

Supplement 1: Technical Appendix on Sampling Strategy

Participants in this survey study were part of an online panel maintained by Survey Sampling International (SSI), a survey research company. SSI originally recruited panel members using a variety of opt-in methods. These included online banners, TV ads, e-mails, apps, social media influencers, and websites. This diverse recruitment strategy helps to maintain the heterogeneity of the panel. All participants in the SSI panel undergo rigorous quality controls within the SSI Dynamix sampling platform before they are included in any survey sample. SSI's panel includes roughly 7 million individuals.

For this study, sampling occurred as follows: Whenever an individual panel member logged in to SSI's system and indicated availability to participate in a survey, the Dynamix platform then used a dynamic algorithm to randomize them to one of the multiple surveys currently available. This randomization algorithm adjusted the probability of a respondent being assigned to a particular survey based on both respondent demographic characteristics, known medical characteristics, and the needs of the currently fielded surveys. SSI retains information on participant characteristics based on information provided at the time of panel enrollment, as well as additional information provided in subsequent queries. We pre-determined the number of completed surveys required for this study (750), and randomization continued until the total number of completes were achieved.

Participants who were randomized to be presented with our survey and who entered it were then presented with four screening questions to ensure they met our inclusion criteria (age >18 years, currently taking a PPI, a reported diagnosis of GERD, and having a primary care provider). These were the first four questions in the survey. Only individuals who met all inclusion criteria were allowed to complete the survey.

A trial run of the survey was conducted July 11 and July 12, 2017 to ensure proper data capture. The survey functioned properly, and these initial 164 survey entries were included in the analysis. The survey re-opened for the full survey cohort on July 21, 2017, and by July 25, 2017 the quota of 750 completers was met. Specifically, 1431 individuals started the survey and completed the screening questions, of whom 755 met our inclusion criteria and completed the survey. 93 individuals opened the survey but did not complete any questions.

PPI 2.0

Start of Block: Introduction and eligibility questions

Q1 This survey contains questions regarding your knowledge and thoughts about a group of medications called proton pump inhibitors (PPIs). Please don't ask other people about how to answer the questions, or read about the topic online. Please answer each question to the best of your ability after reading through all possible response options. There are no “right” answers to the questions – we are simply interested in your opinions and experiences.

Your answers will be completely anonymous and will be kept confidential. The entire survey will take about 10-15 minutes.

The University of Michigan Institutional Review Board Health Sciences and Behavioral Sciences has determined that this study is exempt from IRB oversight.

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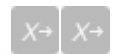
Q2

Let's begin. First we will ask some questions to make sure that you qualify for this study.



Q3 What is your age in years?

▼ less than 18 years old (17) ... Older than 104 (105)



Q4 Do you **currently** take any of the following medications?

Choose only one medication; if you are currently taking more than one of these, choose the one you have been on longest. These medications are collectively called proton pump inhibitors or "PPIs," a term we will use throughout the survey.

- ☐ Prilosec/Zegerid (generic name: omeprazole) (1)
- ☐ Protonix (generic name: pantoprazole) (2)
- ☐ Nexium (generic name: esomeprazole) (3)
- ☐ Prevacid (generic name: lansoprazole) (4)
- ☐ Dexilant (generic name: dexlansoprazole) (5)
- ☐ Aciphex (generic name: rabeprazole) (6)
- ☐ Not taking any of these medications currently (7)

Skip To: Q6 If Do you currently take any of the following medications? Choose only one medication; if you are cu... = Not taking any of these medications currently

Page Break



Q5 Do you use \${Q4/ChoiceGroup/SelectedChoices} for the treatment of gastro-esophageal reflux disease (GERD)? This condition goes by many different names, including acid reflux and heartburn.

☐ Yes (1)

☐ No (2)



Q6 Do you have a primary healthcare provider?

☐ Yes (1)

☐ No (2)

End of Block: Introduction and eligibility questions

Start of Block: Ineligible end of survey

Q7 Thank you for your interest in taking this survey. Unfortunately, you are not eligible to complete the survey. We appreciate your time.

