

EMPOWERING ACTION: EXOCRINE PANCREATIC INSUFFICIENCY MANAGEMENT IN PANCREATIC CANCER

JULY 2025

OVERVIEW

Background

In the United States, the lack of formal, comprehensive clinical practice guidelines or national recommendations on EPI and PERT management in pancreatic cancer leaves a critical gap in care. But our patients can't wait for perfect data—they need high-value care now. This executive summary presents key insights from **"From Overlooked to Essential: U.S. Consensus Statements on Identifying and Managing Exocrine Pancreatic Insufficiency in Pancreatic Oncology Practice,"** a white paper developed by Canopy Cancer Collective with support of The Pancreatic Cancer Action Network.

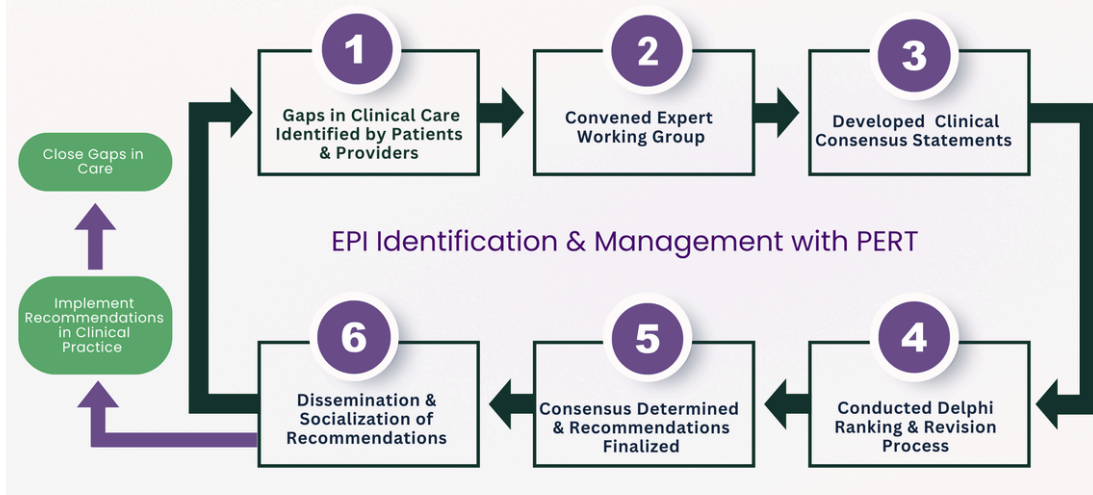
Key Contribution of This Work

This summary introduces a new guiding framework, grounded in available evidence and clinical practice, that expands on existing pancreatic adenocarcinoma guidelines with comprehensive clinical recommendations to support clinical decision-making in identifying and managing exocrine pancreatic insufficiency (EPI) (see *"Insight Panel 2"*).

Developed by a Multidisciplinary Expert Panel

Canopy convened a diverse Expert Working Group (EWG) of 12 individuals with highly specialized expertise in pancreatic oncology clinical practice, including registered dietitians, nurse practitioners, physician assistants, and doctoral-level dietitians. Several members are Board Certified Specialists in Oncology Nutrition. The EWG members represent eight academic and community cancer centers, serving a broadly diverse population of patients with EPI due to pancreatic cancer in cancer centers nationwide.

BLENDING EVIDENCE AND INSIGHT TO DEVELOP CLINICAL CONSENSUS STATEMENTS



This summary, created in partnership with AbbVie, highlights key points from the Canopy Cancer Collective and Pancreatic Cancer Action Network's white paper. For the complete document, visit <https://canopycancer.org/epi-pertwhitepaper>. AbbVie provided financial sponsorship but was not involved in the white paper's methodology, data collection, analysis, or development. Authors received no compensation from AbbVie for their contributions.

abbvie

What We Know, What's Missing, and What Needs to Change?

EPI is common in patients with pancreatic cancer (see “Insight Panel 1” for prevalence rates). The condition can result from pancreatic resection¹, duct obstruction from tumors or fibrosis, loss of gland function, and/or pancreatitis from surgical or radiation treatment trauma². **Yet, EPI remains widely underdiagnosed³ and undertreated⁴ in clinical practice,** despite its distressing symptoms⁵ and impact on patient lives⁶.

