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# Proton Pump Inhibitor Overuse in India: An Emerging Public Health Challenge: A Narrative Review

**Dr Gunjan Khurana**

Department of Community Medicine, AIIMS Rishikesh

**Abstract**

Proton pump inhibitors, or PPIs, are among the most commonly prescribed drug classes in the world because of their effectiveness in treating gastrointestinal diseases caused by acid reflux.A significant percentage of PPI prescriptions may be written without obvious clinical grounds, according to mounting data from India and a number of other nations. This overuse trend has significant public health ramifications.The prevalence, causes, clinical effects, and financial burden of improper PPI usage in India's healthcare system are all summarized in this narrative review.Inappropriate PPI prescribing is widespread, with estimates ranging from 33% to 91%, according to hospital-based research carried out in tertiary care facilities in India. This pattern seems to be caused by a number of factors, such as easy access to over-the-counter medications, frequent co-prescription with nonsteroidal anti-inflammatory drugs even in patients with low gastrointestinal risk, poor adherence to evidence-based prescribing guidelines, and a lack of knowledge among healthcare professionals about the possible negative effects of long-term use. Although PPIs are generally considered safe, unnecessary long-term exposure has been linked to a number of adverse outcomes, such as Clostridioides difficile infection, vitamin B12 deficiency, hypomagnesemia, acute interstitial nephritis, chronic kidney disease, and an increased risk of fractures.

With PPI expenses making up as much as 19.93% of total outpatient pharmaceutical prices in Indian settings, the financial burden is enormous. Although recent international and regional consensus guidelines on PPI rationalization have emerged, their implementation in India remains limited. This review concludes that a multifaceted strategy encompassing prescriber education, electronic clinical decision support, pharmacist-led medication review, structured deprescribing protocols, and regulatory tightening of over-the-counter access is urgently needed to curtail PPI overuse in India and safeguard public health.

**Keywords**: proton pump inhibitors; inappropriate prescribing; public health; India; deprescribing; adverse drug reactions; rational use of medicines

## 1. Introduction

Proton pump inhibitors (PPIs) have revolutionized the management of acid-related gastrointestinal disorders since the introduction of omeprazole in the late 1980s. The hydrogen-potassium adenosine triphosphatase (H+/K+ ATPase) enzyme system on the luminal surface of gastric parietal cells is irreversibly inhibited by these medications, which include omeprazole, esomeprazole, pantoprazole, rabeprazole, lansoprazole, and dexlansoprazole. This results in a significant and long-lasting decrease in gastric acid secretion [1]. Their therapeutic effectiveness in treating illnesses including Helicobacter pylori

infection, peptic ulcer disease (PUD), gastroesophageal reflux disease (GERD), and Zollinger-Ellison syndrome is well-established, and they have continuously been among the best-selling drug classes globally [2].

PPI prescriptions have increased globally despite their therapeutic value, outpacing the epidemiological frequency of diseases that require their usage. Between 40% and 65% of PPI prescriptions in hospital and outpatient settings are incorrect, missing valid clinical grounds or exceeding approved therapeutic durations, according to numerous research from developed nations [3, 4].Because long-term PPI therapy has been linked to a number of negative side effects, such as enteric infections, bone fractures, chronic kidney disease, and nutritional deficiencies, when not clinically justified, this pattern of overuse has been recognized as a serious public health concern[5,6].

Examining PPI usage in India is particularly difficult due to diverse healthcare system, which includes primary and secondary care facilities, tertiary academic institutions, and a robust commercial pharmaceutical industry.The Indian pharmaceutical market, valued at approximately USD 55 billion in 2025, is among the largest in the world, and gastrointestinal drugs constitute a major therapeutic segment [7,8]. Inappropriate PPI prescribing rates ranging from 33% to 91% in various hospital settings have been reported in a number of single-center studies from India [9,10,11], but no thorough analysis has combined these results to fully evaluate the extent of the issue.

The objective of this narrative review is to methodically assess the available data regarding PPI usage as a public health issue in India. Specifically, this review seeks to: (a) describe the prevalence of inappropriate PPI prescribing in Indian healthcare settings; (b) examine the clinical and economic burden associated with their overuse; (c) explore the healthcare system– and patient-related factors that contribute to inappropriate prescribing practices; (d) critically appraise the available evidence on the association between prolonged or unnecessary PPI use and adverse health outcomes; and (e) provide doable, research-based strategies to encourage the sensible use of PPIs in the Indian healthcare system.