End of Block: Ineligible end of survey

Start of Block: PPI Adverse Effects

Q8 Good news. You qualify for the survey. We will continue the survey now.



Q9 How concerned are you about significant long term side effects from your [\\${Q4/ChoiceGroup/SelectedChoices}](#)?

- ☐ I'm **not at all** concerned (1)
 - ☐ I'm **slightly** concerned (2)
 - ☐ I'm **somewhat** concerned (3)
 - ☐ I'm **extremely** concerned (4)
-



Q10 Have you ever tried stopping your [\\${Q4/ChoiceGroup/SelectedChoices}](#) because of concern about long term side effects?

- ☐ Yes (1)
 - ☐ No (2)
-



Q11 Have you ever tried reducing the amount of [\\${Q4/ChoiceGroup/SelectedChoices}](#) you take because of concern about long term side effects?

- ☐ Yes (1)
 - ☐ No (2)
-



Q12 Do you believe that your [\\${Q4/ChoiceGroup/SelectedChoices}](#) has caused you any long term side effects?

- ☐ Yes (1)
 - ☐ No (2)
-

Display This Question:

If Do you believe that your [\\${q://QIDbothe89/ChoiceGroup/SelectedChoices}](#) has caused you any long term si... = Yes

Q13 What side effect(s) do you believe it caused?



Q14 How familiar are you with any reports linking proton pump inhibitors (PPIs), like [\\${Q4/ChoiceGroup/SelectedChoices}](#), to long term side effects?

- ☐ Not at all familiar (1)
- ☐ Slightly familiar (2)
- ☐ Somewhat familiar (3)
- ☐ Extremely familiar (4)

Skip To: Q16 If How familiar are you with any reports linking proton pump inhibitors (PPIs), like ... = Not at all familiar

Q15 Please write in any specific side effects from proton pump inhibitors that you are aware of, **whether or not you have experienced them**. If you're not sure of the specific side effects, you can write in, "I'm not sure."

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Q16 Has a healthcare provider ever talked with you about **possible long term side effects of proton pump inhibitors (PPIs), like** **#{Q4/ChoiceGroup/SelectedChoices}**?

- ☐ Yes (1)
- ☐ No, not that I recall (2)
-



Q17 Has a healthcare provider ever talked with you about **the risks versus the benefits of taking** **#{Q4/ChoiceGroup/SelectedChoices}** **for your specific medical condition?**

- ☐ Yes (1)
- ☐ No, not that I recall (2)
-



Q18 Has a healthcare provider ever recommended that you try **to reduce the dose or how often you take your** **#{Q4/ChoiceGroup/SelectedChoices}**?

- ☐ Yes (1)
- ☐ No, not that I recall (2)
-



Q19 Has a healthcare provider ever recommended that you try **to stop your** **#{Q4/ChoiceGroup/SelectedChoices}**?

- ☐ Yes (1)
- ☐ No, not that I recall (2)
-



Q20 How willing would you be to **reduce the dose or how often you take** your [\\${Q4/ChoiceGroup/SelectedChoices}](#) if your primary healthcare provider recommended it because of possible long term side effects?

- ☐ Very **unwilling** (1)
 - ☐ Somewhat **unwilling** (2)
 - ☐ Somewhat **willing** (3)
 - ☐ Very **willing** (4)
-



Q21 How willing would you be to **stop** your [\\${Q4/ChoiceGroup/SelectedChoices}](#) if your **primary healthcare provider** recommended it because of possible long term side effects?

- ☐ Very **unwilling** (1)
 - ☐ Somewhat **unwilling** (2)
 - ☐ Somewhat **willing** (3)
 - ☐ Very **willing** (4)
-

Q22 How willing would you be to **stop** your [\\${Q4/ChoiceGroup/SelectedChoices}](#) if a **gastroenterologist (digestive disease specialist)** recommended it because of possible long term side effects?

- ☐ Very **unwilling** (1)
- ☐ Somewhat **unwilling** (2)
- ☐ Somewhat **willing** (3)
- ☐ Very **willing** (4)

Q23 How willing would you be to **stop** your [\\${Q4/ChoiceGroup/SelectedChoices}](#) if a **pharmacist** recommended it because of possible long term side effects?

