

# Reductions in Gastrointestinal Intolerance, Healthcare Resource Utilization and Cost Associated with a Plant-Based Peptide Enteral Formula with Fruit and Vegetable Ingredients: Retrospective Analysis of Children and Adults in Post-Acute Care

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**Purpose:** Peptide-based enteral nutrition (EN) formulas are an alternative to standard EN formulas for patients with gastrointestinal (GI) intolerance. Evidence supports GI tolerance benefits of either peptide-based EN or EN containing fruits and vegetables. However, there is a lack of research on plant-based peptide EN with added fruit and vegetable ingredients.

**Patients and Methods:** This retrospective study analyzed United States (US) claims data on children (1–13 years) and adults (≥14 years) receiving plant-based peptide formulas with fruit and vegetable ingredients in post-acute care. Demographics, GI tolerance, healthcare resource utilization (HCRU) and costs were captured. Clinical and health economic outcomes were compared 6 months pre-index and 1-, 3- and 6-months post-index in both cohorts.

**Results:** In total, data from 91 children and 82 adults were analyzed. Mean (standard deviation [SD]) age was 5.5 (3.0) years in children and 49.0 (20.5) years in adults. Significantly fewer children and adults experienced any GI intolerance symptoms at all post-index time points compared with pre-index ( $p < 0.001$ ). Significant reductions in individual GI symptoms including constipation, diarrhea, nausea and vomiting were observed in children and adults at all post-index time points compared with pre-index ( $p < 0.05$ ). Significantly lower adjusted HCRU costs for inpatient and outpatient visits were reported at all post-index time points compared with pre-index for children. For adults, significant reductions in adjusted costs were reported for emergency, inpatient, outpatient, and urgent care at all post-index time points when compared with pre-index. Total adjusted costs were significantly reduced from \$473,857 at pre-index to \$273,134 at 3 months post-index ( $p < 0.05$ ) for children, and from \$676,456 at pre-index to \$427,576 at 6 months post-index ( $p < 0.001$ ) for adults.

**Conclusion:** Children and adults prescribed plant-based peptide formulas with fruit and vegetable ingredients showed significant reductions in GI intolerance symptoms, HCRU and associated costs post-hospital discharge.

**Keywords:** pediatric nutrition, peptide tube feeding, healthcare resource utilization, real food enteral formulas, intolerance, real-world evidence

## Introduction

Enteral nutrition (EN) is the standard of care for patients with a functional gastrointestinal (GI) system who cannot meet their nutritional needs orally.<sup>1,2</sup> Initiated during acute care in hospital, EN continues to be administered following

discharge at home or in a care facility setting (post-acute care).<sup>2,3</sup> The prevalence of EN as part of post-acute care has increased in the United States (US) in recent decades, from 152,000 patients in 1992 to 436,874 patients in 2013,<sup>4,5</sup> due to its clinical and economic benefits in both children and adults.

Patients are typically initiated on standard EN formulas containing intact protein sources.<sup>6</sup> However, up to 50% of patients have been reported to experience GI intolerance, including symptoms such as nausea and vomiting, diarrhea or constipation, abdominal pain, and bloating,<sup>7–9</sup> which can adversely impact their nutritional status and overall well-being.<sup>8</sup> Although there are currently no consensus guidelines on how to manage GI intolerance in adults or children receiving EN,<sup>10</sup> peptide-based formulas (PBF) are used in clinical practice as an alternative to standard polymeric EN formulas as they are designed to enhance digestion and absorption.<sup>10,11</sup> Studies have demonstrated the benefits of PBF on GI symptoms and reduced healthcare resource utilization (HCRU) in adults in acute and post-acute care settings.<sup>9,12–16</sup>

There is a growing preference towards real food formulas with blenderized whole foods or added fruits and vegetables, as improvements in GI symptoms have been observed in children switching to EN formulas with food-derived ingredients.<sup>17</sup> The improvements observed with formulas containing real food ingredients are thought to be due to the benefit of varying fiber types and amount on gut microbiota compared with standard EN.<sup>17–19</sup> Additionally, healthcare professionals, patients, and caregivers are requesting EN formulas that include real food and recognizable ingredients.<sup>1,3</sup> However, there is a lack of research on peptide-based EN formulas that also include fruit and vegetable ingredients.<sup>7,20,21</sup> Plant-based EN formulas have also become increasingly popular among patients with food allergies or experiencing GI intolerance symptoms with standard EN formulas.<sup>22,23</sup>

This retrospective review of real-world data is a first study to assess GI intolerance occurrence and symptoms, HCRU, and associated costs up to 6 months before and after the initiation of a plant-based peptide enteral formula containing fruit and vegetable ingredients in children and adults receiving EN in a post-acute care setting.