PERT is the recognized standard of care for EPI, and breaks down fats, proteins, and carbohydrates in the duodenum and proximal small intestine, acting like digestive enzymes physiologically secreted by the pancreas, improving maldigestion and malabsorption of EPI.

Methods & Approach

The consensus statements were developed through a **structured and evidence-based approach, which included a modified Delphi methodology⁹.** It integrated an iterative, targeted literature review with qualitative research that leveraged human-centered design principles¹⁰ to assess care team and patient *experiences with EPI and PERT, and uncover unmet clinical and nonclinical needs.*

Where empirical evidence from literature was limited or conflicting, synthesized expert opinion from the EWG ensured recommendations were both evidence-based and grounded in clinical experience through its systematic combination of qualitative insights and expert consensus rounds. While systematic review using GRADE assessment is considered the gold standard for clinical practice guidelines, its traditional methodology was not feasible given the project timeline^{11, 12}, making this combined approach a balance of rigor and practicality.

Clinical Insights Panel 1

EPI PREVALENCE RATES: WHAT CLINICIANS SHOULD KNOW

- **Postoperative EPI occurs in 10–100% of patients,** depending on procedure type and remaining gland function⁷.
- **In unresectable disease, EPI affects 50–100% of patients and may worsen over time—**exocrine function can decline by ~10% per month⁸.

Clinical Insights Panel 2

WHAT IS THE CURRENT GAP IN CLINICAL PRACTICE?

Existing guidance acknowledges the importance of addressing EPI with PERT, but provides limited guidance on how to identify and manage EPI, initiate and adjust PERT and how teams work together to deliver PERT effectively.

As a result, detailed information on optimal EPI management is still largely undefined in practice—highlighting the need for a guiding framework to support clinical decision-making.

¹ Dominguez-Muñoz, J. E., et al. (2024). European guidelines for the diagnosis and treatment of pancreatic exocrine insufficiency. *United European Gastroenterology Journal*, 13(1), 125–172. <https://doi.org/10.1002/ueg2.12674>

² Ghodeif, A. O., & Azer, S. A. (2023). Pancreatic Insufficiency. In *StatPearls*.

³ Landers et al. (2014). Pancreatic enzyme replacement therapy (PERT) for malabsorption in patients with metastatic pancreatic cancer. *BMJ Supportive & Palliative Care*, 6(1), 75–79. <https://doi.org/10.1136/bmjspcare-2014-000694>

⁴ Forsmark et al. (2020). The use of pancreatic enzyme replacement therapy in patients with a diagnosis of chronic pancreatitis and pancreatic cancer in the US is infrequent and inconsistent. *Alimentary Pharmacology & Therapeutics*, 51(10), 958–967. <https://doi.org/10.1111/apt.15698>

⁵ Barkin et al. (2024). Real-world patient experience with pancreatic enzyme replacement therapy in the treatment of exocrine pancreatic insufficiency. *Pancreas*, 53(1), e16–e21. <https://doi.org/10.1097/MPA.0000000000002273>

⁶ Trestini et al. (2021). Pancreatic enzyme replacement therapy in patients undergoing first-line gemcitabine plus nab-paclitaxel for advanced pancreatic adenocarcinoma. *Frontiers in Oncology*, 11, 688889. <https://doi.org/10.3389/fonc.2021.688889>

⁷ Roeyen et al. (2022). Expert opinion on management of pancreatic exocrine insufficiency in pancreatic cancer. *ESMO Open*, 7(1), 100386. <https://doi.org/10.1016/j.esmoop.2022.100386>

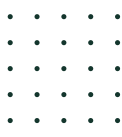
⁸ Powell, C. (2003). The Delphi technique: Myths and realities. *Journal of Advanced Nursing*, 41(4), 376–382. <https://doi.org/10.1046/j.1365-2648.2024.02537.x>

⁹ Teisberg et al. (2020). Defining and implementing value-based health care: A strategic framework. *Academic Medicine*, 95(5), 682–685. <https://doi.org/10.1097/ACM.00000000000003122>

¹⁰ Al Duhaillib et al. (2024). GRADE pearls and pitfalls—Part I: Systematic reviews and meta-analyses. *Acta Anaesthesiologica Scandinavica*, 68(5), 584–592. <https://doi.org/10.1111/aas.14386>

¹¹ Guyatt et al. (2008). GRADE: An emerging consensus on rating quality of evidence and strength of recommendations. *BMJ*, 336(7650), 924–926. <https://doi.org/10.1136/bmj.39489.470347.AD>

