

Abstract

Background: Vitamin D is a key immunomodulator that plays a role in calcium and phosphate absorption. Vitamin D deficiency has been recognized as a risk factor for post-thyroidectomy hypocalcemia. The majority of vitamin D is synthesized cutaneously, with its production dependent on sunlight exposure. Seasonal differences in sunlight exposure may influence vitamin D levels and, consequently, the risk of hypocalcemia. Hypocalcemia is a common complication following total thyroidectomy, affecting approximately 15-30% of postoperative patients. This study aimed to analyze whether seasonal differences contribute to the development of post-thyroidectomy hypocalcemia.

Methods: A retrospective analysis was conducted using TrinetX, a de-identified patient database. A total of 6,886 patients who underwent total thyroidectomy between December 1, 2022, and December 31, 2023, were identified. Patients were grouped into seasonal cohorts based on the meteorological definition of seasons (Winter: December-February; Spring: March-May; Summer: June-August; Autumn: September-November). Cohorts were controlled for age, sex race. Those with a history of calcium or Vitamin D supplementation, chronic kidney disease or related comorbidities were excluded. Hypocalcemia was defined as serum levels less than 8.5 mg/dL. PTH, Vitamin D, and phosphorous levels were also assessed.

Results: When comparing the spring cohort to the winter cohort (n=1,146), the risk of hypocalcemia was 18.7% versus 15.5%, respectively ($p < 0.01$). No significant differences in hypocalcemia risk were observed between other seasonal groups. Differences in levels of 25-Hydroxy-vitamin D, PTH, and phosphorus were also not significant between groups.

Conclusions: Seasonal differences appear to influence the risk of post-thyroidectomy hypocalcemia, with patients undergoing surgery in the spring experiencing a higher risk compared to those in winter. These findings challenge the hypothesis that decreased sun exposure in the colder months could be associated with a risk of postoperative hypocalcemia. Further research is warranted to explore the underlying mechanisms of these seasonal variations

Introduction

- Total thyroidectomy is a common procedure, and transient hypocalcemia is its most frequent complication, affecting ~15-30% of patients¹.
- Vitamin D plays a crucial role in calcium absorption and parathyroid hormone (PTH) regulation.²
- Previous studies suggest that seasonal variation in sunlight exposure may influence postoperative calcium homeostasis, however these studies are limited by small, single-center cohorts.³

Objective - to determine whether seasonal differences affect the incidence of hypocalcemia following total thyroidectomy using large, multi-institutional U.S. database.