- ☐ Very **unwilling** (1)
- ☐ Somewhat **unwilling** (2)
- ☐ Somewhat **willing** (3)
- ☐ Very **willing** (4)
-



Q24 Now imagine that your **primary healthcare provider** has recommended that you **stop** your [\\${Q4/ChoiceGroup/SelectedChoices}](#) because of possible long term side effects.

How **willing** would you be to stop [\\${Q4/ChoiceGroup/SelectedChoices}](#) if the provider ...

	Very unwilling (1)	Somewhat unwilling (2)	Somewhat willing (3)	Very willing (4)
... said you could go back on your current dose of medication in the future if needed (2)	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
... gave you a less powerful acid-blocking medication to use instead (3)	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
... slowly lowered the dose of your \${Q4/ChoiceGroup/SelectedChoices} to make sure you didn't have problems while coming off of it (4)	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>

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Q25 Which, if any, of the following conditions or risks are you aware of having been linked to proton pump inhibitors (PPIs), like [\\${Q4/ChoiceGroup/SelectedChoices}](#)? Select all answers that apply. If you are not aware of any of these conditions having been linked to proton pump inhibitors, select the "none of the above" choice.

- ☐ chronic kidney disease (1)
- ☐ Clostridium difficile (C diff, an infection that causes diarrhea) (2)
- ☐ death (20)
- ☐ dementia (3)
- ☐ fracture of a bone (4)
- ☐ heart attack (5)
- ☐ osteoporosis or osteopenia (weakening of the bones) (6)
- ☐ pneumonia (7)
- ☐ stroke (8)
- ☐ vitamin B12 deficiency (9)
- ☐ vitamin D deficiency (10)
- ☐ none of the above (11)

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Q26 Have you ever been diagnosed with any of the following conditions while taking [\\${Q4/ChoiceGroup/SelectedChoices}](#) or another proton pump inhibitor (PPI)? Select all answers that apply. If none of them, select the "none of the above" choice.

- ☐ chronic kidney disease (1)
- ☐ Clostridium difficile (C diff, an infection that causes diarrhea) (2)
- ☐ dementia (3)
- ☐ fracture of a bone (4)
- ☐ heart attack (5)
- ☐ osteoporosis or osteopenia (weakening of the bones) (6)
- ☐ pneumonia (7)
- ☐ stroke (8)
- ☐ vitamin B12 deficiency (9)
- ☐ vitamin D deficiency (10)
- ☐ none of the above (11)

Display This Question:

If Have you ever been diagnosed with any of the following conditions while taking ... != none of the above



Q27 You indicated that you were diagnosed with [\\${Q26/ChoiceGroup/SelectedChoices}](#). Did your healthcare provider discuss stopping the proton pump inhibitor (PPI) after the diagnosis?

- ☐ Yes (1)
- ☐ No, not that I recall (2)



Q28 What is your comfort level asking your primary healthcare provider about whether you can reduce or stop your [\\${Q4/ChoiceGroup/SelectedChoices}](#)?

- ☐ Very **uncomfortable** (1)
- ☐ Somewhat **uncomfortable** (2)
- ☐ Somewhat **comfortable** (3)
- ☐ Very **comfortable** (4)



Q29 Do you think you would be able to manage your acid reflux or heartburn symptoms without taking [\\${Q4/ChoiceGroup/SelectedChoices}](#)?

- ☐ Definitely **yes** (1)
- ☐ Probably **yes** (2)
- ☐ Probably **no** (3)
- ☐ Definitely **no** (4)

End of Block: PPI Adverse Effects

Start of Block: GERD Symptoms

Q30 Now we will ask some questions about your heartburn or acid reflux symptoms.



Q31 In the past two weeks, how bad have your heartburn or acid reflux symptoms been?

- ☐ No symptoms (1)
 - ☐ Symptoms are noticeable but not bothersome (2)
 - ☐ Symptoms are bothersome every day but do not change your daily activity (3)
 - ☐ Symptoms interfere with your daily activity (4)
 - ☐ Symptoms are incapacitating and you are unable to do some daily activities (5)
-



Q32 How much improvement in your heartburn or reflux symptoms have you had since being on [\\${Q4/ChoiceGroup/SelectedChoices}](#)?