U.S. CONSENSUS STATEMENTS ON IDENTIFYING AND MANAGING EPI IN PANCREATIC ONCOLOGY PRACTICE



Consensus Statement and Level of Agreement* (%)

1. In the U.S., there are no widely accepted and adopted clinical guidelines or formalized published care pathways specifically in pancreatic oncology for identifying EPI and managing with PERT.	88%
2. EPI is underrecognized and undertreated. Evidence shows that if addressed, PERT may improve QOL and support adherence to oncology treatment. We have an ethical obligation to act on existing evidence: EPI identification and treatment must be standard in pancreatic cancer care and integrated into oncology guidelines, multidisciplinary planning, and tumor boards. Every patient deserves timely relief from the avoidable suffering EPI causes.	88%
3. All patients with pancreatic cancer should be screened for EPI, and re-screened at interval time points thereafter.	94%
4. Screening for EPI should begin at the earliest signs of a pancreatic mass with clinical symptoms, ideally before cancer treatment initiation, as side effects from treatment may distort evaluation of EPI.	100%
5. Screening should be done in the simplest and most feasible way given clinical infrastructure, staffing, and processes, to allow for treatment initiation if needed. Currently, screening may be done by patient self-report (PRO) if reviewed by a clinician, or by care team members (nurses, nurse navigators, registered dietitians, advanced practice providers, oncologists, gastroenterologists, primary care providers) who can coordinate with a prescribing provider if EPI is identified. Prescribing providers should follow up to ensure PERT is taken correctly and symptoms are managed.	100%
6. Given the high prevalence of EPI in this patient population, EPI can be diagnosed in pancreatic cancer patients through routine screening that combines assessment of clinical symptoms and nutritional status, without the need for pancreatic function tests (such as fecal elastase -1).	88%
7. EPI can be suspected when a patient presents with unintentional weight loss despite adequate food intake, plus at least one additional symptom, OR a patient presents with two to three EPI-related symptoms [†] even in the absence of unintentional weight loss despite adequate food intake.	81%
8. If EPI is found, PERT should always be offered or attempted.	94%
9. The suggested starting dose for a meal should be at least 48,000 - 72,000 units of pancrelipase, and about half the amount per snack. A formulation with the highest appropriate dose should be prescribed to decrease pill burden and cost.	94%
10. Patient education on PERT should occur when prescription is given and reinforced thereafter. Patients should be educated to inquire about increasing dose if EPI symptoms persist. A sliding scale for self-titration may be helpful.	100%
11. A patient on PERT should be routinely monitored for dose adjustments, especially within the first 1-2 weeks after initiating therapy and with the onset of any new or worsening symptoms.	94%
12. Active collaboration between the multidisciplinary team (i.e. oncology, gastroenterology, dietitians, palliative care, social work, navigation, primary care etc.) represents a best practice in the management of patients with EPI.	100%
13. Practical considerations for prescribing PERT should include the cost to the patient, factoring in insurance coverage and any available financial assistance programs, along with pill burden in the context of their full treatment plan, and any religious beliefs or dietary restrictions that may affect adherence.	100%
14. For patients with documented extreme financial need who have exhausted all standard financial assistance options for PERT, under certain circumstances with discretion, it is reasonable for providers to consider educating patients about non-standardized methods of accessing enzymes (e.g., OTC, international sources) for only enzyme brands that have a quality third-party certification. However, patients must also be educated that: 1) supplements are not standardized or regulated; 2) utility and safety are unknown; 3) potency and/or quality varies.	100%

Disclaimer: This document reflects a subset of consensus statements and recommendations drawn from the full white paper. It is intended as a concise summary and does not represent the complete scope of the expert panel's findings. Some of the statements in this summary may have been modified from the original consensus statements. For full methodology, detailed results, and the complete list of consensus statements, please refer to the [full white paper](#).