This study aims to provide a basis for clinical, educational, and policy approaches targeted at addressing this significant public health issue by combining the existing body of research.

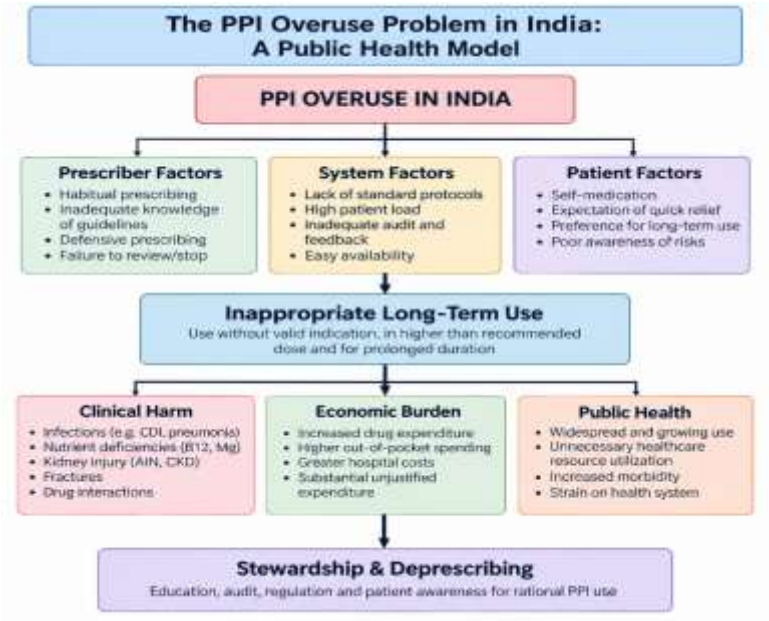


**Figure 1. The PPI Overuse Problem in India: A Public Health Model**

## 2. Pharmacology and Mechanism of Action

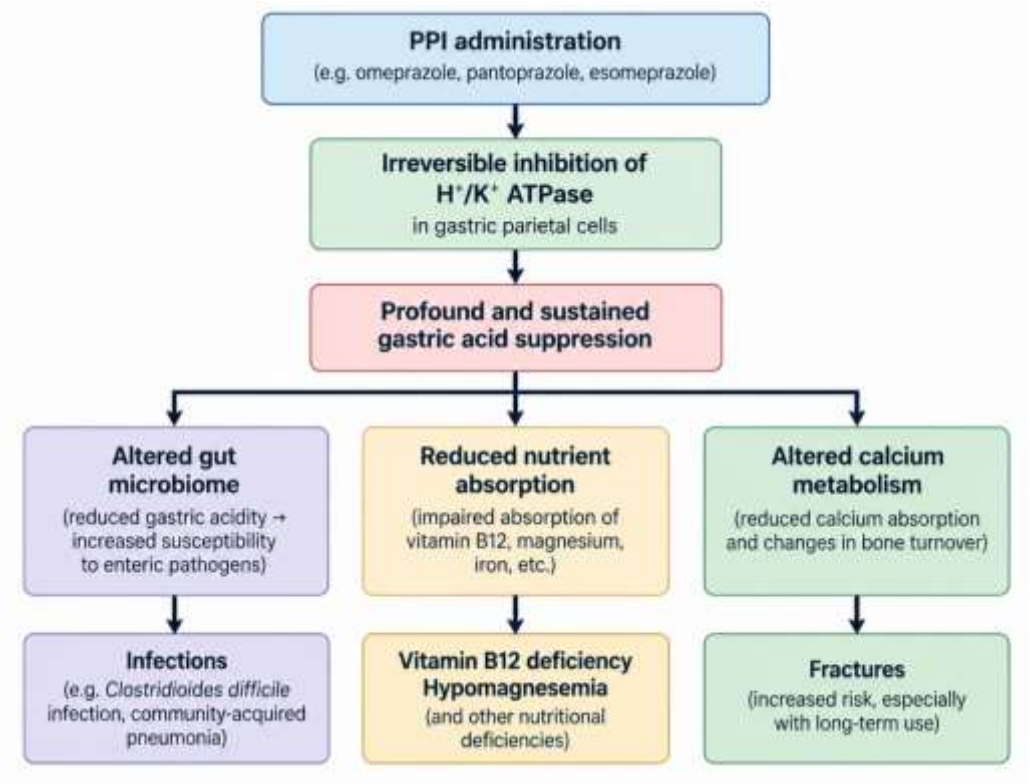


**Figure 2. Mechanism of Action of PPIs and Pathways to Adverse Effects**

Proton pump inhibitors are prodrugs that require acid-mediated activation in the secretory canaliculi of gastric parietal cells.When taken orally, the inactive substance is absorbed in the small intestine and carried to the parietal cells by the circulation, where it builds up in the secretory canaliculi's acidic environment. In this instance, the prodrug goes through a number of chemical changes before creating a reactive sulfenamide intermediate that covalently attaches to cysteine residues on the luminal surface of the H+/K+ ATPase enzyme, rendering it permanently inactive. [1,12]. Because the restoration of acid secretory capability depends on the manufacture of new pump enzymes, which is fueled by regular cellular turnover and usually takes 24 to 72 hours, this mechanism guarantees prolonged acid suppression. [12,13].

The five PPIs most commonly available in India are omeprazole, esomeprazole (the S-enantiomer of omeprazole), pantoprazole, rabeprazole, and lansoprazole. Dexlansoprazole and dexrabeprazole, the R-enantiomers of lansoprazole and rabeprazole respectively, have also been introduced in the Indian market. Despite having a similar mode of action, these drugs have different