significant associations. Change-score models related the current-day minus previous-day electrolyte change to the current-day source-recorded transition indicator and were exploratory because within-day ordering was unavailable. Sustained de-escalation was defined among source-recorded step-down events with at least one follow-up record on calendar day +1 or +2 as no recorded step-up and no increase above the step-down day's maximum support level on either available follow-up day. Events with neither follow-up day were unclassifiable. Additional analyses included adjustment for acid–base status and relevant treatments, within-patient effects, lagged measurements, and alternative longitudinal models.** For the duplicate-trajectory sensitivity analysis, duplicated trajectories were defined as **different patients sharing identical processed day-to-day electrolyte sequences after data preparation** and did not represent repeated admissions or duplicate patient records. The incident-IMV

analysis was limited to feasibility assessment because only seven eligible new onsets followed a non-IMV day. No adjusted onset model was fitted, and same-day IMV comparisons were descriptive. Analyses were performed using R version 4.4.2 and Python version 3.12, with all 12 primary estimates independently reproduced in both environments. Additional analyses and results are presented in the Supplementary Material.

3. Results

During the study period, 554 children were admitted to the PICU with a diagnosis of LRTIs. Of these, 31 were excluded because of incomplete clinical data and 179 because of accompanying comorbidities, leaving 344 children in the study cohort. Demographic and clinical characteristics are shown in Table 1.

Table 1. Demographic and Clinical Characteristics of the Analysis Cohort

The analysis cohort included 344 children contributing 1,993 observed patient-days. The median age was 14.0 months, and 47.4% of patients were female. HFNC was the most frequently used respiratory support modality, accounting for 46.6% of support-days. During follow-up, step-up and step-down transitions occurred on 3.6% and 16.7% of patient-days, respectively. The median PICU length of stay was 4 days, and overall mortality was 1.5% (Table 1). Cohort reconciliation, outcome availability, and daily maximum respiratory-support transitions are summarized in Supplementary Figure S1.

The associations between previous-day electrolyte levels and next-day respiratory support transitions were evaluated using adjusted longitudinal models (Table 2).

Table 2. Population-averaged Associations with Next-day Respiratory-support Transitions

In the primary longitudinal analysis, none of the six previous-day electrolyte levels was significantly associated with next-day escalation of respiratory support after false-discovery-rate correction (all $q > 0.05$). In contrast, after covariate adjustment, higher previous-day calcium levels were associated with an increased likelihood of next-day de-escalation (adjusted OR 1.27 per SD increase, 95% CI 1.13–1.44, $p < 0.001$, $q < 0.001$). No significant associations with de-escalation were observed for sodium, potassium, chloride, magnesium, or phosphorus after multiple-testing correction (Table 2).

The adjusted associations between previous-day electrolyte levels and next-day respiratory support escalation and de-escalation are illustrated in Figure 1. Complete model estimates, exposure standardization constants, and independent software verification are provided in Supplementary Table S1.

Figure 1. Associations Between Previous-Day Electrolyte Levels and Next-Day Respiratory Support Transitions

As illustrated in Figure 1, none of the evaluated electrolytes showed a significant association with next-day respiratory support escalation. In contrast, calcium was the only electrolyte significantly associated

with next-day de-escalation after false-discovery-rate correction, whereas the confidence intervals for all other electrolytes crossed unity.

Given that calcium was the only electrolyte significantly associated with respiratory support de-escalation, further analyses were performed to assess the robustness and characteristics of this association. The calcium–de-escalation association remained significant across sustained de-escalation, within-patient analyses, and models additionally adjusted for acid–base parameters and relevant treatments (Table 3).

Table 3. Extension and Sensitivity Analyses for the Previous-day Calcium–de-escalation Association

The association between higher previous-day calcium levels and respiratory support de-escalation remained robust across multiple sensitivity analyses. It persisted for sustained de-escalation and after additional adjustment for acid–base status and relevant treatments. The within-patient calcium component was statistically significant, whereas the between-patient component was not statistically significant (Table 3).

