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Review

Fecal elastase test in diagnosing exocrine pancreatic insufficiency: The web of science and scopus bibliometric analysis (1984–2024)

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Abstract. *Background:* Exocrine pancreatic insufficiency (EPI) is a condition characterized by impaired nutrient digestion due to insufficient enzyme secretion, leading to steatorrhea and weight loss. Fecal elastase (FE) is a reliable non-invasive biomarker for diagnosing EPI and detecting enzymatic dysfunction. *Aims and Methods:* This study provides a bibliometric analysis of the role for the diagnosis of FE, using Scopus and Web of Science databases (1984–2024). Data merging, statistical analyses, and visualizations were conducted using RStudio and the Bibliometrix R package. *Results:* A total of 385 publications from 188 sources were analyzed. The peak year was 2022 with 38 publications, followed by a decline to 17 in 2023. The United States leads with 136 publications and international cooperation with 26 joint projects, especially with Poland, Italy and the UK. Germany showed the highest scientific citations impact (2,024). The most prolific institutions were Haukeland University Hospital in Norway and Poznan University of Medical Sciences in Poland. The Pancreatology journal stand out as one of the leading scientific publications on EPI. *Conclusions:* Overall, this analysis provides a comprehensive overview of the research landscape, identifies critical areas for future investigation, and emphasizes the need to strengthen interdisciplinary collaboration to drive global advancements in the diagnosis of EPI. (www.actabiomedica.it)

Key words: exocrine pancreatic insufficiency, fecal elastase, pancreatic function marker, pancreatic insufficiencies, pancreatic enzyme activity

Introduction

Exocrine pancreatic insufficiency (EPI) is defined by the inadequate digestion of both macronutrients and micronutrients due to insufficient delivery of pancreatic exocrine enzymes into the duodenum (1), causing pancreatic steatorrhea, weight loss, and a potential decline in quality of life (2,3). EPI develops as a result of various diseases, including chronic pancreatitis, in which insufficiency occurs in 30–90% of patients (4); cystic fibrosis, affecting 85% of patients (5); and pancreatic cancer, particularly after surgical interventions, impacting 80–90% of patients (6). Additionally, EPI may occur after surgical procedures on the digestive system in 20–50% of cases (7). Additionally, some sources suggest that other conditions, such as diabetes mellitus, celiac disease, inflammatory bowel disease, diseases of iron overload (haemochromatosis and β-thalassemia) (8) and human immunodeficiency virus (HIV)/acquired immunodeficiency syndrome (AIDS), as well as genetic and congenital pathologies, may also be associated with the development of EPI (9). Over the past decades, many tests have been developed to assess EPI, which are divided into direct and

indirect methods of measuring the exocrine function of this organ (10). Direct tests, which involve obtaining pancreatic secretions through duodenal intubation after stimulation of the pancreas with exogenous hormones or intestinal nutrients, are considered the most accurate method for assessing pancreatic function. However, they are expensive, invasive, and technically challenging, which significantly limits their practical application in clinical settings (11). The gold standard for diagnosing fat malabsorption involves a 72-hour stool collection during a 100 g fat-per-day diet, with malabsorption confirmed at >7 g of fat excreted per day and severe steatorrhea defined as ≥15 g per day (12). The 72-hour stool collection method for assessing steatorrhea has several drawbacks, including inconvenience for the patient, the need for strict adherence to a high-fat diet, and challenges associated with the prolonged storage and transportation of samples (13). One of the widely recognized clinical biomarkers for diagnosing exocrine pancreatic function is serum immunoreactive trypsinogen levels (14). Serum trypsinogen levels are used for the neonatal screening of cystic fibrosis and meconium ileus. While the test is particularly useful in pediatrics, its application in adults is limited, because amylase and lipase are currently considered the preferred biomarkers (15, 16). The 13C-mixed triglyceride breath test (13C-MTG) evaluates fat digestion by pancreatic lipase through the recovery rate of 13CO2 over a 6-hour period, after consuming a meal containing 250 mg of 13C-MTG, making it a valuable tool for diagnosing EPI (17). Studies have shown that the 13C-MTG breath test demonstrates a sensitivity of 90-100% and a specificity of 90-92% when compared to endoscopic secretin studies and 72-hour fecal fat measurements (18). A notable advantage of this method is its applicability for evaluating treatment response (19). Scientists aimed to simplify the test procedure; however, reducing the CO2 measurement time to less than 4 hours results in lower specificity, although the sensitivity of the test remains high (20). The test may also yield false-positive results in patients with non-pancreatic steatorrhea, such as in severe diseases of the duodenal mucosa, while its main drawbacks remain its high cost and longer duration compared to FE levels (21). Updated clinical guidelines designate the fecal elastase (FE) test as the preferred diagnostic modality for assessing PEI (22). The FE measures elastase-1, a pancreatic enzyme that binds bile salts and resists degradation as it passes through the gastrointestinal tract (23). FE levels above 200 μg/g in stool suggest normal exocrine pancreatic function, while concentrations between 100 and 200 μg/g indicate mild to moderate PEI, and levels below 100 μg/g reflect severe PEI (24). FE stands out among other indirect tests for its simplicity, non-invasiveness, and stability of results even with sample storage (21,25). Unlike the 72-hour fecal fat test, which is labor-intensive and inconvenient, FE requires only a single random sample (26). Compared to serum trypsinogen, which is less sensitive in early dysfunction, FE provides more reliable results in moderate and severe insufficiency, additionally, FE is unaffected by enzyme supplementation, making it the preferred choice for routine assessment of exocrine pancreatic function, though it may be less sensitive in detecting mild insufficiency (27). One of the main advantages of this test is its use of ELISA with specific monoclonal antibodies against human elastase-1, making it relatively inexpensive, accessible, and convenient, as it requires less than 1 gram of stool (28). Despite drawbacks such as relatively low sensitivity in detecting mild PEI and the requirement for solid stool samples for analysis, FE has proven to be a reliable diagnostic tool for PEI (29). Based on the presented data, FE test represents a potentially useful and valuable tool for diagnosing and long-term monitoring of exocrine pancreatic function. After conducting an extensive review of FE, we became interested in its application in EPI due to its sensitivity, accessibility and non-invasiveness. Therefore, this formed the basis for conducting our bibliometric analysis. This comprehensive approach helps pinpoint evolving trends and key aspects of the disease (30,32). The method uses quantitative approaches to evaluate the influence and development of academic publications, providing valuable insights into emerging trends, significant studies, and prominent contributors within a particular field of research (33). The database documented only one previous bibliometric analysis on EPI (34). This made us interested in prospectively examining research in this area, as the difficulties in diagnosing EPI and its serious impact on patients' quality of life highlight the need for a more in-depth and

comprehensive study of this condition. Moreover, despite the growing number of publications in this area, no specifically focused bibliometric analysis of the role of the FE in EPI is available in the databases. Therefore, our study was performed for a better analysis of FE as a reliable and non-invasive test for diagnosing EPI, and to document the research field's development process over the years.

Methods

Search strategy

This bibliometric analysis investigates the use of FE as a marker for EPI, based on data from the Scopus and Web of Science databases spanning 1968 to 2024, collected in September 2024. Inclusion criteria were strictly limited to original research and review articles published in English that directly addressed FE in the context of diagnosing EPI. Publications of other types, as well as studies conducted on animal models, were excluded. To standardize the search, specific keywords such as "fecal elastase" and "exocrine pancreatic insufficiency, were included. To enhance search precision, Boolean operators were applied, along with Medical Subject Headings (MeSH) terms (https://www.nlm.nih.gov/mesh/meshhome.html), which enabled the construction of a precise search formula and ensured the maximum relevance of the results (Table 1). After removing duplicate, we exported publications from Web of Science and BibTeX from Scopus, and thereafter we processed and saved in RStudio for xlsx final format analysis (Figure 1).

