

Abstract

Background: The use of digestive enzymes like pancrealipase and related compounds has not been well-characterized. There are both prescription medications and nonprescription supplements that contain a range of digestive enzymes, which may impact the gut microbiome in diverse ways. Our aim was to describe the use of digestive enzymes (prescription and non-prescription) by US adults and children and reported reasons.

Methods: We used data from the National Health and Nutrition Examination Survey from 1999 to 2020 to assess prescription and nonprescription supplement use in the prior 30 days. We evaluated ingredient lists to identify those including digestive enzymes. We then compared trends in use over time and by sex, age, race/ethnicity, education, income, self-reported dietary and health measures, and alcohol use.

Results: Prescription and nonprescription digestive enzyme use was stable from 1999 to 2020. Prevalence of use of nonprescription digestive enzyme-containing products was 2.3% for all age groups (95% confidence interval (CI) 2.1-2.6, Table 2). Prevalence of prescription digestive enzymes was 0.05% overall (95% CI 0.03-0.07, Table). Rates of non-prescription digestive enzymes were significantly higher in older age groups (Table 2). Individuals aged 60 years and older were the most likely to take prescription digestive enzymes (0.2% prevalence, p=0.006 compared to <60 years). There were no significant gender-related differences in digestive enzyme use. Non-Hispanic white individuals were significantly more likely to use non-prescription digestive enzymes than other racial/ethnic groups (p<0.001). There was significantly more non-prescription digestive enzyme use by individuals who had higher household incomes (p<0.001), and had some college education or more (p<0.001 compared to less than a 9th grade education). The most common reasons for use were to improve and maintain overall health and to get more energy. Only 13% of people on non-prescription digestive enzyme supplements reported that the product was recommended by a healthcare provider.

Discussion: Around 5.3 million people in the United States take nonprescription digestive enzymes. Higher income, older, more educated, non-Hispanic white people who have ever used alcohol are more likely to take nonprescription enzymes. They are most often used without the recommendation of a healthcare provider.

Introduction

- Digestive enzymes like amylase, lipase, and related compounds are licensed for use in pancreatic insufficiency.
- The use of these enzymes in non-prescription supplements has not been well-characterized.
- Non-prescription supplements contain a range of products with purported enzymatic use, which may impact the gut microbiome in diverse ways.
- Our primary objective was to describe the use of non-prescription digestive enzymes by US adults and children and reported reasons.
- Our secondary objective was to describe the trends in digestive enzyme use over time.

Methods and Materials

Data: Centers for Disease Control and Prevention's National Health and Nutrition Examination Survey (NHANES).

Years used: 2009-2010, 2011-2012, 2013-2014, 2015-2016, 2017-2020. Note: because of the COVID-19 Pandemic, data from 2019-2020 were not fully collected. A sample of the data were included with the 2017-2018 data as a 2017-2020 release that maintains representative weighting.

Data forms used: Demographics, Dietary Supplements and Prescription Medications

Exposure: identification of digestive enzymes was based on text review of ingredient lists for supplements. Probiotics were identified using the same method but selecting for relevant probiotic terms.

Table 1. List of Key Terms for Ingredients

Ingredient Key Term	
Acid Maltase	Lactase
Alpha Galactosidase	Lipase
Aminopeptidase	Pancreas
Amylase	Pancreatin
Amyloglucosidase	Pancrelipase
Aspergillopepsin	Papain
Beta-glucanase	Papaya
Bile	Pectinase
Bromelain	Pepsin
Carbenzyme	Peptidase
Cellulase	Peptizyme
Cerecalase	Phytase
Chymotrypsin	Protease
Digeseb	Stomach
Digezyme	Trypsin
Enzymes	Xylanase
Fibrazyme	

Analytic method: Proportions and 95% confidence intervals were calculated using survey weights and the Rao-Scott likelihood method. Multivariable analysis using quasipoisson models.

Analysis software: R {survey}

Ethics: Deidentified publicly available government database. No prior institutional ethics approval required.