The dose–response pattern and temporal characteristics of the association between calcium levels and respiratory support de-escalation were further explored, as illustrated in Figure 2. Detailed dose-response and temporal estimates are provided in Supplementary Table S2.

Figure 2. Dose-response and Temporal Specificity of the Calcium–de-escalation Association

Further evaluation of the calcium–de-escalation association suggested an exploratory nonlinear pattern (quadratic $p = 0.045$) that should be interpreted cautiously. Temporal analyses indicated that the association was strongest for calcium measured on the immediately preceding day (Figure 2).

Additional secondary and exploratory analyses were generally consistent with the primary findings. Change-score analyses did not identify significant associations between day-to-day electrolyte changes and same-day source-recorded respiratory support transitions after multiple-testing correction. Because within-day ordering was unavailable, these exploratory estimates were not prospective. Calcium was associated with a higher discrete-time hazard of first de-escalation (adjusted HR 1.19 per SD, 95% CI 1.05–1.34, $q = 0.034$), whereas the ordinal transition estimate was directionally similar but imprecise (proportional OR 1.13, 95% CI 0.98–1.32, $q = 0.595$). At the patient level, greater hypomagnesemia burden was associated with a higher IMV-day rate and more observed PICU days, whereas hypophosphatemia burden was not. These analyses were exploratory and hypothesis-generating. Only seven eligible incident IMV events occurred, precluding an adjusted onset model. Same-day IMV comparisons were therefore descriptive. Selected secondary and exploratory estimates are provided in Supplementary Table S2.

4. Discussion

In this longitudinal study of critically ill children with LRTIs, serum calcium was the only tested electrolyte associated with next-day de-escalation of respiratory support after correction for multiple testing, whereas none of the evaluated electrolytes was associated with respiratory support escalation. The association between higher calcium levels and de-escalation remained consistent across multiple sensitivity analyses, including sustained de-escalation and additional adjustment for acid–base status and relevant treatments. The within-patient calcium component was statistically significant, whereas the between-patient component was not. Periods of relatively higher calcium levels within the same patient were associated with a greater likelihood of subsequent respiratory support de-escalation. Taken together, these findings suggest a distinct longitudinal relationship between calcium status and respiratory recovery, while supporting a more limited role for other routinely measured electrolytes in short-term respiratory support transitions.

The association observed between higher calcium levels and respiratory support de-escalation is biologically plausible given the central role of calcium in neuromuscular transmission and muscle contraction. Previous studies have generally examined calcium at a single time point in relation to hypocalcemia, illness severity, or adverse outcomes [11,12,18,19]. In contrast, one pediatric study did not identify a significant association between calcium disturbance and the use of IMV, suggesting that the relationship between calcium status and respiratory support may not be straightforward [5]. In our data, the calcium signal was specific to de-escalation. The within-patient component was statistically significant, whereas the between-patient component was not. This suggests that calcium may reflect changes occurring during the recovery phase rather than simply distinguishing more severely ill children from less severely ill ones.

Several findings in our analysis support the interpretation of calcium as a potential marker of respiratory recovery rather than a causal determinant of de-escalation. The association was strongest for calcium measured on the immediately preceding day, was attenuated at longer lag intervals, but a similar association was observed in the reverse-time analysis. This bidirectional signal limits directional interpretation. The exploratory dose-response curve was nonlinear and should be interpreted cautiously. Together with the persistence of the association for sustained de-escalation, these findings suggest that calcium levels may track a transient physiological recovery state surrounding reductions in respiratory support. Importantly, the present data do not imply that increasing or correcting calcium would itself facilitate de-escalation. Instead, serial calcium measurements may have potential value as an adjunctive biochemical marker of respiratory improvement.

In contrast to calcium, neither magnesium nor phosphorus was associated with day-to-day escalation or de-escalation of respiratory support in the primary longitudinal analyses. This finding is noteworthy because disturbances in both electrolytes have been investigated in relation to respiratory muscle dysfunction, mechanical ventilation, and adverse outcomes in critically ill patients, with mixed findings [6,8–10,17,21,22]. In the present cohort, however, the exploratory patient-level analysis showed that a greater cumulative burden of hypomagnesemia was associated with a higher IMV-day rate and more observed PICU days, despite the absence of an association with daily respiratory support transitions.