*Classification of extent of agreement in consensus: Strong Consensus is 90% or more of participants agree or strongly agree; Consensus is 70% - 89% of participants agree or strongly agree; Majority Agreement but not consensus is 50% - 69% of participants agree or strongly agree; No Consensus is 0 - 49% of participants agree or strongly agree. Adapted from "Clinical nutrition as part of the treatment pathway of pancreatic cancer patients: an expert consensus," by A. Carrato et al, 2021, Clin Transl Oncol, 24(1):112-126 (<https://doi.org/10.1007/s12094-021-02674-x>). Copyright 2021 by the authors who adapted content from another source. Our adaptation is based solely on Carrato et al.'s version, licensed under CC BY 4.0 (<http://creativecommons.org/licenses/by/4.0/>). This does not imply endorsement by the original or intermediate authors or publishers. Changes include: (1) percentage values were slightly adjusted to reflect our methodology; (2) "or strongly agree" was added to clarify the agreement scale; and (3) a note was added that majority agreement does not constitute formal consensus.

[†] For a list of symptoms, see the 'Early and Late Symptoms of EPI' sections on the following page.

PRACTICAL STRATEGIES FOR BUILDING AND APPLYING A CLINICAL FRAMEWORK

Recognizing the Symptoms EPI

Early Symptoms of EPI¹³

- Abdominal bloating
- Excessive flatulence
- Abnormal stool frequency
- Abdominal pain, cramping, or discomfort

Late Symptoms of EPI¹⁴

- Frequent, loose, fatty and/or oily stools
- Unintentional weight loss despite adequate oral intake
- Fat-soluble vitamin deficiencies
- Steatorrhea, characterized by bulky, foul-smelling, oily stools



Screening Your Patients for EPI: Where to Start

- **Screen Early: Proactive identification is key. EPI often worsens over time due to disease progression, treatment side effects, or post-surgical changes¹⁵. Routine re-screening can help identify changes before they escalate¹⁶.**
- **Consider confounding factors, and when in doubt, test: If symptoms are unclear or complicated by co-existing conditions¹⁷, consider confirming EPI with an indirect diagnostic test, like the fecal elastase-1 (FE-1). Identify overlapping symptoms with cancer or cancer treatment, considering the impact of chemotherapy and pain medications on stool quality and how it may mask EPI¹⁸.**
- **Currently, there is no validated algorithm with a definitive number or hierarchy of signs or symptoms to determine the presence of EPI or start patients on PERT. Below is a preliminary algorithm designed by the EWG to help clinicians recognize EPI early and initiate timely treatment:**

Start PERT if:
Unintentional weight loss (despite adequate intake)
+ 1 > additional EPI symptom
OR
2-3 EPI-related symptoms
(other than unintentional weight loss)

Multidisciplinary Team-Based Management of EPI: Recommendations from Literature & the Expert Working Group

Effective identification and management of EPI requires a coordinated, multidisciplinary approach¹⁹. Key professionals involved in this effort include:

- Oncologists and nurse practitioners: often the first point of contact, responsible for identifying patients at high risk for EPI and initiating screening.
- Oncology dietitians: essential for nutritional assessments, correlation of dietary intake with symptoms, and guiding PERT use (e.g., recommending initiation and starting dose, assessing need for adjustments to optimize treatment outcomes)²⁰.
- Gastroenterologists: provide specialized evaluation and support for complex or unclear cases.
- Palliative care teams: integrate symptom management and quality of life considerations.
- Pharmacists: advise on appropriate enzyme formulations, dosing, and patient education.

Why it matters:

EPI frequently falls into a gray zone on care teams, where no single provider assumes clear ownership. This leads to fragmented care and missed opportunities to intervene. Shared responsibility across disciplines, paired with clear communication and workflows, is critical to ensure patients are identified early and supported throughout the continuum of care. By assigning clear roles, defining workflows, and creating team-based accountability for EPI screening, treatment initiation, and follow-up, health care teams can begin to address gaps in care of pancreatic cancer patients with EPI.

13, 14 Berry, A. J., & Bilbo, A. (2024). Exocrine pancreatic insufficiency and pancreatic exocrine replacement therapy in clinical practice. *Nutrition in Clinical Practice*, 39(51). <https://doi.org/10.1002/ncp.11124>

15 Roeyen et al. (2022). Expert opinion on management of pancreatic exocrine insufficiency in pancreatic cancer. *ESMO Open*, 7(1), 100386. <https://doi.org/10.1093/esmo/obab011>