pharmacokinetic characteristics, such as bioavailability, metabolism (mostly through hepatic cytochrome P450 enzymes, including CYP2C19 and CYP3A4), and the possibility of drug-drug interactions[14]. For example, among the PPIs, pantoprazole has the lowest affinity for CYP2C19, making it comparatively less vulnerable to pharmacogenetic variability in metabolism [14]. Rabeprazole, on the other hand, undergoes predominantly non-enzymatic reduction, resulting in fewer drug interactions [14].

Despite these pharmacological variations, all PPIs are quite successful at reducing the production of stomach acid; with a typical once-daily dosage, they can reduce triggered acid secretion by more than 90%.This potency, while therapeutically advantageous, also underlies the potential for harm when these agents are used without adequate clinical justification. The profound suppression of gastric acidity

diminishes a critical barrier against ingested pathogens, impairs the absorption of certain nutrients requiring acidic environments for solubilization, and may alter the gut microbiome in ways that are only beginning to be fully characterized [5,15].

### 3. The prevalence of PPI overuse in India

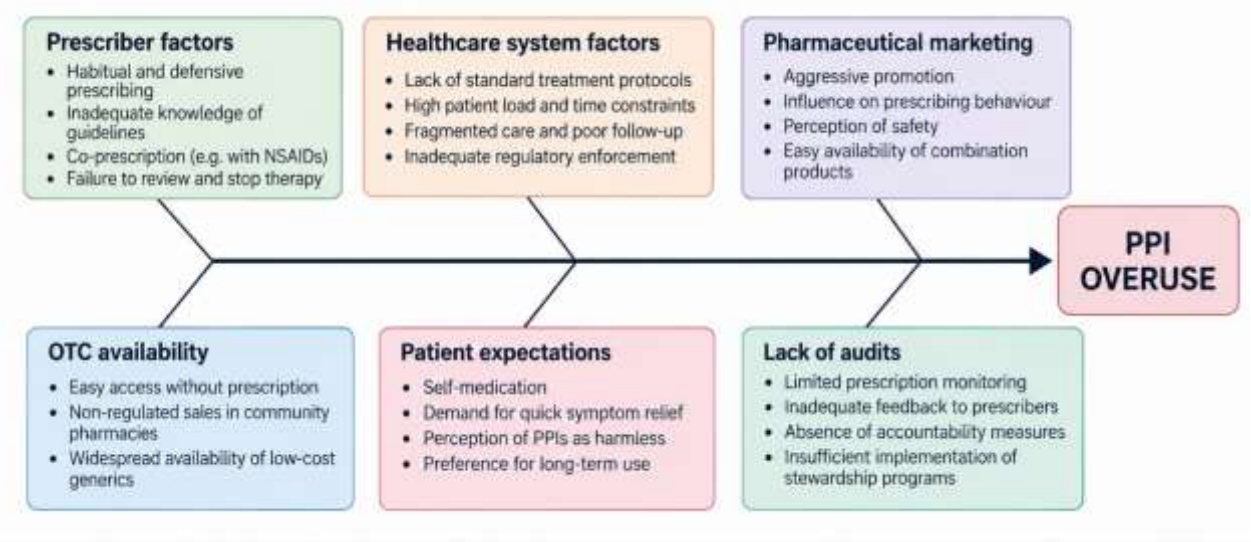


**Figure 3. Root cause analysis of Drivers of PPI Overuse in India**

Hospital-based cross-sectional research have been the main source of the epidemiological characterization of PPI usage in India. These studies collectively show a very alarming trend of incorrect prescribing. To comprehend the extent and kind of PPI overuse at all levels of the Indian healthcare system, a thorough analysis of these studies is necessary.