This apparent discrepancy may reflect the distinct clinical processes captured by these outcomes: an electrolyte disturbance associated with overall illness severity or cumulative ventilatory burden may not necessarily track short-term transitions between respiratory support levels. Given the observational nature of these patient-level analyses and the potential for residual confounding, these findings should be considered hypothesis-generating.

From a clinical perspective, the observed calcium–de-escalation association should not be interpreted as evidence that calcium correction promotes respiratory recovery or facilitates reduction of respiratory support. Rather, serial calcium levels may provide complementary information regarding the evolving recovery state of critically ill children with LRTIs. As calcium is routinely measured and readily available in PICU practice, its longitudinal pattern could potentially serve as an adjunctive biochemical marker alongside clinical assessment when evaluating respiratory recovery. However, calcium levels alone should not guide de-escalation decisions, and the clinical utility of this association requires validation in prospective studies before it can be incorporated into respiratory support management strategies.

Among routinely measured electrolytes, serum calcium was the only tested electrolyte associated with subsequent respiratory support de-escalation in critically ill children with LRTIs, whereas no electrolyte was associated with escalation. The within-patient calcium component was statistically significant, whereas the between-patient component was not. The association was temporally concentrated around the de-escalation period, suggesting that calcium may serve as a potential biochemical marker of respiratory recovery rather than a causal determinant of improvement. Further prospective studies are needed to validate these findings and clarify the clinical utility of longitudinal calcium monitoring in assessing respiratory recovery.

5. Limitations

This study has several limitations. First, its retrospective, single-center design limits causal inference and may reduce the generalizability of the findings. Second, decisions regarding respiratory support escalation and de-escalation were based on clinical judgment and institutional practice. Therefore, unmeasured variation in clinician decision-making may not have been fully captured by the available covariates. Third, the relatively small number of escalation events, particularly incident invasive ventilation, limited statistical power for evaluating respiratory deterioration and precluded a reliable adjusted analysis of new IMV onset. Fourth, only routinely measured serum electrolyte values were available, and factors such as ionized calcium, albumin-adjusted calcium, nutritional status, renal function, and the timing or dose of electrolyte replacement may not have been completely accounted for. Fifth, the positive reverse-time association and the observational design indicate that residual confounding and reverse causality cannot be excluded. Accordingly, the calcium–de-escalation association should be interpreted as reflecting a respiratory recovery state rather than a causal effect or a treatment target. The 30-day cap also truncated observation for some longer recorded stays. Identical processed electrolyte trajectories were observed across different children, which may indicate unresolved duplication in the source data. The source-recorded within-day transition indicators could not

be fully reconstructed from daily maximum support alone. Nevertheless, the longitudinal analysis of nearly 2,000 patient-days, patient-clustered modeling, correction for multiple testing, and consistent sensitivity analyses strengthen the reliability of the observed association.

Abbreviations

CI: confidence interval

CRP: C-reactive protein

ECMO: extracorporeal membrane oxygenation

GEE: generalized estimating equation

HCO₃: bicarbonate

HFNC: high-flow nasal cannula

HR: hazard ratio

IMV: invasive mechanical ventilation

IQR: interquartile range

LRTI: lower respiratory tract infection

NIV: noninvasive ventilation

OR: odds ratio

pCO₂: partial pressure of carbon dioxide

PELOD: Pediatric Logistic Organ Dysfunction

PICU: pediatric intensive care unit

PRISM: Pediatric Risk of Mortality

SD: standard deviation

WBC: white blood cell count

Declarations

Artificial Intelligence (AI) Declaration: No artificial intelligence tools were used to generate, analyze, or interpret the study data. The authors are solely responsible for all scientific content and conclusions presented in this manuscript.

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Author Contributions;

Ayberk Özkavaklı: Conceptualization, Investigation, Data Curation, Writing – Original Draft, Project Administration. **Ayşe Aşık:** Conceptualization, Investigation, Data Curation. **Hüseyin Tunç:** Methodology, Formal Analysis, Writing – Review & Editing. **Muhterem Duyu:** Methodology, Formal Analysis, Writing – Review & Editing.