- ☐ No improvement at all (1)
 - ☐ A little improvement (2)
 - ☐ Moderate improvement (3)
 - ☐ Quite a bit of improvement (4)
 - ☐ Complete resolution of symptoms (5)
-



Q33 How much does your **quality of life** depend on taking [\\${Q4/ChoiceGroup/SelectedChoices}](#)?

- ☐ Not at all (1)
- ☐ A little (2)
- ☐ A moderate amount (3)
- ☐ A great deal (4)



Q34 How much does your **overall health** depend on taking
\${Q4/ChoiceGroup/SelectedChoices}?

- ☐ Not at all (1)
- ☐ A little (2)
- ☐ A moderate amount (3)
- ☐ A great deal (4)

End of Block: GERD Symptoms

Start of Block: Background- PPI Use

Display This Question:

If Do you currently take any of the following medications? Choose only one medication; if you are cu... = Prilosec/Zegerid (generic name: omeprazole)

Or Do you currently take any of the following medications? Choose only one medication; if you are cu... = Nexium (generic name: esomeprazole)

Or Do you currently take any of the following medications? Choose only one medication; if you are cu... = Prevacid (generic name: lansoprazole)



Q35 Do you have to go to a pharmacy window or online pharmacy to fill a prescription for your
\${Q4/ChoiceGroup/SelectedChoices}, or do purchase it "over the counter" without needing a
prescription?

- ☐ From the pharmacy window or online pharmacy (1)
- ☐ I purchase it without a prescription ("over the counter") (2)



Q36 What does it cost you for a **one-month** supply of your [\\${Q4/ChoiceGroup/SelectedChoices}](#)? This is the amount that you have to pay out of pocket for the medicine, after any pharmacy benefits you might have. Please enter the amount in dollars below. If it costs you nothing, enter "0." **Please leave off the "\$" sign.**

X→

Q37 Did a healthcare provider recommend that you start taking a proton pump inhibitor (PPI) initially or did you start taking it on your own?

- ☐ A medical provider recommended starting the medicine (1)
- ☐ I started it on my own (2)

X→

Q38 Have any of the following types of healthcare providers recommended that you take [\\${Q4/ChoiceGroup/SelectedChoices}](#)? Select all that apply.

- ☐ My primary care provider (1)
- ☐ A gastroenterology provider, who specializes in digestive diseases (2)
- ☐ A pulmonology provider, who specializes in the lungs (3)
- ☐ An otolaryngology provider (ear, nose, and throat) (4)
- ☐ A pharmacist (5)
- ☐ Another type of provider (6)
- ☐ I'm not sure (7)

X→

Q39 Have you ever seen a gastroenterologist (digestive disease specialist) about your heartburn or acid reflux?

☐ Yes (1)

☐ No (2)



Q40 In an average week, how many days do you take [\\${Q4/ChoiceGroup/SelectedChoices}](#)?

☐ Less than once a week (1)

☐ 1 day per week (2)

☐ 2 days per week (3)

☐ 3 days per week (4)

☐ 4 days per week (5)

☐ 5 days per week (6)

☐ 6 days per week (7)

☐ 7 days per week (8)



Q41 In an average week, how many days do you take your [\\${Q4/ChoiceGroup/SelectedChoices}](#) **more than once** (i.e., twice or three times in a single day)?

- ☐ Less than once a week, or never (1)
- ☐ 1 day per week (2)
- ☐ 2 days per week (3)
- ☐ 3 days per week (4)
- ☐ 4 days per week (5)
- ☐ 5 days per week (6)
- ☐ 6 days per week (7)
- ☐ 7 days per week (8)



Q42 How long have you been taking proton pump inhibitors (PPIs)? This includes any proton pump inhibitor (PPI) you have been on, not just [\\${Q4/ChoiceGroup/SelectedChoices}](#). If more than one year, round to the closest year.