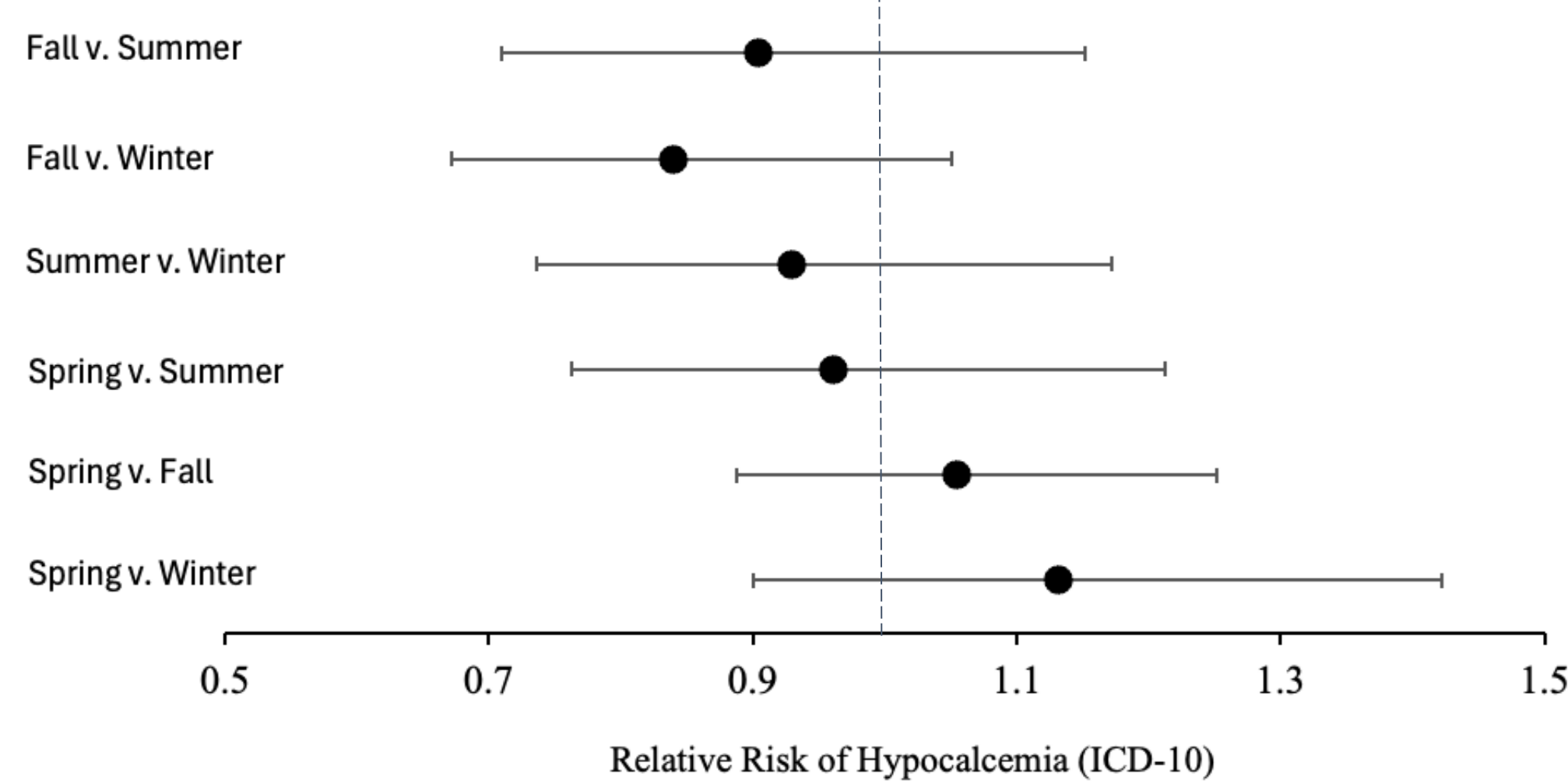
Methods and Materials

- **Study Design** - retrospective cohort design using the TriNetX de-identified national database.
- **Population** - 6,886 patients who underwent total thyroidectomy (Dec 1, 2022 - Dec 31, 2023)
- **Cohorts** - patients grouped by season of surgery according to meteorological definition