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Tables

Table 1. Demographic and Clinical Characteristics of the Analysis Cohort

Characteristic	Value
Children	344
Observed patient-days	1,993
Age, months, median [IQR]	14.0 [4.0–32.0]
Female sex, n (%)	163 (47.4%)
Admission PRISM, median [IQR]	6.0 [3.0–10.0]
Admission PELOD, median [IQR]	4.0 [1.0–10.0]
Admission WBC, median [IQR]	11550.0 [8800.0–15950.0]
Admission CRP, mg/L, median [IQR]	13.3 [3.8–33.3]
Admission Procalcitonin, ng/mL, median [IQR]	0.2 [0.1–0.7]
Total HFNC Duration, days, median [IQR]	2.0 [0.0–4.0]
Total Oxygen Duration, days, median [IQR]	3.0 [2.0–5.0]
Total NIV Duration, days, median [IQR]	0.0 [0.0–0.0]
Total IMV Duration, days, median [IQR]	0.0 [0.0–0.0]
Length of stay in PICU, days, median [IQR]	4.0 [3.0–7.0]
Mortality, n (%)	5 (1.5%)
Sodium, patient mean, mmol/L, mean (SD)	137.9 (1.9)
Potassium, patient mean, mmol/L, mean (SD)	4.5 (0.4)
Chloride, patient mean, mmol/L, mean (SD)	102.0 (2.6)
Calcium, patient mean, mg/dL, mean (SD)	9.4 (0.5)
Magnesium, patient mean, mg/dL, mean (SD)	2.1 (0.2)
Phosphorus, patient mean, mg/dL, mean (SD)	4.5 (0.7)
Support-days at Room air, total, n (%)	421 (21.1%)
Support-days at O ₂ support, total, n (%)	149 (7.5%)
Support-days at HFNC, total, n (%)	928 (46.6%)
Support-days at NIV, total, n (%)	176 (8.8%)
Support-days at IMV, total, n (%)	262 (13.1%)
Support-days at ECMO, total, n (%)	57 (2.9%)
Arterial pH, patient-day, mean (SD)	7.40 (0.06)

Characteristic	Value
pCO ₂ , patient-day, mean (SD)	41.7 (9.2)
Lactate, patient-day, mean (SD)	1.5 (1.5)
HCO ₃ , patient-day, mean (SD)	24.9 (4.0)
Escalation, patient-days, n (%)	71 (3.6%)
De-escalation, patient-days, n (%)	333 (16.7%)
IMV patient-days, n (%)	319 (16.0%)
Electrolyte replacement-days, n (%)	383 (19.2%)
Steroid administration-days, n (%)	1,027 (51.5%)
Furosemide-administration-days, n (%)	202 (10.1%)

Values are median [IQR], mean (SD), or n (%) as indicated. Electrolyte rows summarize the distribution of each child's mean across observed days. Blood-gas rows summarize observed patient-days. Support-category rows classify each day by its maximum recorded level. Escalation and de-escalation rows use separate source-recorded within-day indicators, and IMV patient-days use the same-day IMV indicator, including ECMO days with IMV recorded. Table 2 restricts transition indicators to lag-eligible days.

IQR: interquartile range, WBC: white blood cell count, CRP: C-reactive protein, mg/L: milligrams per liter, ng/mL: nanograms per milliliter, HFNC: high-flow nasal cannula, NIV: noninvasive ventilation, IMV: invasive mechanical ventilation, PICU: pediatric intensive care unit, mmol/L: millimoles per liter, mg/dL: milligrams per deciliter, pCO₂: partial pressure of carbon dioxide, HCO₃: bicarbonate.