## Materials and Methods

### Study Design, Data Sources, and Inclusion Criteria

This retrospective observational study used US claims data to analyze patient demographics, GI intolerance symptoms, HCRU rates, and costs in children and adults in a post-acute care setting. Medical and pharmacy claims were obtained from the Clarivate Real World Evidence Data Repository, a US database which covers 98% of health plans, providing a nationally representative overview.<sup>24</sup> Data were de-identified at the patient level and retrospectively analyzed. The study was not considered human subjects research and was deemed exempt from Institutional Review Board oversight and informed consent under US Code of Federal Regulations 45 Part 46. The study adhered to Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines (Table S1).

Data were collected from records dated between January 2020 and December 2022. The study included two cohorts, pediatric (children aged 1–13 years prescribed the pediatric plant-based peptide enteral formulas with fruit and vegetable ingredients; Compleat® Pediatric Peptide 1.5, Nestlé HealthCare Nutrition, US, [PPPF]) and adults (aged ≥14 years, prescribed the adult plant-based peptide enteral formulas with fruit and vegetable ingredients; Compleat® Peptide 1.5, Nestlé HealthCare Nutrition, US, [APPF]) in a post-acute care setting, with a history of formula use for at least 5 days. Patients were excluded if they were receiving parenteral nutrition or palliative and/or end of life care.

### Outcome Measures

Clinical and health economic outcomes were compared 6 months pre-index and 1 month (28 days), 3 months (84 days) and 6 months (168 days) post-index in both the pediatric and adult cohorts. The index date was defined as the date of hospital discharge. Clinical outcomes included the occurrence and frequency of GI intolerance events and specific GI symptoms (nausea and vomiting, gagging and retching, diarrhea, constipation, flatulence, abdominal distension, and abdominal pain). Health economic outcomes included HCRU (inpatient and outpatient services, emergency department [ED], urgent care, and other places of service including assisted living or intermediate care facilities, and those not identified in the claims) and associated unadjusted and adjusted costs. Imputation was used to fill in missing cost components. To address missing entries, the average cost of the available elements was utilized for each group of age,

gender, and category elements. Patient characteristics, clinical comorbidities and medical history were captured. Outcomes including z-score, weight gain, height and weight parameters were excluded due to missing data. Use of concomitant medications was analyzed at 6 months pre-index and 1, 3, and 6 months post-index.

## Statistical Analyses

Patient demographics and clinical characteristics, comorbidities, GI intolerance, medication use, HCRU rates, and unadjusted costs were analyzed using descriptive statistics (mean, median, and standard deviations). Pre- and post-index outcomes were compared using chi-square or Fisher exact test at an alpha 0.05 level of significance. Adjusted costs were assessed using a multivariate generalized linear model adjusted for age, gender, and comorbidity index score (pediatric comorbidity index [PCI]<sup>25</sup> and Charlson's Comorbidity Index [CCI]<sup>26</sup>). Difference in adjusted costs at pre-and post-index were compared using multivariate *t*-test with an alpha 0.05 level of significance. Univariate analysis and *t*-tests were performed using Python, while descriptive statistics were analyzed in Microsoft<sup>®</sup> Excel.

## Results

### Demographic and Patient Characteristics

In total, 91 children and 82 adults met eligibility criteria for the study. Demographic and patient characteristics, as well as the most common medical diagnoses and comorbidities for children and adults are presented in Table 1. The mean (SD) age was 5.5 (3.0) years in children and 49.0 (20.5) years in adults. The majority of patients were categorized as commercially insured, with 59% and 71% of children and adults, respectively. All US regions were represented in the pediatric and adult populations in this study.

In the pediatric population, the most common medical diagnoses were diseases of the digestive system (79%) and the respiratory system (74%), congenital malformations, deformations and chromosomal abnormalities (74%), and mental, behavioral and developmental disorders (73%) (Table 1). The majority of patients (84%) in the pediatric population had a PCI score  $\geq 4$ , with a mean (SD) of 8.26 (2.93). The most common comorbidities, measured via PCI, in the pediatric population included congenital malformations (73%), developmental delays (60%), and GI conditions (57%). (Table 1).