16 Dominguez-Munoz, J. E., Vujasinovic, M., De La Iglesia, D., Cohen, D., Capurso, C., Gubergits, N., Hegyi, P., Hungin, P., Ockenga, J., Patelio, S., Parkhofer, L., Rebours, V., Rosendahl, J., Salvia, R., Scheers, I., Szentesi, A., Bonovas, S., Piovani, D., Léhr, J. M., & European PEI Multidisciplinary Group. (2024). European guidelines for the diagnosis and treatment of pancreatic exocrine insufficiency: UKG, EPC, EDS, ESPEN, ESPGHAN, ESDO, and ESPCG evidence-based recommendations. *United European Gastroenterology Journal*, 13(1), 125-172. <https://doi.org/10.1002/ueg2.12674>

17, 18 Moore, J. V., Scoggins, C. R., Phillips, P., Egger, M. E., & Martin, R. C. G. (2024). Optimization of exocrine pancreatic insufficiency in pancreatic adenocarcinoma patients. *Nutrients*, 16(20), 3499. <https://doi.org/10.3390/nu16203499>

19 Ghadef, A. O., & Azer, S. A. (2023). Pancreatic insufficiency. In StatPearls. StatPearls Publishing. <http://www.ncbi.nlm.nih.gov/books/NBK555926/>

20 Sohal, D. P. S., Kennedy, E. B., Cinar, P., Conroy, T., Copur, M. S., Crane, C. H., Garrido-Laguna, I., Lau, M. W., Johnson, T., Krishnamurthi, S., Moravek, C., O'Reilly, E. M., Philip, P. A., Pant, S., Shah, M. A., Sahai, V., Uronis, H. E., Zaidi, N., & Laheru, D. (2020). Metastatic pancreatic cancer: ASCO guideline update. *Journal of Clinical Oncology*, 38(27), 3217-3230. <https://doi.org/10.1200/JCO.20.01364>



PERT Dosing & Management: Recommendations from the Expert Working Group

1. Starting Dose

- Minimum starting dose in this patient population should be **48,000–72,000 units of lipase per meal, and 24,000–36,000 units for snacks²¹**.
- Prescribe the **highest appropriate strength to reduce pill burden²² and minimize cost²³**.
- While traditional prescribing references body weight or dietary fat intake, the Expert Working Group consensus suggests **prioritizing clinical judgment for patient-centered dosing, noting that weight-based dosing formulas can lead to inadequate enzyme replacement in high-risk patients with minimal symptoms but severe malabsorption, in an oncologic population.**

2. Appropriate Utilization

- Timing matters: Patients should **take PERT with the first bite of food or sip of drinks²⁴**.
- Reinforce that **low-fat diets are not a substitute**; they can worsen malnutrition²⁵. PERT may help patients resume normal, nutritionally complete diets²⁶.

3. Management & Follow-Up

- Clinical response has been proven within 5–8 days²⁷.
- **Routinely monitor need for dose adjustments, especially within the first 1–2 weeks after initiating therapy and with the onset of any new or worsening symptoms²⁸**.
- If symptoms persist²⁹:
 - Consider adding a proton pump inhibitor (PPI) to reduce gastric acid.
 - Increase the enzyme dose as needed; higher doses are often required.
- **All PERTs carry warnings and precautions regarding fibrosing colonopathy, irritation of the oral mucosa, hyperuricemia, risk of viral transmission, and hypersensitivity reactions. Please see the prescribing information for adverse events specific to each PERT.**
- In patients who have undergone surgery in particular, it is important to adjust the dose based on the surgical procedure and how it alters pancreatic anatomy, as well as residual pancreatic function and dietary fat intake³⁰.

The Importance of Patient Education for PERT Usage, Management, and Adherence: Recommendations from the Expert Working Group

Patient education is essential for maximizing the effectiveness of PERT³¹. Empowering patients with clear, actionable information improves adherence, supports symptom management, and helps them understand when and how to adjust dosing in partnership with their care team.

Key Patient Education Points³²:

- Teach the mechanism of action: PERT contains lipases, proteases, and amylases that mimic natural digestive enzymes, breaking down fats, proteins, and starches in the small intestine. Understanding the mechanism of action helps patients grasp why dosing must be adjusted for different foods, symptoms, or depending on the impact of their specific cancer treatment.
- Encourage two-way communication: Emphasize the importance of reporting symptoms or ongoing issues to their healthcare provider so dosing can be adjusted.
- Address adherence barriers: Discuss strategies to manage common challenges like high pill burden or difficulty swallowing, including alternatives when appropriate.
- Clarify administration timing: Reinforce taking PERT with the first bite of food or sip of drink for optimal efficacy.