Table 2. Population-averaged Associations with Next-day Respiratory-support Transitions

Outcome	Previous-day exposure	N / events	Adjusted OR (95% CI)	p-value	q-value
Next-day Escalation	Sodium	1,649 / 46	0.96 (0.76–1.21)	0.753	0.857
	Potassium	1,649 / 46	1.07 (0.80–1.45)	0.640	0.857
	Chloride	1,642 / 46	0.97 (0.75–1.24)	0.801	0.857
	Calcium	1,643 / 46	1.31 (0.92–1.88)	0.135	0.809
	Magnesium	1,649 / 46	1.09 (0.83–1.43)	0.534	0.857
	Phosphorus	1,648 / 46	1.02 (0.80–1.31)	0.857	0.857
Next-day De-escalation	Sodium	1,649 / 325	1.09 (0.97–1.22)	0.168	0.349
	Potassium	1,649 / 325	1.02 (0.89–1.16)	0.787	0.787
	Chloride	1,642 / 323	0.97 (0.86–1.09)	0.592	0.710
	Calcium	1,643 / 324	1.27 (1.13–1.44)	< 0.001	< 0.001
	Magnesium	1,649 / 325	1.10 (0.96–1.25)	0.175	0.349
	Phosphorus	1,648 / 324	1.05 (0.93–1.20)	0.427	0.640

Odds ratios are reported per empirical standard deviation increase of the previous-day concentration. All models adjust for log PICU day, previous-day respiratory-support level, age, sex, and admission PRISM, using an independence working correlation and patient-cluster sandwich standard errors. q-values use outcome-specific Benjamini–Hochberg correction across the six electrolytes. Exposure means, empirical SDs, and available observations are reported in Supplementary Table S1.

Table 3. Extension and Sensitivity Analyses for the Previous-day Calcium–de-escalation Association

Analysis	Calcium OR (95% CI)	p-value
Primary model (reference)	1.27 (1.13–1.44)	< 0.001
Sustained de-escalation (no recorded re-escalation on available day +1/+2)	1.34 (1.14–1.58)	< 0.001
Within-patient calcium (Mundlak)	1.27 (1.12–1.44)	< 0.001
Between-patient calcium (Mundlak)	1.12 (1.00–1.25)	0.057
+ same-day full acid–base panel	1.26 (1.11–1.43)	< 0.001
+ same-day electrolyte replacement, furosemide, and steroid administration	1.21 (1.07–1.37)	0.003
Excluding all duplicated-trajectory patients	1.25 (1.10–1.41)	< 0.001

All rows model next-day de-escalation and are adjusted as in the primary model, with patient-cluster sandwich standard errors. Odds ratios are reported per empirical standard deviation increase of previous-day calcium. The sustained-de-escalation row classifies source-recorded step-downs with at least one follow-up record on calendar day +1 or +2 and no recorded step-up or higher maximum support on either available follow-up day. These extension analyses are exploratory and were not additionally multiplicity adjusted. Additional numeric results are provided in Supplementary Table S2.