**Table 1** Demographics, Medical Diagnoses, and Comorbidities in the Study Population

Characteristics	Children (N=91)	Adults (N=82)
Age, years		
Mean (SD)	5.5 (3)	49 (20.5)
Sex, N (%)		
Female	45 (49)	46 (56)
Region, N (%)		
Midwest	34 (37)	21 (26)
West	8 (9)	23 (28)
South	23 (25)	24 (29)
Northeast	26 (29)	14 (17)
Payer, N (%)		
Commercial	54 (59)	58 (71)
Medicaid <sup>a</sup>	4 (4)	3 (4)
Others <sup>b</sup>	33 (36)	21 (26)

(Continued)

**Table 1** (Continued).

Characteristics	Children (N=91)	Adults (N=82)
Most common medical diagnoses, N (%)		
Diseases of the digestive system	72 (79)	73 (89)
Diseases of the respiratory system	67 (74)	55 (67)
Congenital malformations deformations and chromosomal abnormalities	67 (74)	15 (18)
Diseases of the nervous system	54 (59)	64 (78)
Mental behavioral and neurodevelopmental disorders	66 (73)	60 (73)
Diseases of the musculoskeletal system and connective tissue	43 (47)	62 (76)
Endocrine nutritional and metabolic diseases	54 (59)	68 (83)
Most common comorbidities, N (%)		
Congenital malformations	66 (73)	–
Developmental delays	55 (60)	–
GI conditions	52 (57)	–
Cancer	–	32 (39)
Chronic pulmonary disease	–	24 (29)
Paraplegia and hemiplegia	–	20 (24)
PCI score $\geq 4$ , N (%)	76 (84)	–
CCI $\geq 3$	–	42 (56)

**Notes:** <sup>a</sup> Medicaid consists of Medicaid, State Medicaid, and Managed Medicaid; <sup>b</sup> Other payer type includes Veteran Affairs, other Government, Tricare among others.

**Abbreviations:** CCI, Charlson Comorbidity Index; GI, gastrointestinal; N, number; PCI, Pediatric Comorbidity Index; SD, standard deviation.