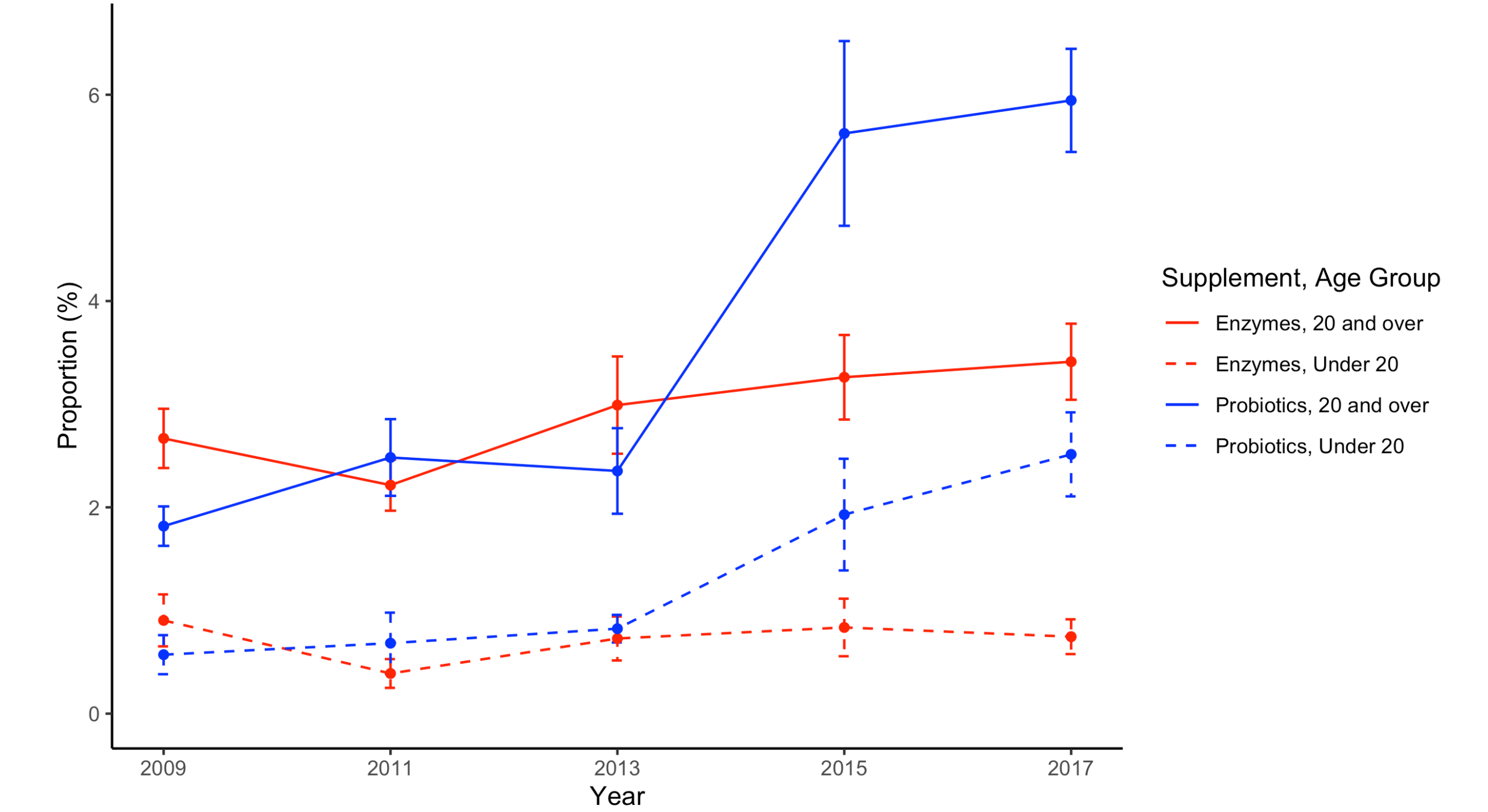
Results

- Overall, 2.3% of the population uses non-supplement digestive enzymes.
- Digestive enzyme use has been stable over time, though recent years suggest it may be becoming more common.
- The most common reasons for use were to improve and maintain overall health and to get more energy.
- Only 13% of people on non-prescription digestive enzyme supplements reported that the product was recommended by a healthcare provider.
- Of the 9,772 unique non-prescription supplements reported by NHANES participants in 2009-2020, 580 (5.9%) contained digestive enzymes; 573 (5.9%) contained probiotics.