Figures

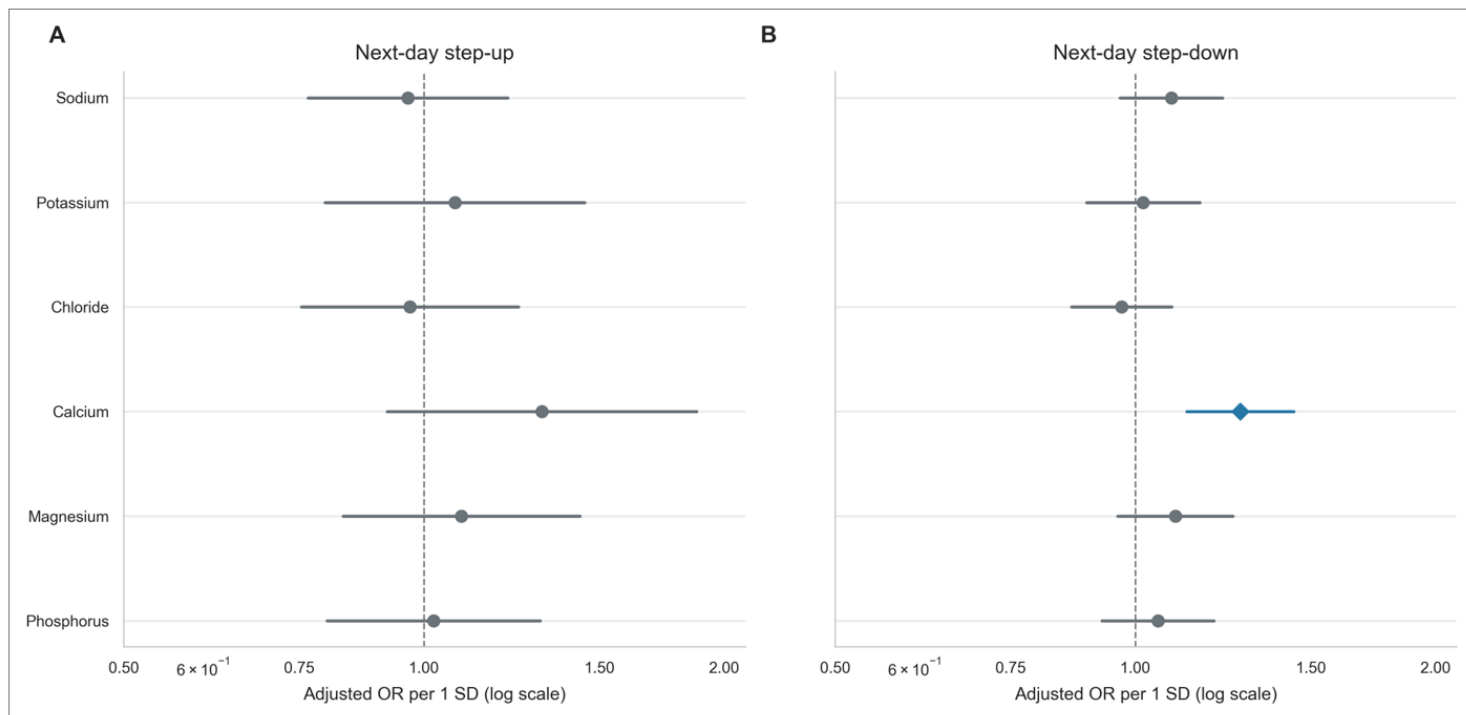


Figure 1

Adjusted associations of previous-day electrolytes with next-day support transitions. Population-averaged odds ratios per one-standard-deviation increase with patient-cluster robust 95% confidence intervals, for next-day step-up (left) and step-down (right). The diamond marks the only association with q-value < 0.05, previous-day calcium and next-day de-escalation.