#### 3.1 Hospital Based Research

Ahad et al. (2021) examined 797 inpatient case profiles from two tertiary care teaching hospitals in South India in a groundbreaking single-day cross-sectional study. They found that 714 (90%) of the patients received PPIs, with pantoprazole making up around 90% of all PPI prescriptions[9]. Notably, 95% of patients in intensive care units received PPIs, and among patients prescribed four or more concurrent medications, 93% were receiving a PPI. Approximately 33% of PPI administrations utilized the intravenous route, with 75% of intravenous use occurring in general wards rather than critical care settings, suggesting that route selection was not consistently aligned with clinical need [9].

In a cross-sectional investigation, Sharma et al. (2019) examined 600 outpatient prescriptions and 500 inpatient records at tertiary care teaching hospital in Delhi[10]. Among inpatients, PPIs were prescribed to 62.2%, with the highest utilization in the medicine department (78.5%). Remarkably, according to established rules, only 7.4% of PPI prescriptions were considered appropriate, whilst a startling 91% were considered improper. Among outpatients, 27% received PPI prescriptions, and 79.74% of inpatient PPIs were administered as injections rather than oral formulations, raising concerns about both the indication and route of administration. Complete dosing information was documented in only 9.9% of inpatient and 30.2% of outpatient prescriptions, indicating a pervasive deficiency in prescription quality [10].

In a more recent study, Patil et al. (2026) evaluated 120 inpatients and 50 outpatients at a teaching hospital in Karnataka to determine if PPI prescriptions were reasonable in accordance with National Institute for Health and Care Excellence (NICE) standards[11]. Among inpatients, 80 (66.67%) prescriptions were

classified as appropriate and 40 (33.33%) as inappropriate. The predominant categories of inappropriateness included prophylaxis in low-risk patients co-prescribed with NSAIDs (40%), and prescriptions with no documented indication (57.15%). Among outpatients, the inappropriate prescribing rate was 77.78%, driven primarily by prophylaxis in low-risk patients receiving NSAIDs (77.78%) and prescriptions lacking clear indications (22.22%). Pantoprazole 40 mg was the dominant PPI, accounting for 95.83% of inpatient and 93.07% of discharge prescriptions [11].

In order to assess the financial effects of incorrect PPI use, Venkataraman et al. (2020) carried out a prospective observational study among 253 inpatients in a rural tertiary care hospital in Karnataka[16]. The study identified significant levels of irrational PPI prescribing, with a notable proportion of prescriptions deviating from recommended indications, dosages, or durations.Irrational PPI use created a quantifiable financial burden, according to the cost analysis, using funds that could have been used for more clinically sound treatment approaches. These findings were corroborated by a study from a tertiary care hospital in Dehradun, where total prescription costs of Indian Rupees (INR) 304,118 were analyzed, of which INR 76,984 (25.31%) was attributable to PPI expenditure, with unjustified PPI use accounting for INR 23,558 (31% of total PPI cost) [17].

According to a study by the medicine department at the Maulana Azad Medical College in Delhi, PPIs made up INR 120,085 (11.95%) of the INR 1,004,102 spent on all drugs for inpatients and outpatients. Outpatients' pharmacy spending on PPIs was significantly higher, at 19.93% [18]. These numbers highlight the large amount of medical resources devoted to PPI medication, many of which may be clinically unnecessary.

**3.2 Outpatient and Community Settings**

The widespread availability of PPIs as over the counter (OTC) drugs, aggressive pharmaceutical marketing, and weak regulatory enforcement of prescription requirements all contribute to the overuse of PPIs in outpatient and community settings in India. PPI usage patterns between prescription-based and self-medicated users were compared in a cross-sectional study by Kaushal and Sarala (2026) that was carried out among a number of neighborhood pharmacies in Kolar, Karnataka [19]. Just 170 (33.3%) of the 510 patients had a valid prescription, whereas 340 (66.7%) received PPIs by self-medication.This finding highlights how readily PPIs may be purchased in India devoid of medical consultation, a trend that significantly increases the risk of improper usage without medical supervision.