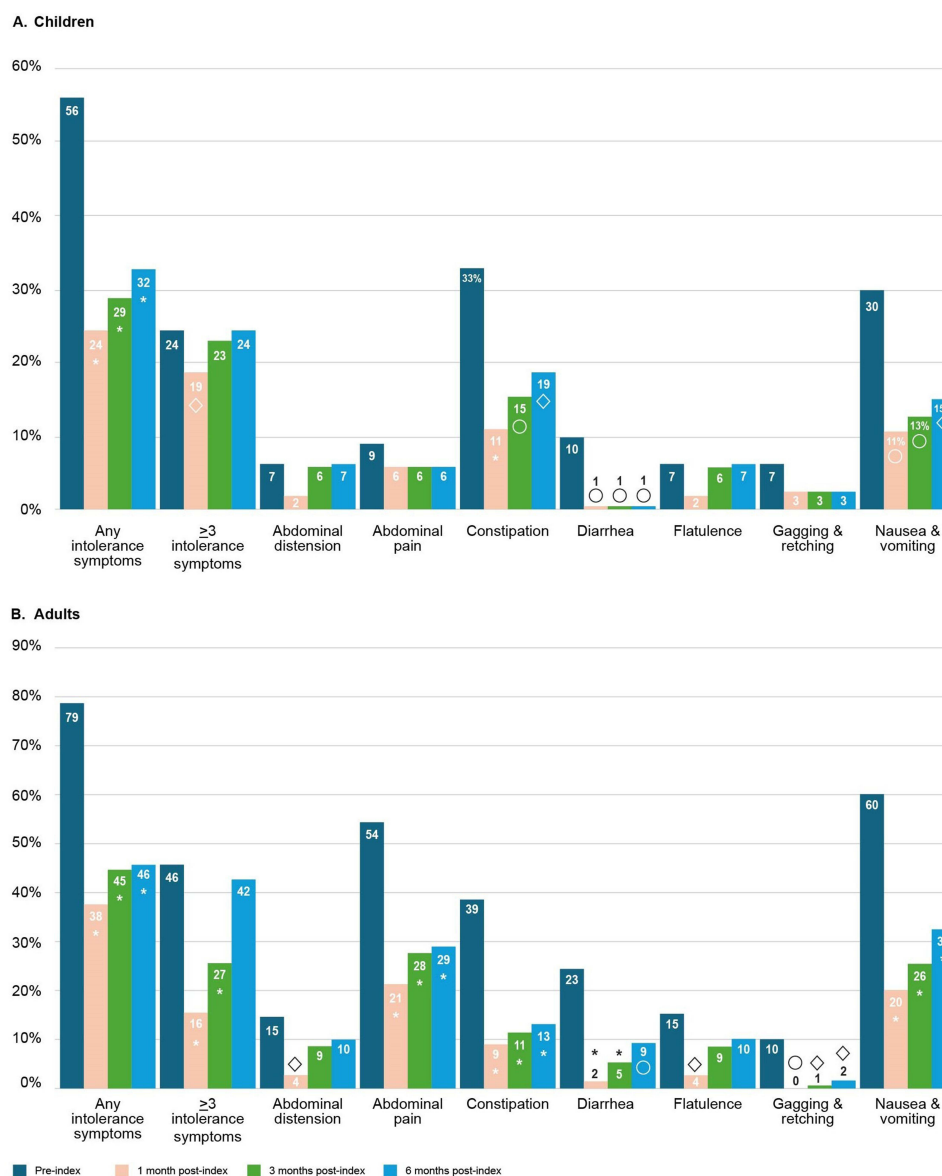
In the adult population, the most common medical diagnoses were diseases of the digestive system (89%), endocrine nutritional and metabolic diseases (83%), diseases of the nervous system (78%), the musculoskeletal system and connective tissue (76%), and mental, behavioral and neurodevelopmental disorders (73%) (Table 1). The mean (SD) CCI weighted score was 10.05 (3.44), and 56% of patients with comorbidities had a CCI  $\geq 3$ . The most common comorbidities, measured via CCI, included cancer (39%), chronic pulmonary disease (29%), and paraplegia and hemiplegia (24%) (Table 1).

Data on concomitant medications were available for 57 children and 66 adults. Anti-infective agents, GI drugs, CNS treatments, and autonomic drugs were the most commonly reported treatment categories, in both children and adults. A summary of concomitant medications pre- and post-index can be found in the supporting information (Table S2).

## Children

### Gastrointestinal Intolerance

Significantly fewer children receiving PPPF experienced any GI intolerance symptoms at all post-index time points compared with pre-index ( $p < 0.001$  for all) (Figure 1A). Significant reductions in individual GI symptoms including constipation, diarrhea, and nausea and vomiting were observed for children receiving PPPF at all post-index time points compared with pre-index ( $p < 0.05$ ) (Figure 1A). The effect of PPPF on GI symptoms for adults are detailed below and shown in Figure 1B.