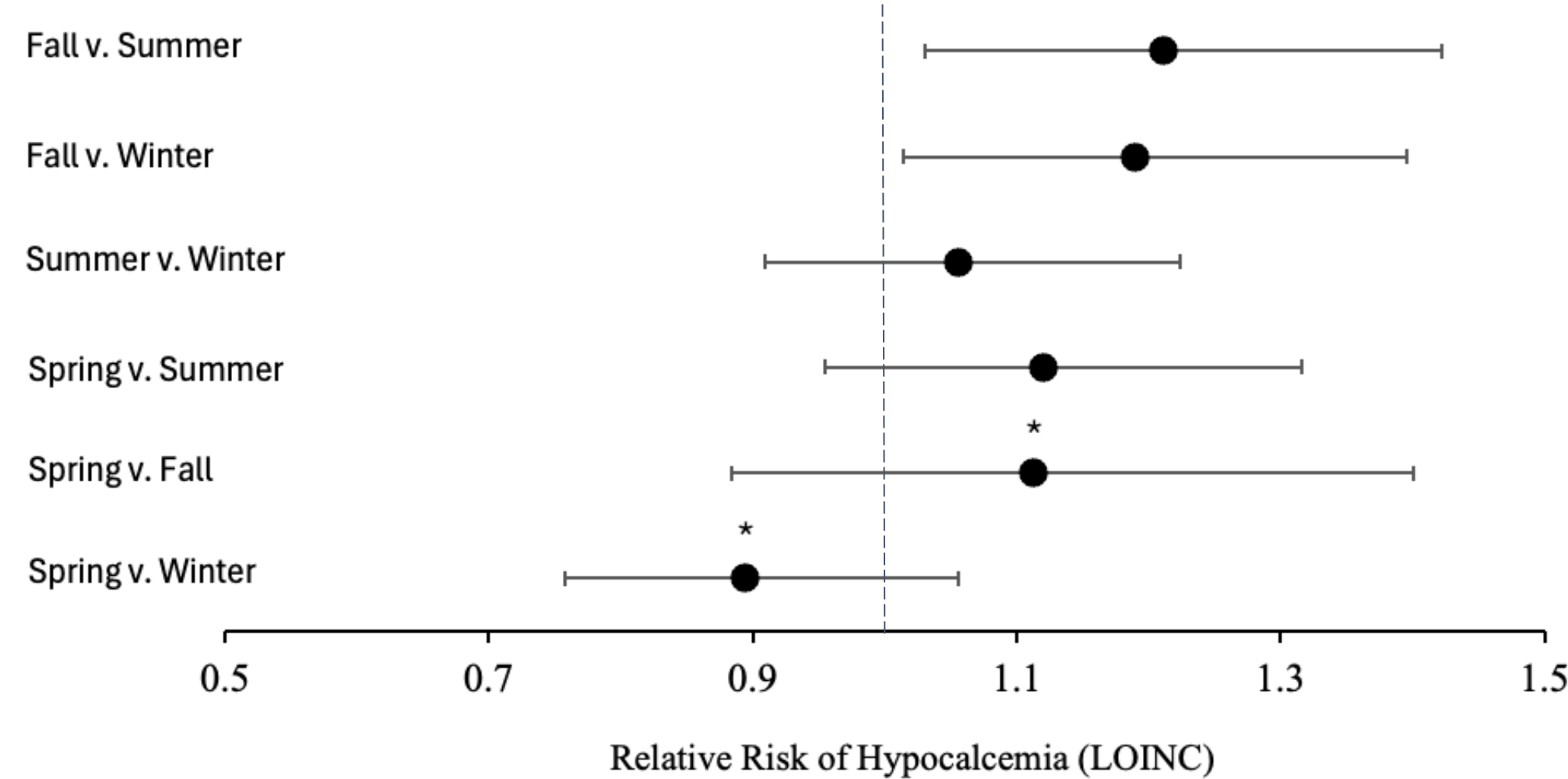
Dec	Jan	Feb	Mar	Apr	May	Jun	Jul	Aug	Sep	Oct	Nov
Winter			Spring			Summer			Autumn		

- **Exclusion Criteria** - prior calcium or vitamin D supplementation, chronic kidney disease, or other related metabolic comorbidities
- **Outcomes of Interest**
 - **Primary:** postoperative hypocalcemia (serum calcium < 8.5 mg/dL)
 - **Secondary:** serum PTH, 25-hydroxyvitamin D, and phosphorus levels
- **Analysis** - cohorts controlled for age, sex, and race using 1:1 propensity score matching. Statistical significance set at $p < 0.05$