A study assessing inappropriate long-term PPI use in a general medicine outpatient department at a tertiary care hospital in India found that among 120 patients receiving long-term PPI therapy (defined as eight weeks or more), 70 (58.3%; 95% CI: 49.1-67.0%) had inappropriate long-term use [20].Prophylaxis without known risk factors (21.4%), nonspecific dyspepsia without diagnostic confirmation (35.7%), and undocumented reasons (28.6%) were the most common incorrect indications. Only 32.5% of patients had a documented indication for PPI usage, which shows extremely poor documentation quality.Factors independently associated with inappropriate use included prescription by general practitioners (OR: 3.8), polypharmacy (OR: 2.9), therapy duration exceeding one year (OR: 4.2), and self-prescription (OR: 5.6) [20]. These findings suggest that inappropriate long-term PPI use is the norm rather than the exception in Indian outpatient settings.

According to a survey conducted among 1000 physicians in India, PPI prescriptions for acid reflux disorders are quite prevalent, and there is significant variation in both prescription practices and adherence to guidelines [21]. Furthermore, studies on the attitude and knowledge of resident doctors in emergency departments of tertiary care hospitals in North India found that 36% of residents prescribed acid

suppressive drugs for the majority of their patients, with acute gastritis being the most commonly cited indication, despite the limited evidence supporting routine PPI use for this condition [22]. According to a similar study carried out in Pune, 82.5% of resident physicians recommended acid-suppressive medications for acute gastritis, and these prescriptions were frequently motivated by unit or consultant protocol rather than personal clinical judgment [23].

**3.3 Self-Medication and Over-the-Counter Availability**

The widespread use of PPI self-medication is one of the highly concerning features of India's abuse problem. Under the Indian pharmaceutical regulatory system, some PPI formulations may be sold as Schedule H medications (requiring a prescription), while others may be sold as Schedule H1 pharmaceuticals (requiring record-keeping). PPIs are often provided without legal prescriptions, especially in rural and semi-urban regions, and implementation of such laws at the retail pharmacy level is still not uniform [24].

The cross-sectional study from Kolar district revealed that self-medicated PPI users had significantly lower knowledge regarding potential side effects compared to prescription users, and the most common reason for self-medication was previous experience with the medication followed by pharmacist recommendation [19]. This conclusion is particularly concerning since it suggests that pharmacists, who should serve as gatekeepers for appropriate prescription usage, may inadvertently promote PPI abuse by writing prescriptions for minor, self-limiting symptoms without carrying out a comprehensive clinical assessment. The habit of self-medication with these powerful acid-suppressive drugs has been further solidified by the cultural normality of PPI use for common digestive problems, which is further supported by direct-to-consumer pharmaceutical advertising.