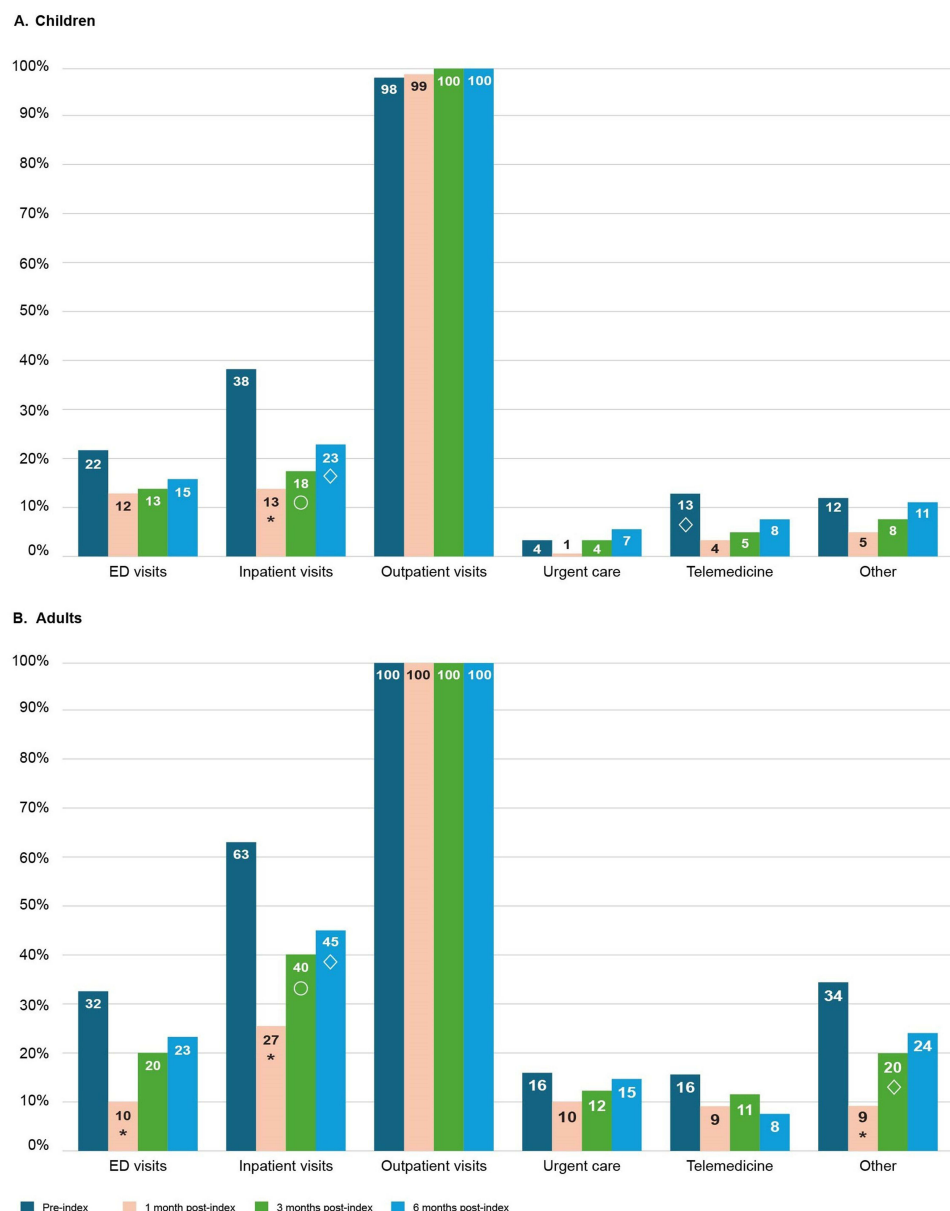
**Figure 1** GI intolerance symptoms pre- and post-index in children (**A**) and adults (**B**) receiving a plant-based peptide formula with fruit and vegetable ingredients. P-values (pre- vs post-index) were calculated using chi-squared test; ◇ p<0.05, ○ p<0.01, \* p<0.001.

## Healthcare Resource Utilization

Compared with the pre-index time period, there were significant reductions in the proportion of patients requiring inpatient visits up to 6 months post-index ( $p<0.05$ ), and telemedicine appointments at 1 month post-index ( $p<0.05$ ) (Figure 2A). A significant reduction in the mean number of outpatient visits was observed at all post-index time points (Figure S1). The mean numbers for all visit types are available in the supporting information (Figure S1). The effect of PPPF on healthcare resource utilization for adults are detailed below and shown in Figure 2B.

## Healthcare Resource Costs

For children receiving PPPF, significantly lower adjusted total HCRU costs were observed up to 3 months post-index, compared with pre-index ( $p<0.05$ ) (Table 2). Significantly lower adjusted mean HCRU costs for inpatient and outpatient visits were observed up to 6 months post-index compared with pre-index ( $p<0.05$ ) (Table 2).



**Figure 2** Percentage of children (A) and adults (B) requiring care pre- and post-index. Other places of services include assisted living or intermediate care facilities, and those not identified in the claims. P-values (pre- vs post-index) were calculated using chi-squared test;  $\diamond$   $p < 0.05$ ,  $\circ$   $p < 0.01$ , \*  $p < 0.001$ .

**Abbreviation:** ED, emergency department.

## Adults

### Gastrointestinal Intolerance

Significantly fewer adults receiving APPF experienced any GI intolerance symptoms and  $\geq 3$  GI intolerance symptoms at all post-index time points compared with pre-index ( $p < 0.001$  for all) (Figure 1B). Significant reductions in individual GI symptoms including abdominal pain, constipation, diarrhea, gagging and retching, and nausea and vomiting were observed for adults receiving APPF at all post-index time points compared with pre-index ( $p < 0.05$ ) (Figure 1B).