Study selection and data extraction

The selection of articles was conducted in two stages based on the inclusion criteria. Initially, two authors (B.T. and M.M.) independently reviewed the titles and abstracts of the articles retrieved through the search strategy. Articles that received approval from both authors proceeded to full-text analysis. If there was any disagreement, the final decision was made after consultation with a third author (Y.B.).

Performance analysis

For analysis and visualization, we utilized Bibliometrix R (http://www.bibliometrix.org) in RStudio v.4.3.2 (Posit Software, PBC, Boston, Massachusetts, USA), Biblioshiny, and Flourish.studio (https://flourish.studio/).

Results

Summary of published scientific articles

The study analyzed a total of 385 documents from 188 sources, spanning the period from 1984 to 2024. The documents demonstrate a steady Annual Growth Rate of 5.5%, reflecting sustained interest and relevance, with an average document age of 10.7 years. Contributions from 2,138 authors were included in

Table 1. Search strategy and key queries

Code	Queries
#1	"Exocrine Pancreatic Insufficiencies" OR "Insufficiencies, Exocrine Pancreatic" OR "Insufficiency, Exocrine Pancreatic" OR "Pancreatic Insufficiencies, Exocrine" OR "Pancreatic Insufficiency, Exocrine" OR "Pancreatic Insufficiency" OR "Insufficiencies, Pancreatic" OR "Insufficiency, Pancreatic" OR "Pancreatic Insufficiencies"
#2	"Fecal elastase test" OR "Elastase-1" OR "Pancreatic elastase" OR "Stool elastase" OR "Fecal pancreatic elastase" OR "Exocrine pancreatic function test" OR "Fecal elastase-1 level" OR "Pancreatic enzyme activity" OR "Elastase deficiency" OR "Exocrine pancreatic insufficiency (EPI) marker" OR "Stool pancreatic elastase" OR "Elastase enzyme activity in stool" OR "Pancreatic function marker" OR "Digestive enzyme testing" OR "Chronic pancreatitis marker" OR "Malabsorption diagnosis"
#3	#1 AND #2

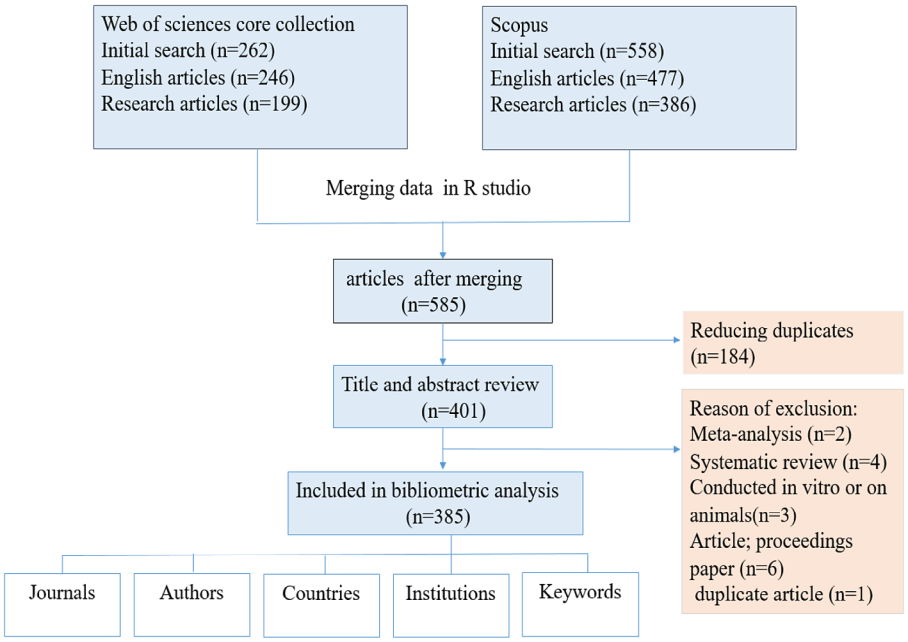

Figure 1. Search process

the analysis, achieving an average of 23.53 citations per document over the past decade. Approximately 8% of these authors participated in collaborative research efforts.

Annual analysis of publications and citations

Until 1995, research on the role of FE in EPI was scarce, with some years showing no publications at all. Since 1996, interest in this topic has grown, leading to a steady increase in the number of studies. The peak was observed in 2022, when 38 publications were released. However, in 2023, the number of publications declined to 17, indicating a possible shift in research focus or priorities. Citation analysis reveals that 1996 had the highest average number of citations per article (186), suggesting a strong scientific impact of publications from that period. In contrast, earlier years, such as 1987, showed significantly lower citation rates (11 per article). Over the past few years (2020–2023), citation activity has remained relatively stable, reflecting continued relevance of the topic in scientific literature (Figure 2).

Countries and affiliations

As shown in Figure 3a, the United States stands out as the country with the highest number of published articles — 136 publications during the study period. Germany ranked second, contributing 91 publications on EPI and the role of FE in its diagnosis. The USA also showed significant activity in international cooperation with 26 joint projects, especially with Poland, Italy and the UK. In addition, Germany and the UK follow with 23 and 18 collaborations respectively, highlighting their significant role in the global partnership (Figure 3b). It is worth noting that the above-mentioned countries are also leaders among the most cited countries. Germany holds the leading position with a total of 2,024 citations, underscoring the substantial scientific impact of its publications. The United States follows with 983 citations, while Italy ranks third with 856 citations. Belgium stands out for achieving the highest average citation rate, with 59 citations per publication annually. These statistics underscore the substantial contributions of these countries to advancing knowledge in the diagnosis of EPI (Table 2).

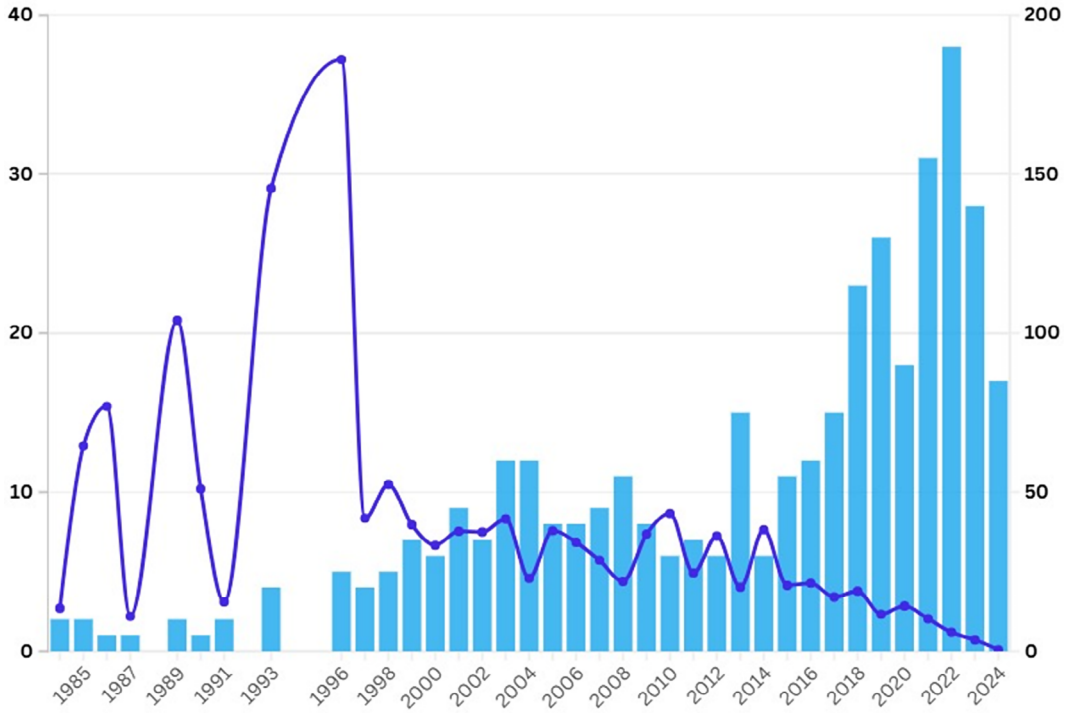

Figure 2. Annual publication and citation trends over time (1984–2024)

Haukeland University Hospital in Norway leads with 25 publications, highlighting its significant contribution to research. Norway demonstrates a strong presence, as the University of Bergen also ranks among the top institutions with 21 publications, confirming the country's prominent role in the field. Poland holds the second position through the Poznan University of Medical Sciences, also with 21 publications. Italy, Germany, and Denmark are well-represented, with the University of Verona contributing 16 publications, while University Medicine Greifswald and Justus Liebig University Giessen in Germany contribute 13 and 11 publications, respectively (Table 3).