Please refer to the full prescribing information for specific information on each PERT.

A Call to Action from the Expert Working Group

Patients can't wait for perfect data: they need high-value care now. By standardizing practices based on the best available evidence, health care providers can reduce variability, improve patient outcomes, and address the long-standing gap in EPI management in pancreatic oncology care. This isn't about overhauling everything; it's about small, strategic steps. Implementing one recommendation and watching what happens. Sharing what we learn and building from there. This is how we move from ideas to impact, and how transformation happens in care delivery.

21 National Comprehensive Cancer Network. (2025). NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®): NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Pancreatic Adenocarcinoma (Version 2.2025). Retrieved from NCCN.org.

22 Imrie, C. W., Connell, G., Hall, R. I., & Charney, R. M. (2010). Review article: Enzyme supplementation in cystic fibrosis, chronic pancreatitis, pancreatic and periampullary cancer. *Alimentary Pharmacology & Therapeutics*, 32(1), 1–25. <https://doi.org/10.1111/j.1365-2036.2010.04437.x>

23 Gupta, A., Premnath, N., Beg, M. S., Khara, R., & Dussetina, S. (2021). Projected 30-day out-of-pocket and total spending on pancreatic enzyme replacement therapy under medicare part D. *Journal of Clinical Oncology*, 39(3_suppl), 401–401. https://doi.org/10.1200/JCO.2021.39.3_suppl.401

24 Whitcomb, D. C., et al. (2020). Chronic Pancreatitis: An Update. *The American Journal of Gastroenterology*, 115(3), 322–339. <https://doi.org/10.14309/ajg.0000000000000526>

25 Dominguez-Munoz, J. E., Drewes, A. M., Lindkvist, B., Ewald, N., Czako, L., Rosendahl, J., Lohr, J. M., & HaPanEU/UEG Working Group. (2018). Recommendations from the United European Gastroenterology evidence-based guidelines for the diagnosis and therapy of chronic pancreatitis. *Pancreatology: official journal of the International Association of Pancreatology (IAP) ... [et al.]*, 18(8), 847–854. <https://doi.org/10.1016/j.pan.2018.09.016>

26 Dominguez-Munoz, J. E. (2011). Pancreatic enzyme therapy for pancreatic exocrine insufficiency. *Gastroenterology & hepatology*, 7(6), 401–403.

27 Trapnell, B. C., McGuinness, K., Graff, G. R., Boyd, D., Beckmann, K., Caras, S. Efficacy and safety of Creon 24,000 in subjects with exocrine pancreatic insufficiency due to cystic fibrosis. *J. Cyst. Fibros* 2009, 8, 370–377. [CrossRef]

28 Lohr, J. M., Dominguez-Munoz, E., Rosendahl, J., Besselink, M., Mayerle, J., Lerch, M. M., Haas, S., Akisik, F., Kartalis, N., Iglesias-Garcia, J., Keller, J., Boermeester, M., Werner, J., Dumonceau, J., Fockens, P., Drewes, A., Ceyhan, G., Lindkvist, B., Drenth, J., ... HaPanEU/UEG Working Group. (2017). United European Gastroenterology evidence-based guidelines for the diagnosis and therapy of chronic pancreatitis (HaPanEU). *United European Gastroenterology Journal*, 5(2), 153–199. <https://doi.org/10.1177/205064016684695>

29 Garcia, M. A. G., Imam, S., Braun, U. K., Jackson, L. K. Rational Prescribing of Pancreatic Enzymes for Patients with Pancreatic Cancer. *Pharmacy* 2024, 12, 47. <https://doi.org/10.3390/pharmacy2020047>

30 Silken, E. C. M., Cahen, D. L., Van Eijck, C., Kuipers, E. J., & Bruno, M. J. (2012). The daily practice of pancreatic enzyme replacement therapy after pancreatic surgery: A northern European survey. *Journal of Gastrointestinal Surgery*, 16(8), 1487–1492. <https://doi.org/10.1007/s11805-012-1927-1>

31, 32 Barkin, J. A., Harb, D., Kort, J., & Barkin, J. S. (2024). Real-world patient experience with pancreatic enzyme replacement therapy in the treatment of exocrine pancreatic insufficiency. *Pancreas*, 53(1), e16–e21. <https://doi.org/10.1097/MPA.0000000000002273>