### Healthcare Resource Utilization

For adults receiving APPF, there was a significant reduction in the percent of patients requiring inpatient visits up to 6 months post-index compared with pre-index ( $p < 0.05$ ), as well as a significant reduction in the proportion of patients requiring ED visits ( $p < 0.05$ ) and other HCRU ( $p < 0.05$ ) up to 1 month and 3 months post-index, respectively (Figure 2B).

**Table 2** Adjusted Costs Associated with Healthcare Resource Utilization Pre- and Post-Index in Children and Adults Receiving PBF

Characteristics	ED Visits	Inpatient Visits	Outpatient Visits	Urgent care	Other <sup>d</sup>	Total
Children						
Pre-index	\$14,931 (1951)	\$127,371 (16,799)	\$255,792 (6449)	\$9,085 (3123)	\$51,891 (17,998)	<b>\$459,069</b>
1 month post-index	\$6,900 (753) <sup>b</sup>	\$36,946 (9266) <sup>c</sup>	\$46,908 (1418) <sup>c</sup>	\$18,634 (-)	\$23,114 (9008)	<b>\$132,501<sup>c</sup></b>
3 months post-index	\$9,760 (1470)	\$60,905 (18,676) <sup>a</sup>	\$113,982 (2693) <sup>c</sup>	\$9,816 (3324)	\$40,007 (14399)	<b>\$234,470<sup>a</sup></b>
6 months post-index	\$9744 (1532)	\$67,507 (16,884) <sup>a</sup>	\$193,784 (4763) <sup>c</sup>	\$7,653 (2557)	\$54,369 (18,845)	<b>\$333,058</b>
Adults						
Pre-index	\$58,795 (\$9703)	\$135,783 (13,757)	\$398,180 (22,828)	\$23,728 (4720)	\$33,155 (972)	<b>\$649,641</b>
1 month post-index	\$22,483 (\$6156) <sup>b</sup>	\$57,549 (12,980) <sup>c</sup>	\$63,177 (2242) <sup>c</sup>	\$7,221 (574) <sup>b</sup>	\$15,580 (5111) <sup>a</sup>	<b>\$166,011<sup>c</sup></b>
3 months post-index	\$33,284 (5031) <sup>a</sup>	\$88,092 (19,388) <sup>a</sup>	\$150,837 (6658) <sup>c</sup>	\$9573 (1613) <sup>a</sup>	\$28,564 (9865)	<b>\$310,349<sup>c</sup></b>
6 months post-index	\$27,752 (4109) <sup>b</sup>	\$82,827 (11,804) <sup>b</sup>	\$235,996 (13,116) <sup>c</sup>	\$9,316 (1389) <sup>a</sup>	\$31,502 (8416)	<b>\$387,393<sup>c</sup></b>

**Notes:** Multivariate GLM model adjusted for age, gender, comorbidity scores; multivariate t-Test (pre-index vs post-index), alpha=0.05 level of significance <sup>a</sup> p<0.05; <sup>b</sup> p<0.01; <sup>c</sup> p<0.001; <sup>d</sup> Other places of service include assisted living or intermediate care facilities, and those not identified in the claims. Total costs are presented in bold.

**Abbreviations:** ED, emergency department; PBF, peptide-based formula; SE, standard error; USD, United States Dollar.

A significant reduction in mean outpatient visits was observed at all post-index time points. The mean number of visits is available in the supporting information ([Figure S1](#)).

### Healthcare Resource Costs

Significantly lower adjusted total HCRU costs were observed up to 6 months post-index, compared with pre-index, in adults receiving APPF (p<0.001) ([Table 2](#)). Significantly lower adjusted mean HCRU costs were observed up to 6 months post-index compared with pre-index for ED visits, inpatient visits, outpatient visits, and urgent care (p<0.05) ([Table 2](#)).

## Discussion

This retrospective observational study analyzed data on GI tolerance and HCRU in children and adults receiving a plant-based, peptide enteral formula containing fruit and vegetable ingredients in a post-acute care setting. Outcomes were compared in the 6-month period before the date of hospital discharge (index date) with those up to 6 months after the index date. The peptide-based EN formulas in this study contain hydrolyzed pea protein, which provides a plant-based option designed to enhance digestion and absorption in patients experiencing intolerance symptoms with a standard polymeric formula. An EN formula containing hydrolyzed pea protein was recently reported to maintain or improve tolerance in children transitioning from a hypoallergenic formula.<sup>22</sup> The formulas in the present study also contain fruit and vegetable ingredients, for which there is a lack of data for peptide-based formulas in currently available literature.