The number off publications and citations by different authors

Author Pezzili R demonstrated long-term publication activity from 1997 to 2020, with a significant citation impact, reaching 102 citations in 1999. Similarly, author Walkowiak Jaroslaw exhibited sustained citation influence over an extended period, spanning from 1999 to 2020. In 2002, Walkowiak J. collaborated with author Herzig Karl-Heinz Heinz and their joint work became the most cited article of that period, receiving 73 citations. Author Herzig also demonstrated consistent productivity, maintaining her publication activity from 1999 to 2011. Author Frulloni began his work in 2010 and stood out among other authors for the largest number of citations – 149 (Figure 4). The top three cited authors are Walkowiak J from Poznan University of Medical Sciences in Poland with 19 articles and an H-index of 39, Herzig K from Oulun Yliopisto in Finland with 13 articles and an H-index of 61, and Pezzilli R from the Department of Gastroenterology at Polyclinic of Sant' Orsola in Italy with 10 articles and an H-index of 50. A complete list of the most relevant cited authors is represented in Figure 4 and Table 4.

Journal publications

We identified 12 major journals as the most relevant for researchers in this field, aligning with

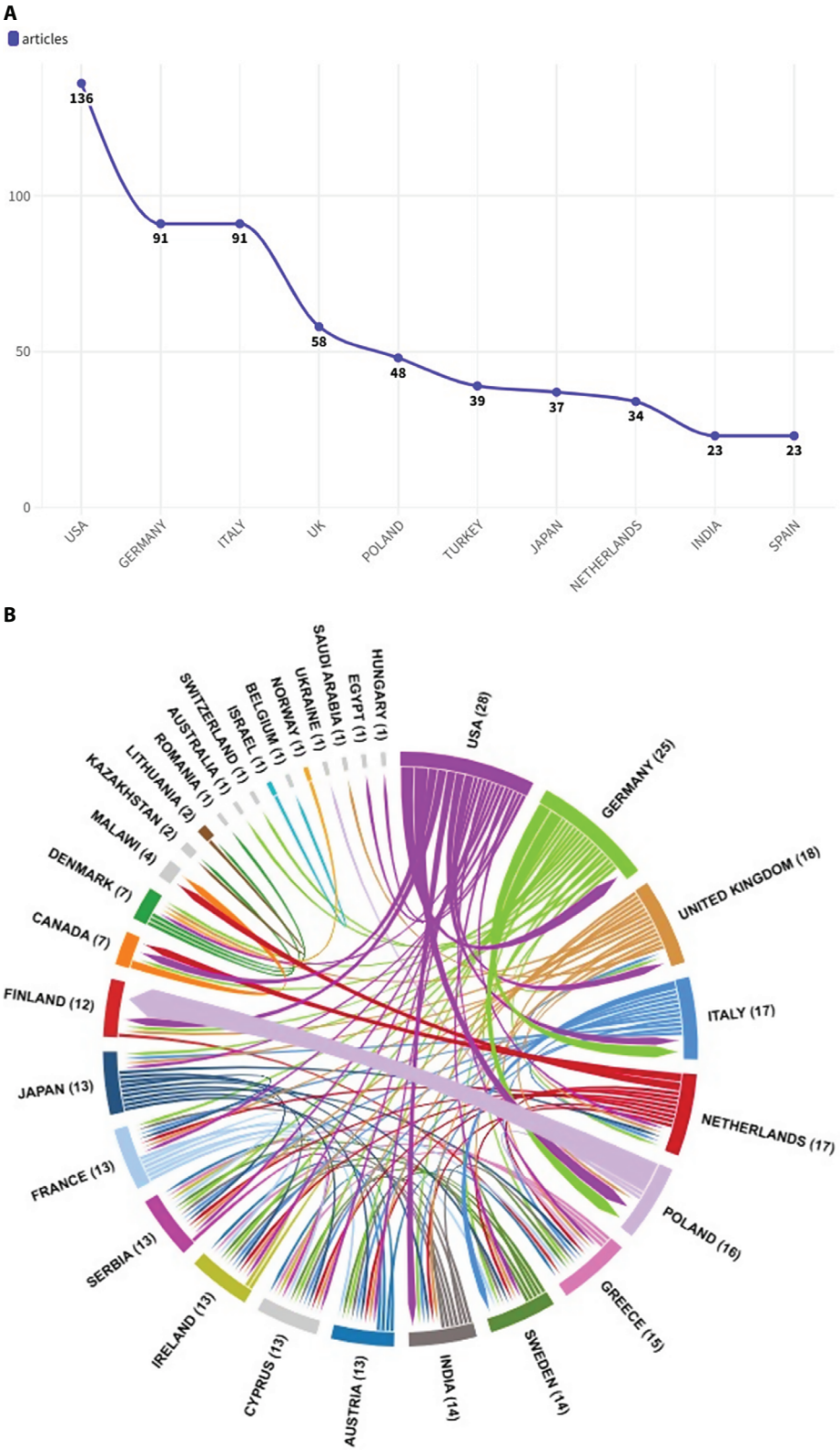

Figure 3. Top 10 countries with the highest number of articles and the collaboration network.

Table 2. Most cited countries

Rank	Country	Total citations	Average article citations
1	Germany	2024	46,00
2	USA	983	19,70
3	Italy	856	32,90
4	United Kingdom	635	19,80
5	Poland	411	20,60
6	Netherlands	357	25,50
7	Belgium	297	59,40
8	China	251	20,90
9	Korea	235	26,10
10	Japan	214	15,30

Table 3. Most relevant affiliations

Rank	Affiliation	Articles	Country
1	Haukeland University Hospital	25	Norway
2	Poznan University of Medical Sciences	21	Poland
3	University of Bergen	21	Norway
4	University of Verona	16	Italy
5	University Medicine Greifswald	13	Germany
6	Shinshu University	12	Japan
7	University of Sheffield	12	England
8	Aalborg University Hospital	11	Denmark
9	Justus Liebig University Giessen	11	Germany
10	Aalborg University	10	Denmark

Bradford's law, which states that a small number of core journals produce the majority of articles in a given discipline (35). These journals, all highly peer-reviewed, are located in zone 1, demonstrating their significance as key sources and their concentration at the forefront of the field (Figure 5). The top three journals contributing to research in this field are *Pancreatology*, which leads with 26 articles focused on EPI and FE, followed by *Pancreas* and the *Journal of Pediatric Gastroenterology and Nutrition*, each publishing over 20 articles. These journals demonstrate significant influence and interest in advancing knowledge within this domain. It is noteworthy that 70% of all the journals rank in the top quartile (Q1) in the Science Citation Index Expanded (SCIE) (Figure 5 and Table 5).

Most relevant documents and trend topics.