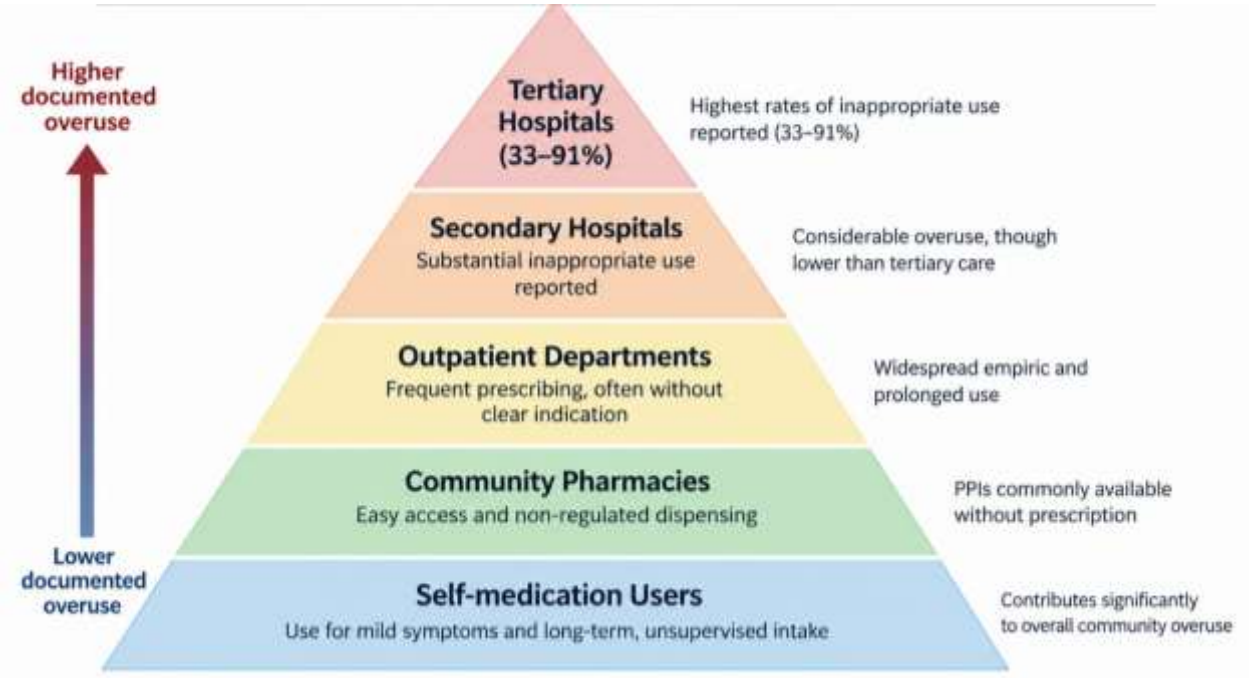


**Figure 4. Spectrum of PPI Overuse Across Indian Healthcare Settings**

## 4. Clinical and Economic Consequences of PPI Overuse


**Figure 5. Clinical Consequences**

Inappropriate PPI use has negative effects on public health and the healthcare system as a whole in addition to the individual patient. This section looks at the economic repercussions of such usage as well as the clinical side effects linked to unjustified long-term PPI exposure.

### 4.1 Adverse Health Effects

#### 4.1.1 Infections

A higher risk of enteric infections has been repeatedly linked to PPI suppression of gastric acid, which is an essential first-line defense against ingested bacteria.An umbrella review of 11 meta-analyses examining the association between PPI use and Clostridioides difficile infection (CDI) found that all included meta-analyses reported a positive association, with pooled odds ratios ranging from 1.26 to 2.34 [25]. The most robust estimates, reported by Trifan et al. (2017) and Deshpande et al. (2015), demonstrated ORs of 1.99 (95% CI: 1.73-2.30) and 2.15 (95% CI: 1.81-2.55), respectively, indicating a doubling of CDI risk among PPI users [25,26]. A dose-response analysis further confirmed that the risk of CDI increases with both the dose and duration of PPI therapy [27].In the Indian context, where CDI rates in healthcare settings are already alarming and antimicrobial resistance can pose a major threat to public health, with an estimated 987,254 deaths attributable to bacterial AMR in 2021 [28].

In addition to the CDI, PPI use has been linked to an increased likelihood of spontaneous bacterial peritonitis, small intestine bacterial overgrowth, and community-acquired pneumonia in cirrhosis patients[5]. The mechanism underlying these associations relates to the loss of the acid barrier, which permits colonization of the upper gastrointestinal tract by pathogenic organisms that would otherwise be

eliminated. Given the high burden of infectious diseases in India and the disproportionate impact of healthcare-associated infections on patient outcomes in resource-limited settings, the infectious complications of PPI overuse warrant particular attention from Indian clinicians and policymakers.

**4.1.2 Renal Effects**

Acute interstitial nephritis (AIN) and chronic kidney disease (CKD) are two serious renal problems linked to PPI use. With hazard ratios ranging from 1.10 to 1.50 in adjusted analyses, a number of observational studies and meta-analyses have shown a positive correlation between PPI use and the risk of incident CKD[6,29]. The relationship between PPI use and CKD progression to end-stage renal disease has also been reported, although the evidence is predominantly from observational designs, precluding definitive causal inference [6].

PPI-associated acute interstitial nephritis is an increasingly recognized entity, with PPIs now identified as the most common cause of drug-induced AIN in the outpatient setting [30]. With a median patient age of 78 years and a mean peak serum creatinine of 392 micromol/L, a groundbreaking study by Simpson et al. detailed 15 patients with biopsy-proven AIN linked to PPI usage and showed that renal function improved in all cases after PPI discontinuation [31]. Four cases of PPI-induced AIN reported from India implicated pantoprazole, omeprazole, and esomeprazole, with two patients requiring hemodialysis [32]. The Central Drugs Standard Control Organisation (CDSCO) of India has issued safety communications regarding the risk of PPI-associated kidney injury, highlighting the regulatory awareness of this concern [33].