▼ less than 1 month (1) ... 20 years or longer (25)

End of Block: Background- PPI Use

Start of Block: Alternative Indications for PPI



Q43 Have you ever been diagnosed with any of the following conditions? Please select all answers that apply to you.

- ☐ Stomach or intestinal ulcer diagnosed on endoscopy (a "scope") (1)
 - ☐ Esophagitis, which is irritation in your esophagus that can only be diagnosed by endoscopy (a "scope") (2)
 - ☐ Barrett's esophagus (a pre-cancerous change in the esophagus) (3)
 - ☐ Bleeding from the stomach or intestines (4)
 - ☐ Helicobacter pylori (H pylori), a type of bacteria infection in the stomach (5)
 - ☐ None of the above (6)
-



Q44 Do you currently take any of the following drugs, which are sometimes used after a heart attack, stroke, or stent in a blood vessel?

Plavix (clopidogrel) Brilinta (ticagrelor) Effient (prasugrel)

- ☐ Yes (1)
 - ☐ No (2)
-



Q45 Do you currently take any of the following **anticoagulation or blood thinning medications**?

Coumadin (warfarin) Pradaxa (dabigatran) Eliquis (apixaban) Xarelto (rivaroxaban)
Savaysa (edoxaban)

- ☐ Yes (1)
 - ☐ No (2)
-



Q46 Do you take **aspirin**, and if so, how often?

- ☐ Yes, I take aspirin 4-7 days per week (1)
 - ☐ Yes, I take aspirin 1-3 days per week (2)
 - ☐ Yes, I take aspirin but less than one day per week (3)
 - ☐ No, I don't take any aspirin (4)
-



Q47 Do you use **non-steroidal anti-inflammatory drugs (NSAIDs)**, and if so, how often?

These medications include:

Advil or Motrin (ibuprofen)

Aleve or Naprosyn (naproxen)

Voltaren (diclofenac)

Indocin (indomethacin)

Mobic (meloxicam)

- ☐ Yes, I take NSAIDs 4-7 days per week (1)
 - ☐ Yes, I take NSAIDs 1-3 days per week (2)
 - ☐ Yes, I take NSAIDs but less than once a week (3)
 - ☐ No, I don't take any NSAIDs (4)
-



Q48 Have you taken **steroid pills** every day for at least the last month? The following medications are considered steroids.

prednisone prednisolone methylprednisolone cortisone hydrocortisone
dexamethasone

☐ Yes (1)

☐ No (2)



Q49 Do you take any of the following medications, which are types of medications used for heartburn or reflux but which are different from proton pump inhibitors, and if so, how often?

Tagamet (cimetidine) **Pepcid (famotidine)** **Zantac (ranitidine)** **Axid (nizatidine)**

☐ Yes, 4-7 days per week (1)

☐ Yes, 1-3 days per week (2)

☐ Yes, but less than once a week (3)

☐ No, I don't take any of these medications (4)

End of Block: Alternative Indications for PPI

Start of Block: Demographics



Q50 What is your gender?

- ☐ Male (1)
 - ☐ Female (2)
 - ☐ Transgender, or I prefer to self-describe (3)
 - ☐ I prefer not to say (4)
-



Q51 What is your race? If multiracial, please choose the race that you identify with most.

- ☐ White/Caucasian (1)
 - ☐ African American (2)
 - ☐ Asian (3)
 - ☐ Native American (4)
 - ☐ Pacific Islander (5)
 - ☐ Other (6)
 - ☐ Decline to answer (7)
-



Q52 Do you consider yourself to be Hispanic or Latino/a?

- ☐ Yes (1)
 - ☐ No (2)
 - ☐ Decline to answer (3)
-



Q53 What is the **highest** grade or level of schooling and/or training you completed?

- ☐ Less than 8 years (1)
 - ☐ 8-11 years (2)
 - ☐ 12 years or completed high school or GED (3)
 - ☐ Vocational or technical training (4)
 - ☐ 1-3 years of college/junior college/community college (5)
 - ☐ 4 or more years of college or graduated from college (6)
 - ☐ Graduate or professional school (7)
-



Q54 What is your current marital status?