The author keyword "exocrine pancreatic insufficiency" is the most commonly utilized term in the studied field, appearing 278 times, with its highest frequency recorded in 2021. The keywords "pancreatic elastase" and "pancreas" were used 227 and 101 times, respectively, with their highest frequency in 2019. Interestingly, "chronic pancreatitis" and "cystic fibrosis" have consistently shown high frequency, highlighting their significant role as primary causes of EPI and their importance within the research context. The term "diabetes mellitus" has gained increasing interest, with notable peaks in usage around 2017. These terms have become more prominent due to their association with EPI and the diagnostic significance of FE, emphasizing the relationship between the endocrine and exocrine functions of the pancreas. Additional information on keyword trends is presented in the Table 6.

The thematic map demonstrates key research directions, for example, base themes such as "pancreatic insufficiency", "chronic pancreatitis" and "fecal elastase" occupy a central position, reflecting their importance in the field. Niche themes like "exocrine insufficiency" and "pancreas" are well-developed but less widely utilized. Special attention is drawn to "exocrine insufficiency", "cystic fibrosis" and "fecal elastase-1" which are relevant and promising areas for further research (Figure 6).

The ten most frequently cited papers demonstrate a growing focus on the utility of FE as a sensitive and specific biomarker. These studies also explore its limitations and its associations with conditions such as chronic pancreatitis and diabetes mellitus. For example, the study of Lankisch et al. (36) is devoted to the study of the course of chronic pancreatitis with an emphasis on three key manifestations: pain, exocrine and endocrine pancreatic insufficiency. The outcomes of the disease were assessed, as well as its impact on the functional state of the pancreas, including exocrine and endocrine functions. The results of Löser et al. (37) highlighted the importance of FE in the diagnosis of EPI and concluded that this method is highly sensitive, specific and practical. Another study assessed the diagnostic value of FE in the diagnosis of EPI, emphasizing its key advantage - the independence of results from enzyme replacement therapy, which makes this test a reliable, non-invasive and convenient method for clinical practice (38) (Table 7).

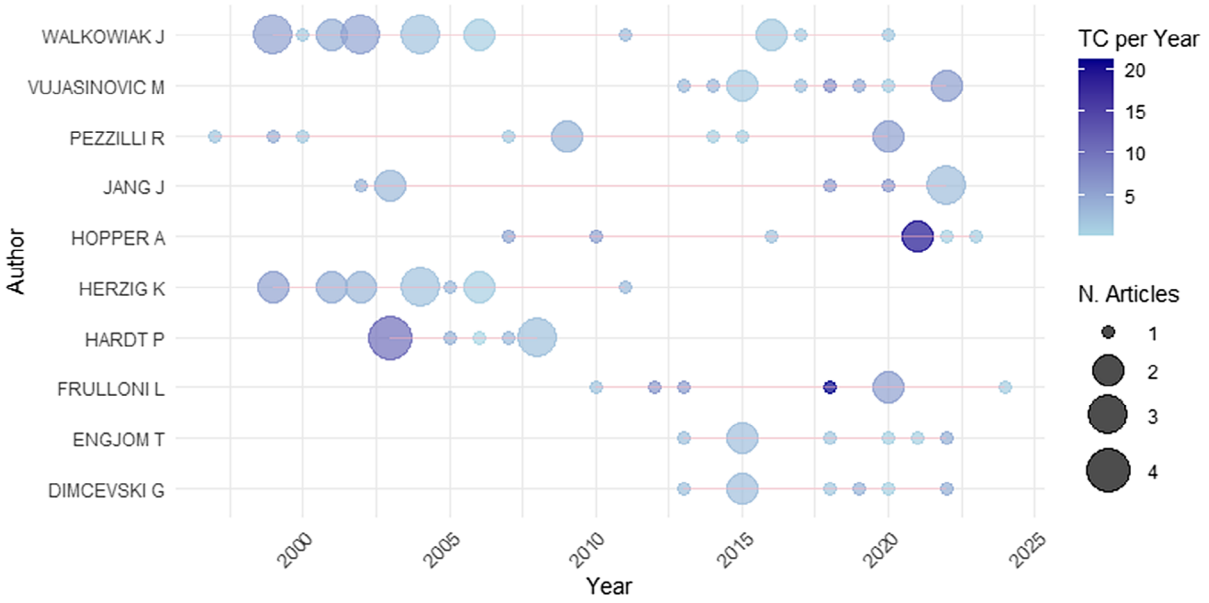

Figure 4. Authors' production over time

Table 4. Most relevant cited authors

Rank	Authors	Articles	H-index	Affiliation
1	Walkowiak, Jaroslaw	19	39	Poznan University of Medical Sciences, Poznan, Poland
2	Herzig, Karl-Heinz Heinz	13	61	Oulun Yliopisto, Finland
3	Pezzilli, Raffaele	10	50	Department of Gastroenterology, Polyclinic of sant'Orsola, Bologna, Italy
4	Hardt, Philip D.	10	27	Third Medical Department and Policlinic, Giessen University Hospital, Germany
5	Vujasinovic, Miroslav	10	23	Department for Digestive Diseases, Karolinska University Hospital, Stockholm, Sweden
6	Jang, Jin-Young	8	54	Department of Surgery, Seoul National University College of Medicine, Seoul, South Korea
7	Hopper, Andrew D	7	25	Department of Gastroenterology, Sheffield Teaching Hospitals NHS Foundation Trust, Sheffield, United Kingdom
8	Frulloni, Luca	7	61	Department of Medicine, University of Verona, Verona, Italy
9	Dimcevski, Georg	7	31	Department of Clinical Medicine, University of Bergen, Bergen, Norway
10	Engjom, Trond	7	14	Department of Medicine, Haukeland University Hospital, Bergen, Norway

Discussion

This bibliometric analysis uncovers significant insights into the research landscape of FE as a diagnostic tool for EPI. While the results reflect notable advancements, they also point out need for further areas of exploration and development. The steady increase in annual publications reflects the growing recognition of the clinical importance of EPI, particularly in diseases such as chronic pancreatitis, cystic fibrosis, and diabetes mellitus. The surge beginning in 1996 corresponds to the introduction of FE