The findings from this study are the first to demonstrate the clinical benefits of a plant-based, peptide EN with fruit and vegetable ingredients for children and adults in a post-acute care setting. Improved GI tolerance was associated with reductions in HCRU, in particular visits to inpatient services for at least 6 months post-index in children and adults. Significant savings in HCRU costs were also observed up to at least 6 months post-index in both populations, compared with pre-index. The reductions in HCRU and significant improvement in clinical outcomes observed with the use of PPF in this study are critical across the continuum of care and for healthcare systems. Healthcare institutions must continue their efforts to reduce clinical complications, inpatient visits, and preventable readmissions, alongside improving patient satisfaction and outcomes to avoid financial penalties due to the Hospital Readmissions Reduction Program.<sup>27</sup>

The results of this analysis are in line with previously published studies on the clinical benefits of an enteral formula containing real food ingredients.<sup>17,28</sup> In a retrospective study conducted in the UK, 85% of children already established on a standard enteral formula reported significant improvements in GI symptoms within 7 days of commencing an enteral formula containing real food ingredients.<sup>28</sup> Plant-based enteral formulas have also demonstrated improved nutritional



outcomes for adults at risk of malnutrition after 28 days, compared with baseline.<sup>29</sup> The improvements observed with real food ingredients and plant-based enteral formulas are thought to be due to the improved GI tolerance and the benefit of higher fiber content on the gut microbiota.<sup>17,28,30</sup> The formulas utilized in this study contain 12 g of fiber per liter, sourced from fruit and vegetable ingredients and from partially hydrolyzed guar gum. The use of fruit and vegetable ingredients may enhance the well-established benefits of peptide-based EN formulas. Findings from this study add to the limited evidence available on PPF with fruit and vegetable ingredients.

This study has a number of methodological strengths. The use of a real-world database encompassing over 98% of US healthcare plans and patient level data for >300 million patients provided a representative sample of children and adults from all US regions. Potential selection bias in the analysis of HCRU costs was minimized by using a multivariate model, adjusted for age, gender, and comorbidity index (PCI or CCI). The sponsor had no role in patient selection, no patient identifiers were collected, and results were not contingent upon sponsor approval. To ensure the validity of findings, the incorporated data and clinical confounders were controlled through appropriate statistics.

In contrast to a clinical study, this analysis is limited by the retrospective design and the use of claims data. Retrospective, claim-based analyses rely on accurate diagnostic and medical coding and any error in the data can potentially affect the results. The real-world data provided by the US claims database do not offer a complete picture, and important information might not be reported, eg, timing and method of EN delivery, severity of the GI symptoms, and availability of nutrition support team. Retrospective analyses can only identify associations between decreased GI symptoms and HCRU in patients receiving PPF, but do not allow for stating causation. Since authors were employees or received direct or indirect payment from the study sponsor for this work, potential biases were minimized by presenting both significant and non-significant results.

Plant-based peptide enteral formulas with fruit and vegetable ingredients are an alternative to standard EN formulas. Future research comparing use of plant-based peptide EN with fruit and vegetable ingredients versus standard EN formulas would be meaningful to understand potential tolerance and/or health economic advantages and appropriate usage of different formula categories.

## Conclusion

Use of a plant-based peptide enteral formula with fruit and vegetable ingredients was associated with significant reductions in GI intolerance symptoms, HCRU and associated costs in children and adults post hospital discharge. This retrospective analysis of real-world national-level data supports the use of a plant-based peptide enteral formula with fruit and vegetable ingredients as a well-tolerated option for EN in children and adults requiring EN support in a post-acute care setting.

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## Disclosure

GJM is employed by KIDZ Medical Services, Hollywood, FL and provided consulting services to Nestlé Health Science on this project. PK, SM, YVK, and KF are employees of Clarivate Data Analytics which was contracted by Nestlé Health Science for this project. PC, AD, and AK are employees of Nestlé Health Science. The authors report no conflicts of interest in this work.

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