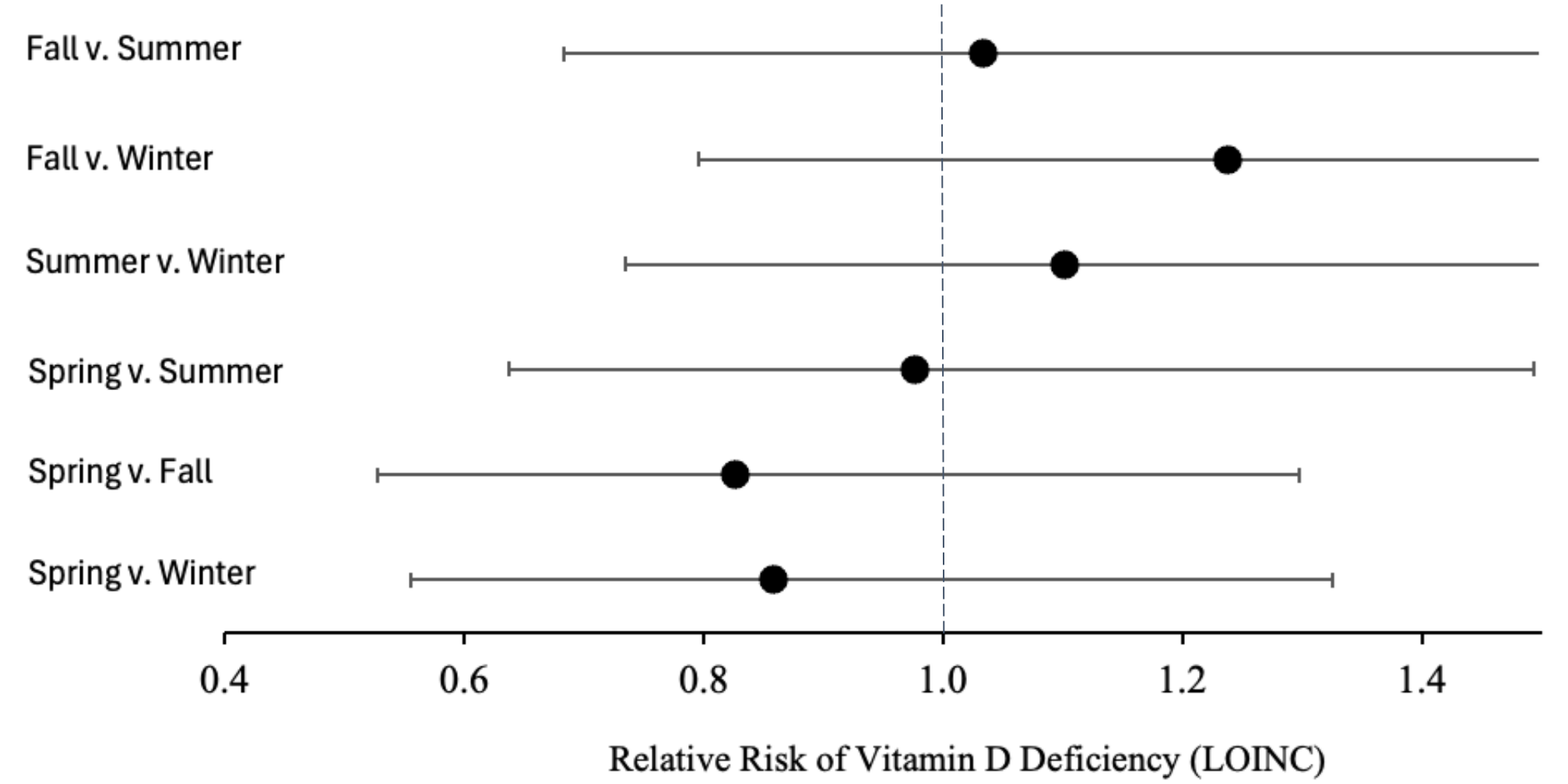
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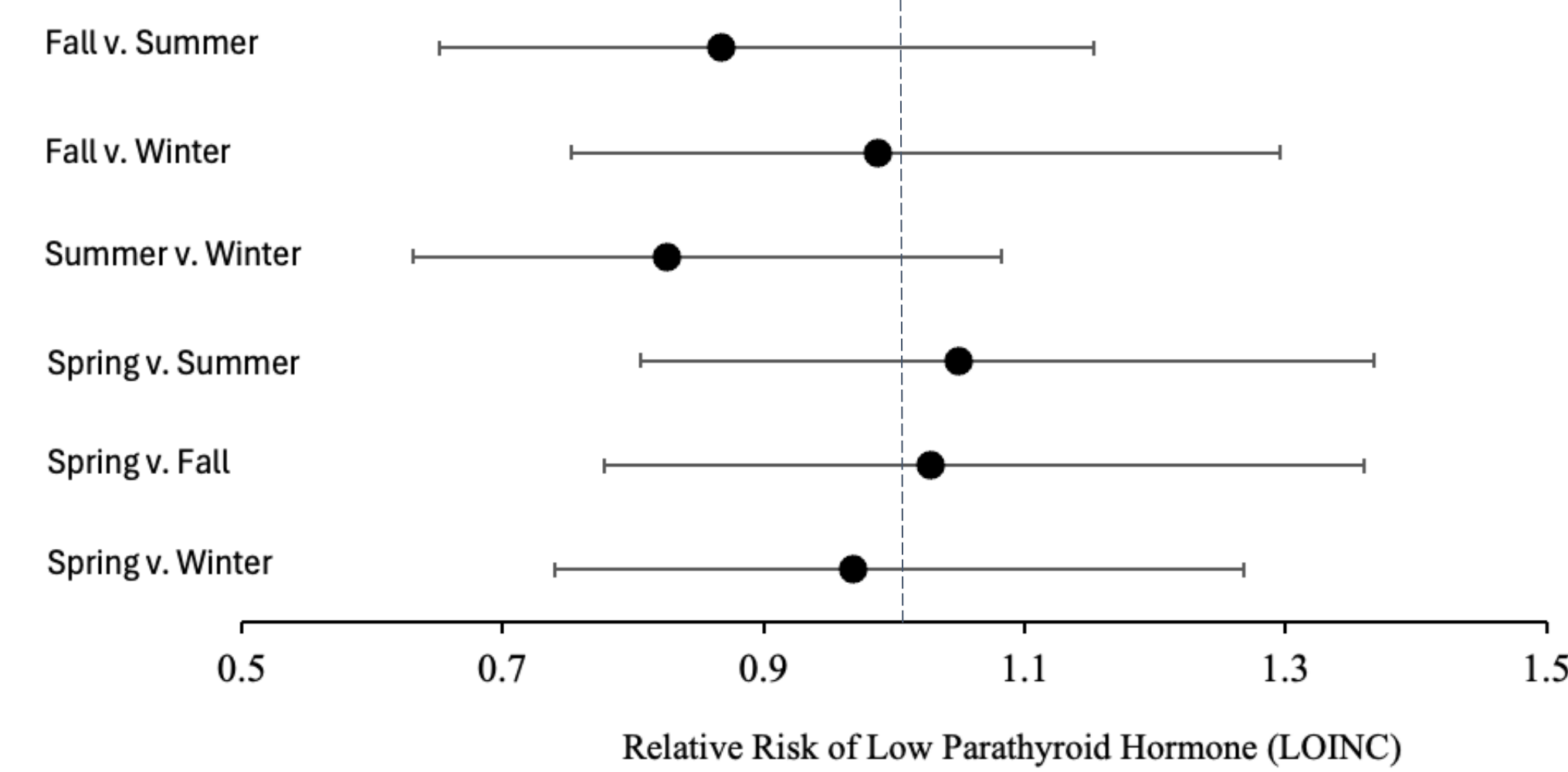