- ☐ Married, or living as married (1)
 - ☐ Widowed (2)
 - ☐ Divorced (3)
 - ☐ Separated (4)
 - ☐ Never married (5)
-



Q55 What is your total household income per year?

- ☐ Less than \$10,000 (1)
- ☐ \$10,000 - \$19,999 (2)
- ☐ \$20,000 - \$29,999 (3)
- ☐ \$30,000 - \$39,999 (4)
- ☐ \$40,000 - \$49,999 (5)
- ☐ \$50,000 - \$59,999 (6)
- ☐ \$60,000 - \$69,999 (7)
- ☐ \$70,000 - \$79,999 (8)
- ☐ \$80,000 - \$89,999 (9)
- ☐ \$90,000 - \$99,999 (10)
- ☐ \$100,000 - \$149,999 (11)
- ☐ More than \$150,000 (12)



Q56 In general, would you say your health is:

- ☐ Excellent (1)
- ☐ Very good (2)
- ☐ Good (3)
- ☐ Fair (4)
- ☐ Poor (5)

End of Block: Demographics

Start of Block: End of Survey

Q57 Thank you for taking the time to complete this survey. Your answers will help us better understand patients' perceptions and knowledge of proton pump inhibitors (PPIs).

Knowledge of possible side effects from proton pump inhibitors (PPIs) is still evolving, and many doctors are still undecided about whether they really have serious long term side effects. If you have any concerns about taking your PPI, you should discuss this with your primary healthcare provider.

End of Block: End of Survey

Supplement 3. Categorization schema for adverse effects written in by patients for question 15.

Categorization	Write-in responses included in this category
Chronic kidney disease	"Bruised kidneys," "Bad on kidneys," "kidney degradation," "kidney damage"
C difficile colitis	"C diff," "Diarrhea"
Death	"Sudden death," "Shorten life span"
Dementia	"Alzheimer's," "memory issues," "affects your brain"
Fracture	"Bone breakage"
Heart attack	"Cardiovascular disease," "heart disease," "heart related," "not good for your heart"
Osteoporosis/osteopenia	"Bone brittleness," "bone density loss," "bone loss," "bone softener"
Pneumonia	
Stroke	
B12 deficiency	
Vitamin D deficiency	
Other	"Anemia," "malabsorption," "vitamin deficits," "iron deficiency," "low calcium," "low magnesium," "disturbed microbiota," "decreased good bacteria"
Not otherwise categorized because overly general or representing an acute reaction	"Cancer," "infection," "stomach issues," "liver injury," "liver failure," "nausea," "vomiting," "rash," "GI issues," "headache," "constipation," "issues with the bowels," "colon problems," "loose stools," "dizziness," "allergic reaction," "organ damage," "vomiting"
Not otherwise categorized because considered acute symptomatic reactions or not a substantiated PPI side effect	"Sleepiness," "abdominal pain," "gas," "blood infections," "damage to esophagus," "dependence," "dry mouth," "stones," "dystonic intestines," "blurred vision," "fever," "stomach ulcers," "fatigue," "intestinal bleeding," "eye strain," "leaky gut," "stomach enzymes," "muscle weakness," "rip in throat tube," "CD," "twitching," "back pain," "cramps," "irregular heart rate," "dependence," "heartburn," "high blood pressure," "joint pain," "over reducing necessary acid"

Supplement 4. Proportion of survey participants endorsing awareness of possible PPI adverse effects. See Supplement 3 for categorization schema.

Adverse effect	Passive recall (%)	Active recall (%)
None of the following	54.0	80.1
Chronic kidney disease (or "kidney disease")	17.4	5.7
Vitamin D deficiency	14.8	0.1
Bone fracture	11.5	0.7
Osteoporosis or osteopenia (or "brittle bones")	10.2	4.9
Vitamin B12 deficiency	6.4	0.4
Heart attack (or "heart disease")	6.2	2.1
Dementia (or "Alzheimer's")	6.1	4.5
<i>C. difficile</i> infection (or "diarrhea")	5.8	2.0
Death	5.2	1.7
Stroke	3.1	0.1
Pneumonia	1.6	0
Others	n/a	2.6

Categories are not mutually exclusive. All participants (N=755).