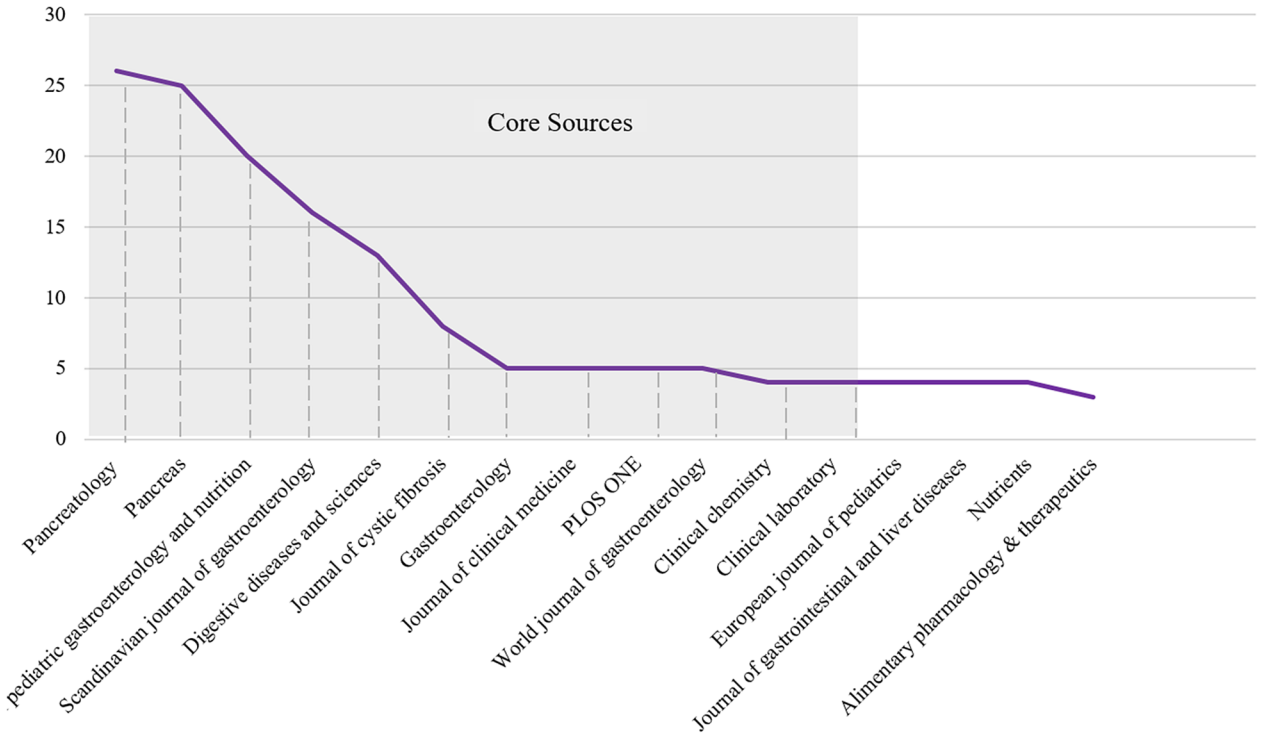

Figure 5. Core sources by Bradford's law

Table 5. Most relevant sources

Rank	Sources name	Articles	CiteScore 2023	IF	JCR category (quartile)
1	Pancreatology	26	7,2	2,8	Medicine: Endocrinology, Diabetes and Metabolism (Q2)
2	Pancreas	25	4,7	1,7	Medicine: Internal Medicine (Q2)
3	Journal of Pediatric Gastroenterology and Nutrition	20	5,3	3,8	Medicine: Pediatrics, Perinatology and Child Health (Q1)
4	Scandinavian Journal of Gastroenterology	14	5,3	2,4	Medicine: Pediatrics, Perinatology and Child Health (Q3)
5	Digestive Diseases and Sciences	10	6,4	2,5	Medicine: Gastroenterology (Q1)
6	Journal of Cystic Fibrosis	8	10,1	4,8	Medicine: Pediatrics, Perinatology and Child Health (Q1)
7	Journal of Clinical Medicine	5	5,7	3,0	Medicine: General Medicine (Q1)
8	PLOS ONE	5	6,2	2,9	Multidisciplinary (Q1)
9	World Journal of Gastroenterology	5	7,8	4,3	Medicine: Gastroenterology (Q1)
10	Clinical Chemistry	4	11,3	7,1	Medicine: General Medicine (Q1)

as a non-invasive biomarker. This innovation significantly lowered the barriers to EPI diagnosis, fostering broader research interest and clinical application. However, the recent decline in publication activity may indicate saturation in certain research areas or challenges in identifying novel approaches. This emphasizes the need for innovative studies exploring the limitations of FE testing, particularly in detecting

mild EPI or differentiating it from other conditions with similar presentations (46).

The concentration of research in high-income countries, such as the USA, Germany, and Italy, underscores the critical role of resources and infrastructure in advancing diagnostic methodologies. Countries with limited research outputs may lack access to advanced diagnostic technologies or funding for longitudinal studies (47). This geographic disparity creates a gap in understanding EPI's prevalence and management in low- and middle-income settings, where the burden of pancreatic diseases may be significant. Enhanced global collaborations could address this imbalance, as seen in successful partnerships between the USA, Poland, and Italy. The work of authors such as Walkowiak et al. (48) has played an important role in studying the diagnostic value of FE, contributing to its widespread use. For example, Herzig's collaborative studies advanced understanding of fecal elastase's robustness compared to other biomarkers, reinforcing its role in non-invasive diagnostics (48,49). However, the observed focus on well-resourced settings raises questions about the generalizability of

Table 6. Trend topics

Term	Frequency	Year (Median)
exocrine pancreatic insufficiency	278	2021
pancreatic elastase	227	2019
pancreas	101	2019
cystic fibrosis	84	2021
diabetes mellitus	79	2017
chronic pancreatitis	76	2015
elastase	71	2015
pancreatitis	68	2009
pancreas function	61	2011
steatorrhea	54	2012

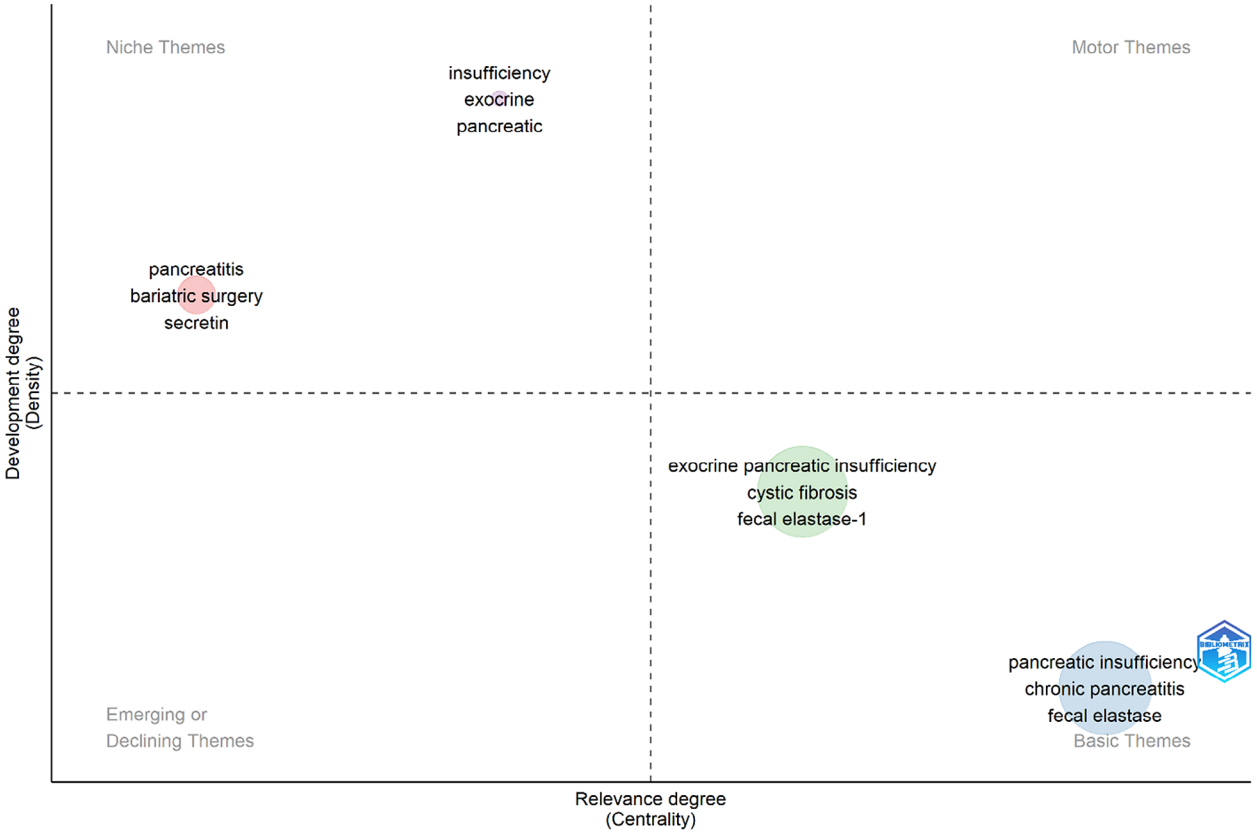

Figure 6. The thematic map of keyword research in articles reviews: thematic significance and recurring terms in the field of study

Table 7. The 10 most frequently cited high-quality papers focusing on EPI and the fecal elastase test