**4.1.3 Bone Metabolism and Fractures**

Numerous studies have examined the relationship between PPI use and osteoporotic fractures. PPI use was linked to a slightly higher incidence of hip fracture (OR: 1.20-1.42), vertebral fracture (OR: 1.50-1.56), and any-site fracture (OR: 1.16-1.20), according to a meta-analysis of 18 observational studies with 244,109 fracture cases[34]. The suggested process entails decreased stomach acid-mediated solubilization of calcium salts, which impairs calcium absorption and causes secondary hyperparathyroidism and hastened bone loss [35]. An updated meta-analysis of 20 observational studies confirmed these findings, reporting an overall hip fracture OR of 1.22 (95% CI: 1.15-1.30), any-site fracture OR of 1.19 (95% CI: 1.12-1.27), and spine fracture OR of 1.53 (95% CI: 1.36-1.73) [36]. Dose-response analyses indicated that both high-dose and low-dose PPI use were associated with elevated fracture risk, though the association was stronger with higher doses and longer durations of therapy [36].In India, where osteoporosis is prevalent, especially among postmenopausal women and the elderly, the risk of fracture associated with excessive PPI exposure is an avoidable factor in morbidity and healthcare costs.

**4.1.4 Nutritional Deficiencies**

Iron, calcium, magnesium, vitamin B12, and other critical micronutrient deficits have been linked to long-term PPI use. Among these relationships, hypomagnesemia is one of the best-characterized; case reports and observational studies show that PPI-associated hypomagnesemia can be severe, resistant to oral magnesium supplementation, and only goes away when PPIs are stopped[37]. A systematic review of long-term PPI use and micronutrient status confirmed significant reductions in serum magnesium, calcium, and vitamin B12 levels among chronic PPI users compared to non-users [38].

Vitamin B12 deficiency is of particular concern because it can lead to megaloblastic anemia, peripheral neuropathy, and cognitive impairment, conditions that may already be prevalent in the elderly Indian population and that are frequently misattributed to other causes. Gastric acid and pepsin are essential for the release of vitamin B12 from dietary protein complexes, and their suppression by PPIs impairs this

process. Several systematic reviews have confirmed the association between PPI use and vitamin B12 deficiency, particularly with durations of therapy exceeding two years [39,40].

#### 4.1.5 Other Adverse Effects

Additional adverse effects associated with long-term PPI use that have been reported in the literature include an association with cardiovascular events, though the evidence is inconsistent and primarily derived from observational studies with significant potential for confounding [41]. The relationship between PPI use and dementia risk remains controversial, with some meta-analyses suggesting a positive association while others have found no significant link [42,43]. Additionally, fundic gland polyps—which are usually benign but may raise diagnostic concerns during endoscopic examination—have been linked to PPI use[44]. The possibility of negative consequences is further increased by drug-drug interactions including PPI-mediated changes in stomach pH and cytochrome P450 enzyme activity, given the high frequency of polypharmacy among long-term PPI users in India[9].