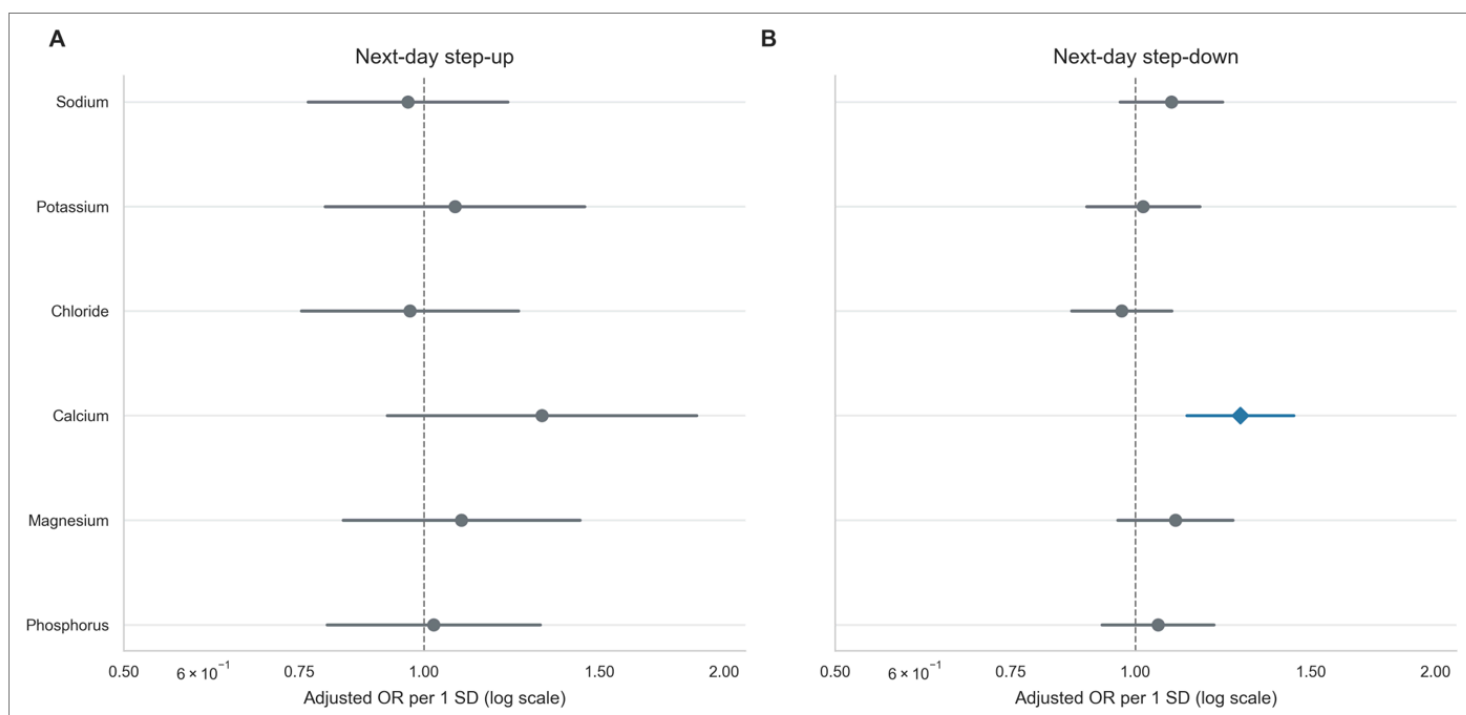


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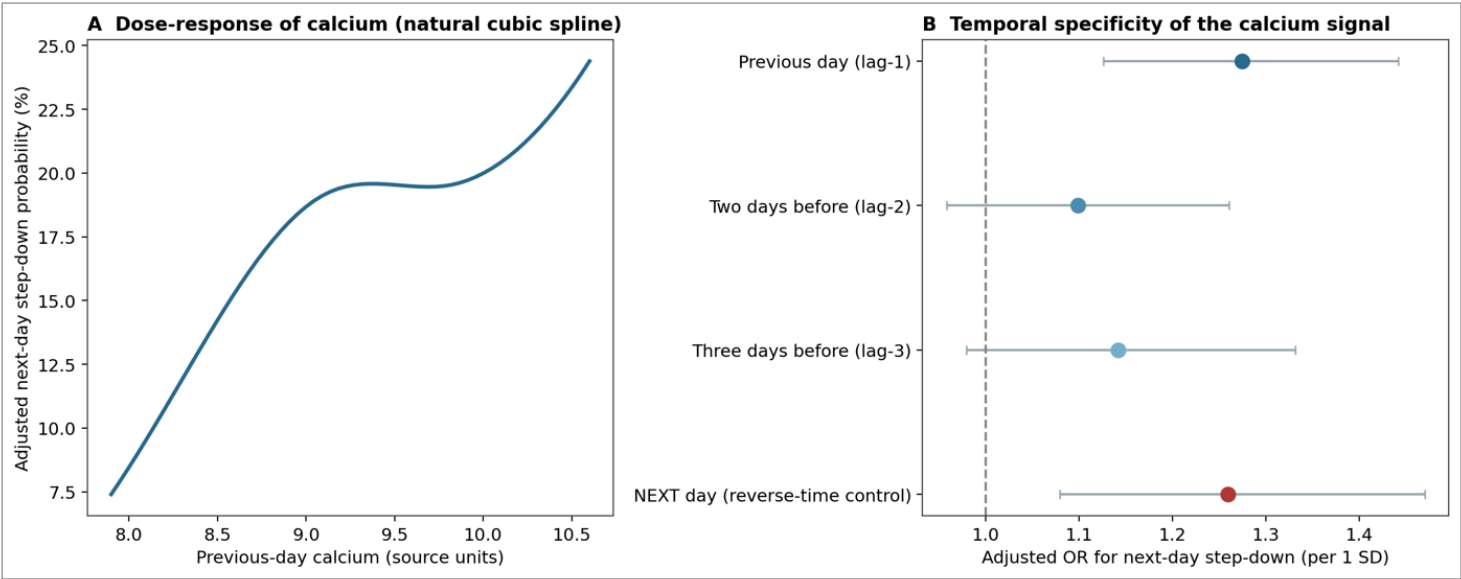