Rank	Article	1st author	TC	TC_Y	Y_P
1	Natural course in chronic pancreatitis. (36)	Lankisch, P	434	13,56	1993
2	Fecal elastase 1: a novel, highly sensitive, and specific tubeless pancreatic function test (37)	Löser, C	425	14,66	1996
3	Immunoreactive elastase I: clinical evaluation of a new noninvasive test of pancreatic function (38)	Stein, J	209	7,21	1996
4	Mixed triglyceride breath test: a noninvasive test of pancreatic lipase activity in the duodenum (39)	Vantrappen, G.	182	5,06	1989
5	Fecal elastase 1: not helpful in diagnosing chronic pancreatitis associated with mild to moderate exocrine pancreatic insufficiency (40)	Lankisch, P	152	5,63	1998
6	A position paper of the International Study Group on Pancreatic Surgery (ISGPS) (41)	Gianotti, L.	149	21,29	2018
7	High prevalence of exocrine pancreatic insufficiency in diabetes mellitus. (42)	Hardt, P	141	6,41	2003
8	Fecal elastase 1 determination in chronic pancreatitis (43)	Gullo, L	102	3,92	1999
9	Use of fecal elastase-1 to classify pancreatic status in patients with cystic fibrosis (44)	Borowitz, D	101	4,81	2004
10	Diabetes mellitus is association of diabetes mellitus with exocrine pancreatopathy: (45)	Mohapatra S	94	10,44	2016

these findings to diverse populations, underscoring the need for more inclusive studies. The role of journals in disseminating and shaping scientific knowledge is evident in this analysis. According to Bradford's Law, the majority of impactful articles are concentrated in a small core of journals (51). The analysis underscores that leading journals with high publication volumes and citation impacts, such as *Pancreatology*, *Pancreas* and the *Journal of Pediatric Gastroenterology and Nutrition*, play a pivotal role in advancing research on FE and its diagnostic significance in EPI. These journals, chosen by authors for their impact, quartile, and reputation, consistently provide platforms for high-quality studies (52), particularly emphasizing the role of FE in diagnosing EPI and its associations with chronic pancreatitis and cystic fibrosis. The high impact factors of journals like the Journal of Clinical Medicine and World Journal of Gastroenterology reflect their ability to reach broader audiences (53), further amplifying the importance of FE in clinical practice. The alignment of these journals with leading quartiles (Q1 and Q2) demonstrates their pivotal role in maintaining rigorous scientific standards. However, the predominance of English-language journals notable aspect a potential language bias, excluding valuable research from non-English-speaking regions (54). Thematic analysis reveals a shift in focus over time. While early studies concentrated on validating FE as a biomarker, recent research has increasingly linked EPI with metabolic disorders like type 2 diabetes mellitus (55). This shift reflects an evolving understanding of the pancreas's dual endocrine and exocrine functions. However, the causal pathways connecting diabetes and EPI remain underexplored. For example, is EPI in diabetes a consequence of metabolic changes, or do underlying genetic or structural factors that predispose individuals to both conditions? (56) Some authors attribute EPI to pancreatic tissue damage caused by chronic hyperglycemia and lipotoxicity (57), oxidative stress and inflammation (58), while others point the attention to primary structural changes such as fibrosis and steatosis that may precede the development of diabetes (59). Genetic studies have identified mutations in CFTR, PRSS1 and SPINK1 as key factors potentially linking the two conditions (60,61). While FE testing and enzyme replacement therapy show promise, their role

in improving metabolic status requires further investigation (62). The simplicity and non-invasiveness of FE testing make it the preferred choice for routine diagnostics (25). However, its limitations, such as reduced sensitivity for mild EPI and reliance on solid stool samples, hinder its universal applicability (63). These limitations necessitate a combined diagnostic approach, incorporating advanced methods like the 13C-mixed triglyceride breath test for more comprehensive assessments (28). Such multi-modal strategies could overcome the drawbacks of individual tests, ensuring accurate diagnosis across a spectrum of EPI severity. Several gaps identified in this analysis suggest directions for future research. Despite FE's established role, studies exploring its utility in specific subpopulations, such as pediatric patients or those with overlapping metabolic and pancreatic conditions, are scarce (64). Additionally, there is a need for comparative studies evaluating FE against emerging biomarkers to determine its relative efficacy (28). Addressing these gaps will not only advance the field but also pave the way for more personalized and effective diagnostic strategies in pancreatic diseases.

Conclusion

This bibliometric analysis highlights significant progress in the study of FE as a diagnostic tool for pancreatic insufficiency. The sustained interest, impactful publications, and active collaborations reflect the critical importance of this research. Future research should focus on global collaboration, interdisciplinary cooperation and resource sharing to reduce the influence of research opportunities between developed and emerging changes, ensuring more equitable knowledge and advances in the diagnosis of EPI. However, the recent plateau in publications emphasizes the need for renewed innovation, particularly in addressing its limitations, such as detecting mild EPI and distinguishing it from other conditions. Overall, this analysis provides a comprehensive overview of the research landscape, identifies critical areas for future investigation, and emphasizes the need to strengthen interdisciplinary collaboration to drive global advancements in the diagnosis of EPI.

Study Limitations: This study focused solely on English-language articles indexed in WoC and Scopus, which could have resulted in language and database biases. Furthermore, the focus on keywords in article titles might have excluded relevant studies, limiting the scope of the analysis. The article alone cannot replace other review methods (e.g., meta-analysis, or systematic review). Serving as merely the first step toward a more comprehensive analysis, bibliometric research is not the final goal of our study but rather a foundation for further, more detailed analytical approaches. At the next stages of the study, a systematic review is planned, involving a broader literature search with the inclusion of additional databases. This will provide a more complete and objective understanding of the research topic and open new directions for further scientific investigations.

Ethic Approval: We would like to inform you that ethical committee approval is not required for this study, as it is a bibliometric analysis. The research does not involve any studies with human participants or animals and therefore does not violate ethical principles for biomedical research.

Conflict of Interest: Each author declares that he has no commercial associations (e.g. consultancies, stock ownership, equity interest, patent/licensing arrangement etc.) that might pose a conflict of interest in connection with the submitted article.

Authors Contribution: conception: KhK, performance of work: MM, YB; interpretation or analysis of data: MM, YB,KK; preparation of the manuscript: RK,MM; revision for important intellectual content: KK,RK ; supervision: KhK. All authors read and approved the final manuscript.

References

1. Perbtani Y, Forsmark CE. Update on the diagnosis and management of exocrine pancreatic insufficiency. F1000Research. 2019;8: e2019.doi:10.12688/f1000research.20779.1
2. Pezzilli R, Morselli Labate AM, Ceciliato R, et al. Quality of life in patients with chronic pancreatitis. Dig Liver Dis. 2005;37(3):181-9. doi:10.1016/j.dld.2004.10.007
3. Fieker A, Philpott J, Armand M. Enzyme replacement therapy for pancreatic insufficiency: Present and future. Clin Exp Gastroenterol. 2011;4(1):4:55-73. doi:10.2147/CEG.S17634
4. Marra-Lopez Valenciano C, Bolado Concejo F, Marín Serrano E, et al. Prevalence of exocrine pancreatic insufficiency in patients with chronic pancreatitis without follow-up. PANCR-EVOL Study. Gastroenterol Hepatol. 2018;41(2):77-86. doi:10.1016/j.gastrohep. 2017.08.002
5. Ritivoiu ME, Drăgoi CM, Matei D, et al. Current and Future Therapeutic Approaches of Exocrine Pancreatic