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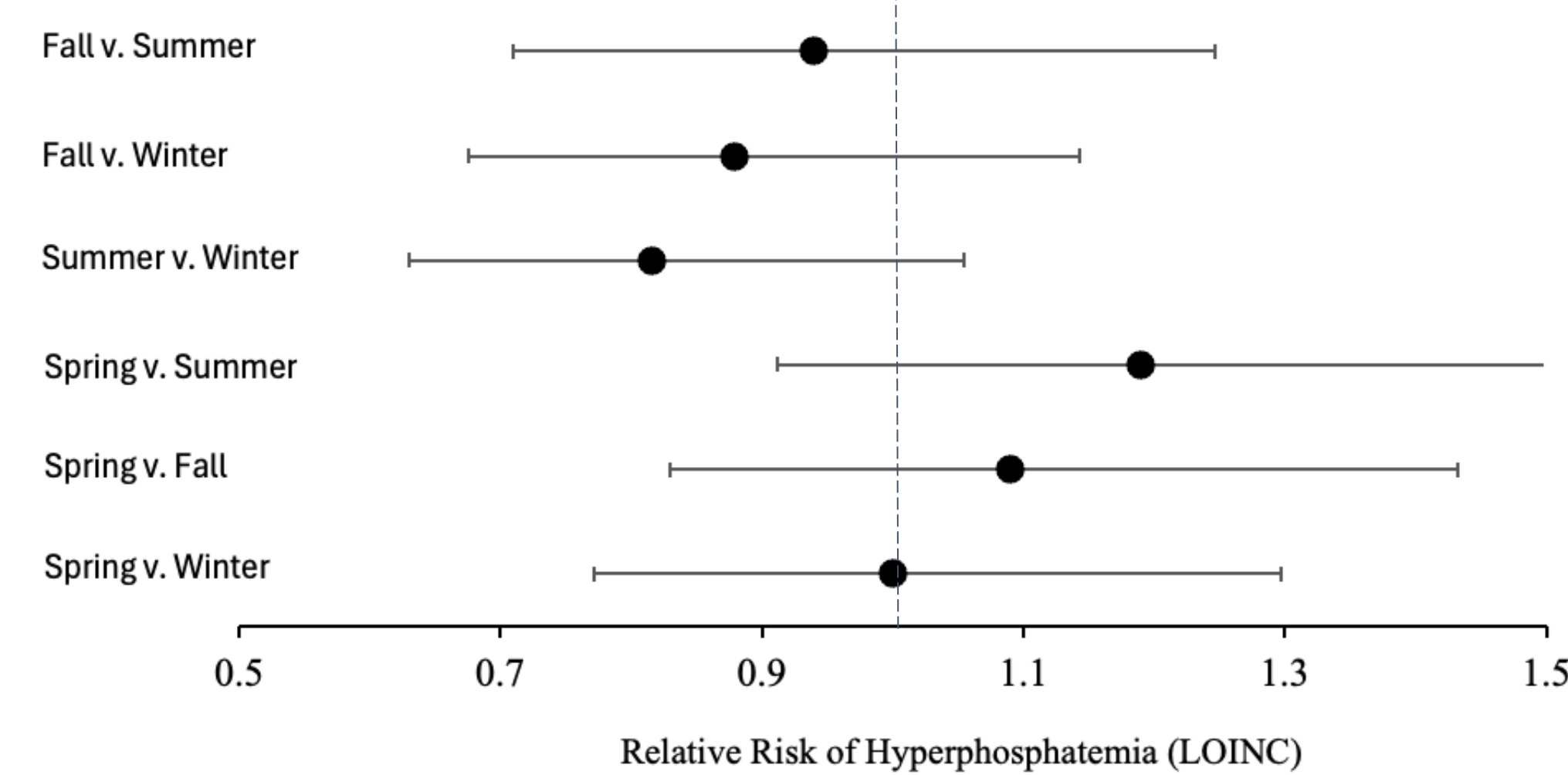