Figure 2

Dose-response and Temporal Specificity of the Calcium-de-escalation Association. (a) Exploratory adjusted probability of next-day de-escalation across previous-day calcium (natural cubic spline with 4 degrees of freedom, covariates at their means): the curve suggests possible nonlinearity but should not be interpreted as establishing a threshold. (b) Odds ratios for calcium measured on the previous day (lag 1), two and three days earlier, and the next day (reverse-time control). The association was strongest at lag 1, while the positive reverse-time estimate indicates temporal co-movement and cautions against a directional interpretation.

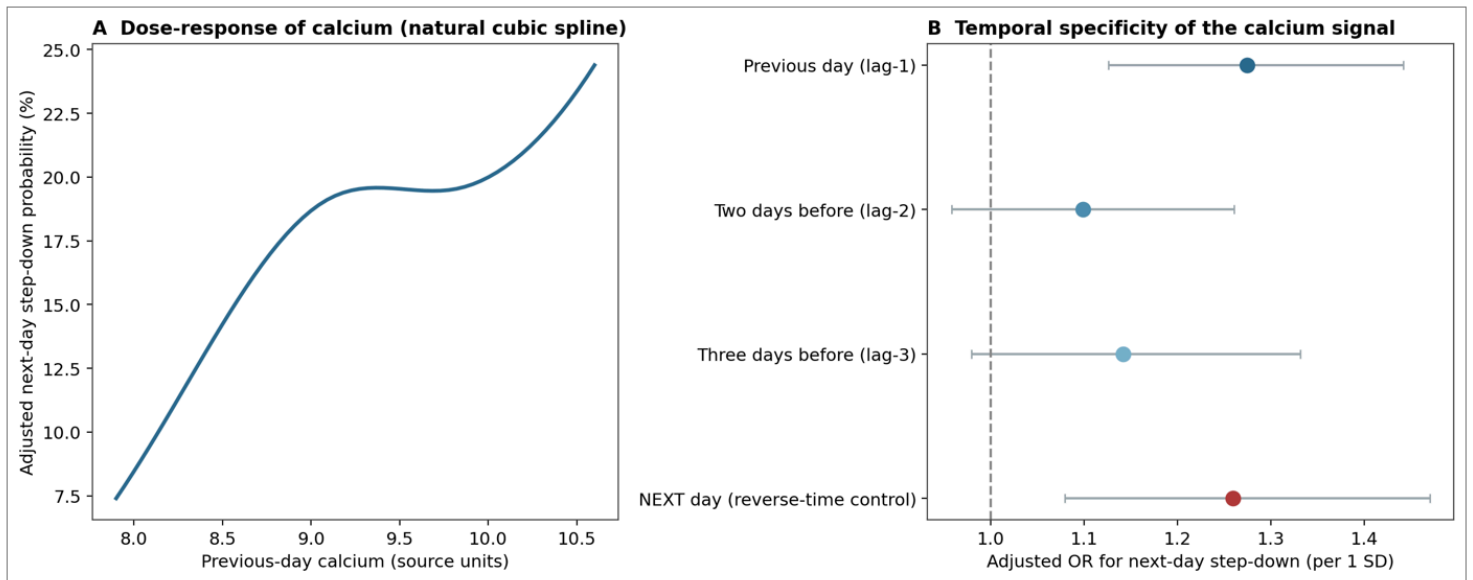


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Supplementary Files

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