Table 2. Association between demographic characteristics and digestive enzyme use.

Characteristics	n	Non-prescription digestive enzymes			Prescription digestive enzymes		
		Estimate (% prev)	SE	p-value	Estimate (% prev)	SE	p-value
Overall	55,147	2.33	0.12		0.05	0.01	
Age Group							
Under 20 years	23270	0.72	0.09	Ref.	0.01	0.01	Ref.
20-39 years	10579	2.68	0.25	<0.001	0.03	0.02	0.43
40-59 years	10521	2.63	0.18	<0.001	0.02	0.01	0.5
60 and over	10777	3.63	0.37	<0.001	0.16	0.04	<0.001
Gender							
Men	27282	2.05	0.15	Ref.	0.05	0.01	Ref.
Women	27865	2.61	0.18	0.01	0.05	0.01	0.66
Race/Ethnicity							
Hispanic	11679	1.68	0.18	Ref.	0.04	0.02	Ref.
Non-Hispanic Asian	4950	2.01	0.28	0.26	0.05	0.04	0.62
Non-Hispanic Black	11027	1.43	0.15	0.3	0.08	0.03	0.17
Non-Hispanic White	14704	2.79	0.21	<0.001	0.05	0.01	0.48
Other	2353	2.35	0.55	0.17	0.07	0.07	0.54
Education (Adults)							
Less than 9th grade	3115	1.27	0.33	Ref.	0.07	0.04	Ref.
9th-11th grade, no HS diploma	4227	1.43	0.29	0.72	0.11	0.05	0.53
High school graduate/GED	7604	1.79	0.23	0.24	0.04	0.02	0.37
Some college or AA degree	7244	3.05	0.24	<0.001	0.09	0.02	0.52
College graduate or above	9645	4.39	0.37	<0.001	0.04	0.01	0.74
Household Percent income to poverty ratio							
PIR≤130%	18929	1.18	0.14	Ref.	0.06	0.02	Ref.
PIR>130%	30467	2.8	0.17	<0.001	0.05	0.01	0.5
Alcohol Use							
Ever	24566	3.11	0.18	Ref.	0.08	0.03	Ref.
Never	4188	2.3	0.38	0.06	0.05	0.03	0.56

Figure 1. Non-prescription supplement use by age group over time.



Discussion

- Based on US population estimates, approximately 7.5 million Americans have used non-prescription digestive enzymes in the prior 30 days.
- Digestive enzymes are included in a wide range of supplements, many of which are not used for digestive purposes.
- Most of the supplements containing digestive enzymes are not used at the recommendation of a healthcare provider.
- The clinical implications of this use are unknown, though some digestive enzyme products have known drug-drug interactions.
- There is a need for further understanding of the effects of these ingredients and their health impacts.

Conclusions

Non-prescription digestive enzyme use is common. They are most often used without the recommendation of a healthcare provider. The implications of this for gastrointestinal health and the microbiome are still not known but may be of important clinical significance.

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References

- Centers for Disease Control and Prevention, National Health and Nutrition Examination Survey. https://www.cdc.gov/nchs/nhanes/about_nhanes.htm
- National Center for Health Statistics Ethics Review Board. Ethics Approval for NHANES. <https://www.cdc.gov/nchs/nhanes/irba98.htm>
- Edakkanambeth Varayil J, Bauer BA, Hurt RT. Over-the-counter enzyme supplements: what a clinician needs to know. *Mayo Clin Proc.* 2014 Sep;89(9):1307-12. doi: 10.1016/j.mayocp.2014.05.015. Epub 2014 Aug 4. PMID: 25103998.