Insufficiency in Children with Cystic Fibrosis in the Era of Personalized Medicine. Pharmaceutics. 2023;15(1):162. doi:10.3390/pharmaceutics15010162
6. Gore J, Romo KG, Peeples J, Noor AA, Uwaifo GI. Exocrine pancreatic insufficiency as a possible predictor of pancreatic cancer development. J Clin Oncol. 2024;42(3_suppl): 679. doi:10.1200/jco.2024.42.3_suppl.679
7. Moore JV., Tom S, Scoggins CR, Philips P, Egger ME, Martin RCG. Exocrine Pancreatic Insufficiency After Pancreatectomy for Malignancy: Systematic Review and Optimal Management Recommendations. J Gastrointest Surg. 2021;25(9):2317-27. doi:10.1007/ s11605-020-04883-1
8. Kimita W, Petrov MS. Iron metabolism and the exocrine pancreas. Clin Chim Acta. 2020;511:167-176. doi:10.1016 /j.cca.2020.10.013
9. Singh VK, Haupt ME, Geller DE, Hall JA, Diez PMQ. Less common etiologies of exocrine pancreatic insufficiency. World J Gastroenterol. 2017;23(39):7059-76. doi:10.3748/wjg . v23.i39.7059
10. Struyvenberg MR, Martin CR, Freedman SD. Practical guide to exocrine pancreatic insufficiency - Breaking the myths. BMC Med. 2017;15(1):29. doi:10.1186/s12916-017 -0783-y
11. Löhr JM, Dominguez-Munoz E, Rosendahl J, et al. United European Gastroenterology evidence-based guidelines for the diagnosis and therapy of chronic pancreatitis (HaPanEU). United Eur Gastroenterol J. 2017;5(2):153-99. doi:10.1177 /2050640616684695
12. Nakajima K, Oshida H, Muneyuki T, Kakei M. Pancrelipase: An evidence-based review of its use for treating pancreatic exocrine insufficiency. Core Evid. 2012;7:77-91. doi:10.2147 /CE.S26705
13. Korostensky M, Martin SR, Swain M, et al. Elimination of 72-Hour Quantitative Fecal Fat Testing by Restriction, Laboratory Consultation, and Evaluation of Specimen Weight and Fat Globules. J Appl Lab Med. 2018;3(3):357-65. doi:10.1373/jalm.2018.026229
14. Li X, Campbell-Thompson M, Wasserfall CH, et al. Serum trypsinogen levels in type 1 diabetes. Diabetes Care. 2017;40(4):577-82. doi:10.2337/dc16-1774
15. Pezzilli R, Talamini G, Gullo L. Behaviour of serum pancreatic enzymes in chronic pancreatitis. Dig Liver Dis. 2000;32(3):233-7. doi:10.1016/s1590-8658(00)80826-9
16. Coverstone AM, Ferkol TW. Early Diagnosis and Intervention in Cystic Fibrosis: Imagining the Unimaginable. Front Pediatr. 2021; 8:608821. doi:10.3389/fped.2020.608821
17. Siuka D, Kumer K, Stabuc B, Stubljar D, Drobne D, Jansa R. Abbreviated 13C-mixed triglyceride breath test for detection of pancreatic exocrine insufficiency performs equally as standard 5-hour test in patients after gastrectomy performed for gastric cancer. Radiol Oncol. 2022;56(3):390-7. doi:10.2478/raon-2022-0034
18. Keller J, Brückel S, Jahr C, Layer P. A modified 13C-mixed triglyceride breath test detects moderate pancreatic exocrine insufficiency. Pancreas. 201; 40:1201-5. doi:10.1097/ MPA .0b013e318220ad98
19. Domínguez-Muñoz JE, Iglesias-García J, Vilariño-Insua M, Iglesias-Rey M. 13C-Mixed Triglyceride Breath Test to Assess Oral Enzyme Substitution Therapy in Patients With Chronic Pancreatitis. Clin Gastroenterol Hepatol. 2007;5(4): 484-8. doi:10.1016/j. cgh.2007.01.004
20. Keller J, Meier V, Wolfram KU, Rosien U, Layer P. Sensitivity and specificity of an abbreviated 13C-mixed triglyceride breath test for measurement of pancreatic exocrine function. United Eur Gastroenterol J. 2014;2(4):288-94. doi:10.1177/2050640614542496
21. Shandro BM, Nagarajah R, Poullis A. Challenges in the management of pancreatic exocrine insufficiency. World J Gastrointest Pharmacol Ther. 2018;9(5):39-46. doi:10.4292 / wjgpt. v9.i5.39
22. Phillips ME, Hopper AD, Leeds JS, et al. Consensus for the management of pancreatic exocrine insufficiency: UK practical guidelines. BMJ Open Gastroenterol. 2021;8(1): e000643. doi:10.1136/bmjgast-2021-000643
23. Shobassy M, Husainat N, Tabash A, Patel K, El-Serag HB, Othman MO. Endoscopic Ultrasound Findings in Patients Diagnosed with Exocrine Pancreatic Insufficiency by Low Fecal Elastase-1. Gastroenterol Res Pract. 2019;2019: 5290642. doi:10.1155 /2019/5290642
24. Jalal M, Leeds JS, Ching HL, et al. Are we missing pancreatic exocrine insufficiency in 'at-risk' groups? Prospective assessment of the current practice and yield of faecal elastase testing in patients with diabetes mellitus, HIV and/or high alcohol intake. Clin Med J R Coll Physicians London. 2023; 23(6):588-93. doi:10.7861/clinmed.2023-0185
25. Domínguez-Muñoz JE, D. Hardt P, Lerch MM, Löhr MJ. Potential for Screening for Pancreatic Exocrine Insufficiency Using the Fecal Elastase-1 Test. Dig Dis Sci. 2017;62(5): 1119-30. doi:10.1007/s10620-017-4524-z
26. Gopi S, Singh N, Yegurla J, et al. Utility of Fecal Elastase-1 to diagnose severe exocrine insufficiency in chronic pancreatitis: Real world experience. Pancreatology. 2023;23(2):151-7. doi:10.1016/j.pan.2023.01.002
27. Lüth S, Teyssen S, Forssmann K, Kölbel C, Krummenauer F, Singer M V. Fecal elastase-1 determination: "Gold standard" of indirect pancreatic function tests? Scand J Gastroenterol. 2001;36(10):1092-9. doi:10.1080/003655201750422729
28. Vanga RR, Tansel A, Sidiq S, El-Serag HB, Othman MO. Diagnostic Performance of Measurement of Fecal Elastase-1 in Detection of Exocrine Pancreatic Insufficiency: Systematic Review and Meta-analysis. Clin Gastroenterol Hepatol. 2018;16(8):1220-8.e4. doi:10.1016/j.cgh.2018.01.027
29. Lindkvist B. Diagnosis and treatment of pancreatic exocrine insufficiency. World J Gastroenterol. 2013;19(42):7258-66. doi:10.3748/wjg.v19.i42.7258
30. Manoj Kumar L, George RJ, P.S A, et al. A Bibliometric Analysis of Study of Associations of Certain Genotypes with the Cardiovascular Form of Diabetic Neuropathy. Biomed Res Int. 2023;4(3):277-82. doi:10.1155/2024/6761451
31. Manoj Kumar L, George RJ, P.S A. Bibliometric Analysis for Medical Research. Indian J Psychol Med. 2023;45(3):277-82. doi:10.1177/02537176221103617