Figure 1. Forest Plots of Seasonal Risk Differences Following Total Thyroidectomy. Forest plots display relative risk (RR) with 95% confidence intervals for seasonal cohort comparisons of postoperative outcomes including A. Hypocalcemia (ICD-10 diagnosis code), B. Hypocalcemia (LOINC, serum calcium < 8.5 mg/dL), C. Vitamin C Deficiency (LOINC, 25-hydroxyvitamin D < 20 ng/mL), D. Low Parathyroid Hormone (LOINC, PTH ≤ 10 pg/mL), E. Hyperphosphatemia (LOINC, phosphate ≥ 4.5 mg/dL). Relative risks > 1 favor higher risk in the first listed season compared with the second. Dashed vertical line indicates the null value (RR = 1).

Discussion

- In this large, multi-institutional cohort, patients undergoing thyroidectomy in Spring had a significantly higher risk of postoperative hypocalcemia compared with Winter.
- This finding contrasts with prior single-center studies suggesting increased risk during winter months due to lower vitamin D levels, highlighting the complexity of seasonal influences on calcium homeostasis.
- No significant seasonal differences were observed in postoperative vitamin D, PTH, or phosphorus, suggesting factors beyond vitamin D status may contribute.
- As a retrospective database study, results are limited by reliance on coding occurrence and laboratory reporting.
- One avenue of consideration could be prior season

Conclusions

In conclusion, this study suggests that seasonality influences the risk of hypocalcemia following total thyroidectomy, with patients undergoing surgery in the spring at greater risk compared to those in winter. With no significant biochemical differences across seasons, these findings challenge conventional assumptions and highlight the need to look beyond vitamin D alone in explaining postoperative calcium homeostasis. If future studies confirm a springtime deficiency, this may guide preoperative indications particularly in regions where such seasonal changes are more largely felt.

Contact

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References

1. Claudius Falch, Jan Hornig, Moritz Senne, Manuel Braun, Alfred Konigsrainer, Andreas Kirschniak, Sven Muller, Factors predicting hypocalcemia after total thyroidectomy – A retrospective cohort analysis, International Journal of Surgery, Volume 55, 2018, Pages 46-50, ISSN 1743-9191, <https://doi.org/10.1016/j.ijso.2018.05.014>.
2. Noureldine SI, Genther DJ, Lopez M, Agrawal N, Tufano RP. Early Predictors of Hypocalcemia After Total Thyroidectomy: An Analysis of 304 Patients Using a Short-Stay Monitoring Protocol. JAMA Otolaryngol Head Neck Surg. 2014;140(11):1006–1013. doi:10.1001/jamaoto.2014.2435
3. Alqahtani SM, Alatawi AS, Alalawi YS. Post-Thyroidectomy Hypocalcemia: A Single-Center Experience. Cureus. 2021 Nov 29;13(11):e20006. doi: 10.7759/cureus.20006. PMID: 34987897; PMCID: PMC8716130.