32. Bekenova NB, Vochshenkova TA, Ablakimova N, et al. Bibliometric analysis and systematic review of environmental, social, and governance disclosure papers: Current topics and recommendations for future research. Indian J Psychol Med. 2022;45(9):1-14. doi:10.1177/02537176221103617
33. Öztürk O, Kocaman R, Kanbach DK. How to design bibliometric research: an overview and a framework proposal. Rev Manag Sci. 2024;18(11):3333-61. doi:10.1007/s11846-024-00738-0
34. Chen G, Wang K, Sha Y, Wang D. Current status and prospect of pancreatic exocrine insufficiency (PEI): A bibliometric and visualized study. Asian J Surg. 2024;47(6):2818-9. doi:10.1016/j.asjsur.2024.02.081
35. Zhang R, Wang Y, Qiu J. Validation of Bradford's Law and Source Journal Characteristics of Papers Mentioned by Twitter: Library and Information Science as Example. Doc Inf Knowl. 2024;41(1):35-47. doi:10.13366/j.dik.2024.01.121
36. Lankisch PG, Löhr-Happe A, Otto J, Creutzfeldt W. Natural course in chronic pancreatitis: Pain, exocrine and endocrine pancreatic insufficiency and prognosis of the disease. Digestion. 1993;54(3):148-55. doi:10.1159/000201029
37. Löser C, Möllgaard A, Fölsch UR. Faecal elastase 1: A novel, highly sensitive, and specific tubeless pancreatic function test. Gut. 1996;39(4):580-6. doi:10.1136/gut.39.4.580
38. Stein J, Jung M, Sziegoleit A, Zeuzem S, Caspary WF, Lembcke B. Immunoreactive elastase I: Clinical evaluation of a new noninvasive test of pancreatic function. Clin Chem. 1996;42(2):222-6. doi:10.1093/clinchem/42.2.222
39. Vantrappen GR, Rutgeerts PJ, Ghoos YF, Hiele MI. Mixed triglyceride breath test: A noninvasive test of pancreatic lipase activity in the duodenum. Gastroenterology. 1989;96(4)1126-34. doi:10.1016/0016-5085(89)91632-6
40. Lankisch PG, Schmidt I, König H, et al. Faecal elastase 1: Not helpful in diagnosing chronic pancreatitis associated with mild to moderate exocrine pancreatic insufficiency. Gut. 1998;42(4):551-4. doi:10.1136/gut.42.4.551
41. Gianotti L, Besselink MG, Sandini M, et al. Nutritional support and therapy in pancreatic surgery: A position paper of the International Study Group on Pancreatic Surgery (ISGPS). Surg (United States). 2018;164(5):1035-48. doi:10.1016/j.surg.2018.05.040
42. Hardt PD, Hauenschild A, Nalop J, et al. High prevalence of exocrine pancreatic insufficiency in diabetes mellitus: A multicenter study screening fecal elastase 1 concentrations in 1,021 diabetic patients. Pancreatology. 2003;3(5):395-402. doi:10.1159/ 000073655
43. Gullo L, Ventrucci M, Tomassetti P, Migliori M, Pezzilli R. Fecal elastase 1 determination in chronic pancreatitis. Dig Dis Sci. 1999;44(1):210-3. doi:10.1023/A:1026691209094
44. Borowitz D, Baker SS, Duffy L, et al. Use of fecal elastase-1 to classify pancreatic status in patients with cystic fibrosis. J Pediatr. 2004;145(3):322-6. doi:10.1016/j.jpeds.2004.04.049
45. Mohapatra S, Majumder S, Smyrk TC, et al. Diabetes Mellitus is Associated with an Exocrine Pancreatopathy: Conclusions from a Review of Literature. Pancreas. 2016;45(8):1104-10. doi:10.1097/MPA.0000000000000609
46. Capurso G, Traini M, Piciucchi M, Signoretti M, Arcidiacono PG. Exocrine pancreatic insufficiency: Prevalence, diagnosis, and management. Clin Exp Gastroenterol. 2019;12:129-39. doi:10.2147/CEG.S168266
47. Kudabayeva K, Tleumagambetova B, Bazargaliyev Y, Kosmuratova R, Zhylkybekova A. Global Trends in LADA Type Diabetes Research: A Bibliometric Analysis of Publications from Web of Science and Scopus, 1994-2024. J Diabetes Res. 2024;2024:4960075. doi:10. 1155/ 2024/4960075
48. Walkowiak J, Herzig KH, Strzykała K, Przysławski J, Krawczyński M. The comparison of fecal elastase-1 and fecal chymotrypsin tests in the assessment of exocrine pancreatic function in cystic fibrosis patients. Pediatr Wspolczesna. 2002;4(3):351-5. ISSN: 15075532
49. Walkowiak J, Herzig KH, Strzykala K, Przyslawski J, Krawczynski M. Fecal elastase-1 is superior to fecal chymotrypsin in the assessment of pancreatic involvement in cystic fibrosis. Pediatrics. 2002;110(1 Pt 1):e7. doi:10.1542/peds.110.1.e7
50. Walkowiak J, Sands D, Nowakowska A, et al. Early decline of pancreatic function in cystic fibrosis patients with class 1 or 2 CFTR mutations. J Pediatr Gastroenterol Nutr. 2005;40(2):199-201. doi:10.1097/00005176-200502000-00022
51. Desai N, Veras L, Gosain A. Using Bradford's law of scattering to identify the core journals of pediatric surgery. J Surg Res. 2018;229:90-95. doi:10.1016/j.jss.2018.03.062
52. Heidenreich A, Eisemann N, Katalinic A, Hübner J. Study results from journals with a higher impact factor are closer to "truth": a meta-epidemiological study. Syst Rev. 2023;12(1):1-9. doi:10.1186/s13643-023-02167-8
53. Law R, Leung D. Journal impact factor: A valid symbol of journal quality? Tour Econ. 2020;26(5):734-42. doi:10.1177/1354816619845590
54. Barja-Ore J, Retamozo-Siancas Y, Fernandez-Giusti A, Guerrero ME, Munive-Degregori A, Mayta-Tovalino F. Trends, collaboration, and visibility of global scientific production on birth complications in pregnant women with tuberculosis: A scientometric study. Int J Mycobacteriology. 2023;12(2):111-6. doi:10.4103/ijmy.ijmy_25_23
55. Bhattamisra SK, Siang TC, Rong CY, et al. Type-3c Diabetes Mellitus, Diabetes of Exocrine Pancreas - An Update. Curr Diabetes Rev. 2019;15(5):382-94. doi:10.2174/1573399815666190115145702
56. Wei Q, Qi L, Lin H, et al. Pathological Mechanisms in Diabetes of the Exocrine Pancreas: What's Known and What's to Know. Front Physiol. 2020;11:570276. doi:10.3389/fphys.2020.570276
57. Mezza T, Cinti F, Giaccari A. Diabetes secondary to pancreatic diseases. Endocrinology (Switzerland).2020;02(August):1-17. doi:10.1007/978-3-030-36694-0_18
58. Zhang C, Xie M, Wang Y, Han T. Tussilagone inhibits inflammation and oxidative stress to alleviate acute pancreatitis. Signa Vitae. 2024;20(1):133-9. doi:10.22514/sv.2024.009

59. Antar SA, Ashour NA, Sharaky M, et al. Diabetes mellitus: Classification, mediators, and complications; A gate to identify potential targets for the development of new effective treatments. Biomed Pharmacother. 2023;168:115734. doi:10.1016/j.biopha.2023.115734
60. Ravi Kanth V. Genetics of acute and chronic pancreatitis: An update. World J Gastrointest Pathophysiol. 2014;5(4): 427-37. doi:10.4291/wjgp.v5.i4.427
61. Vue PM, McFann K, Narkewicz MR. Genetic Mutations in Pediatric Pancreatitis. Pancreas. 2016;45(7):992-6. doi:10.1097/MPA.0000000000000589
62. Moore HN, Chirco AR, Plescia T, et al. Exocrine pancreatic insufficiency after bariatric surgery: a bariatric surgery center of excellence experience. Surg Endosc. 2023;37(2):1466-75. doi:10.1007/s00464-022-09388-3
63. Radlinger B, Ramoser G, Kaser S. Exocrine Pancreatic Insufficiency in Type 1 and Type 2 Diabetes. Curr Diab Rep. 2020;20(6):18. doi:10.1007/s11892-020-01304-0
64. Zheng Y, Mostamand S. Nutrition in children with exocrine pancreatic insufficiency. Front Pediatr. 2023;11:943649. doi:10.3389/fped.2023.943649

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