### 4.2 Economic Burden

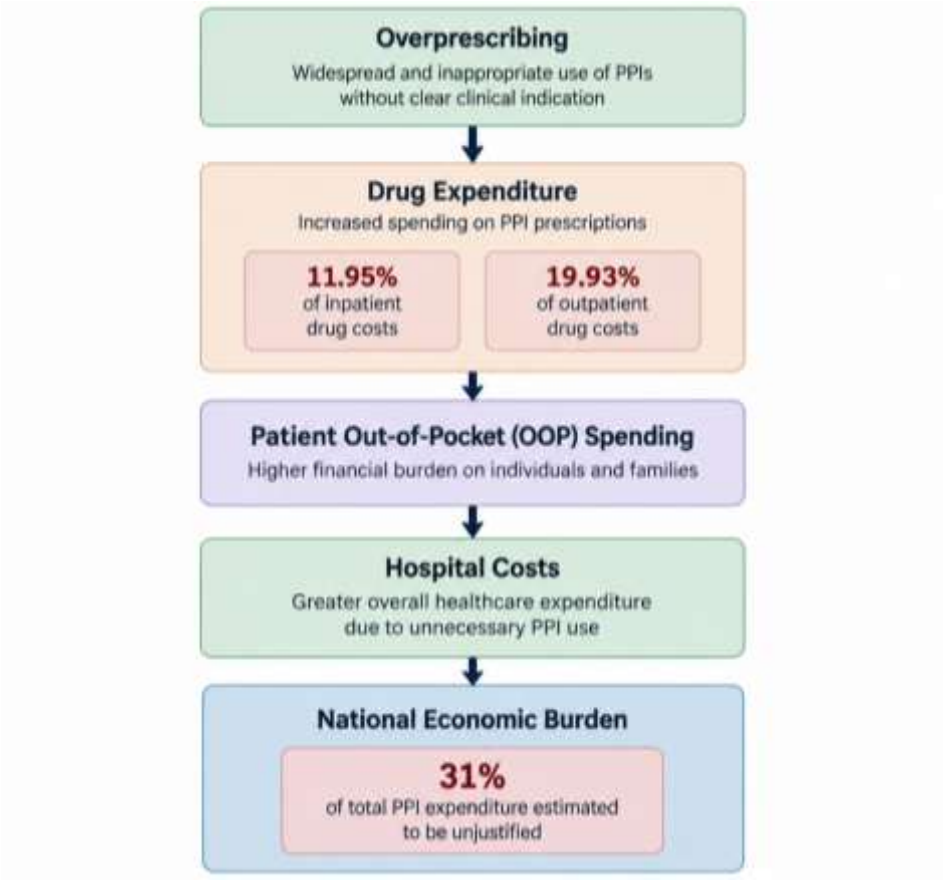


**Figure 6. Economic Burden Pathway**

Although detailed national numbers are not available, PPI usage has a significant economic impact in India. The hospital-based research that is currently available regularly shows that PPIs make up a substantial amount of global pharmaceutical expenditure, with a significant portion of that amount being attributed to an inappropriate use.The study from Delhi found that PPI expenditure constituted 11.95% of total inpatient medication costs and 19.93% of outpatient medication costs [18]. The study from Dehradun reported that 31% of all PPI expenditure was attributable to unjustified use, representing resources that could be redirected to more clinically necessary therapies [17].

Even a small percentage of PPI expenditure attributable to overuse translates into a significant absolute financial burden at the macroeconomic level, given that gastrointestinal medications make up a significant therapeutic segment and that India's domestic pharmaceutical consumption was estimated to be worth INR 201,372 crore (USD 23.5 billion) in FY2024 [7]. A cost variation analysis of PPIs available in the Indian market revealed enormous price disparities across brands, suggesting that branded generic prescribing practices contribute to avoidable healthcare costs when cheaper, therapeutically equivalent alternatives are available [45].The Indian healthcare system, which already finds it difficult to satisfy the needs of a sizable population, is severely burdened by the cumulative impact of needless PPI prescriptions on patient out-of-pocket expenses, insurance claims, and public hospital budgets.

## 5. Contributing Factors to PPI Overuse in India

A multi-level analysis that takes into consideration prescriber, system, patient, and regulatory elements is necessary to understand the causes of PPI overuse in India. These factors all contribute to the ongoing discrepancy between evidence-based prescribing recommendations and actual clinical practice.

### 5.1 Prescriber-Level Factors

Inappropriate PPI use at the prescriber level is caused by a number of circumstances. Research on resident physicians in tertiary care hospitals in India often shows a propensity for empirical PPI prescribing, which is frequently motivated by consultant preferences or unit protocols rather than customized patient evaluation[22,23]. The knowledge gap concerning appropriate indications, dosing, and duration of proton pump inhibitors (PPIs) is notable. A survey conducted among emergency medicine residents in North India revealed that a significant number were unaware of evidence-based guidelines for PPI use and habitually prescribed these medications for conditions like acute gastritis, despite limited evidence supporting routine acid suppression in such cases.[22]. Furthermore, the practice of prescribing PPIs as co-therapy with NSAIDs in patients who lack identifiable risk factors for NSAID-associated gastropathy is widespread, with studies reporting that 40% of inappropriate inpatient prescriptions involved prophylaxis in low-risk patients co-prescribed with NSAIDs [11].

Another significant prescriber-level cause is the failure to reevaluate the ongoing requirement for PPI therapy during care transitions, such as hospital discharge. Without a defined plan for de-escalation or discontinuation, patients who were started on PPIs during hospitalization for stress ulcer prophylaxis are often discharged on these drugs, resulting in lifetime chronic use [20]. Often known as "prescribing inertia" or "legacy prescribing," this phenomenon is a well-known contributor to the inappropriate long-term use of PPIs and is especially common in environments without regular medication review procedures.

### 5.2 System-Level Factors

System-level factors in the Indian healthcare context include the absence of robust antimicrobial stewardship or medication stewardship programs, limited integration of clinical decision support systems into electronic prescribing workflows, and a pharmaceutical industry environment characterized by aggressive promotion of PPIs. The Indian pharmaceutical market is highly competitive, with numerous brands of each PPI molecule available at varying price points, and pharmaceutical representatives frequently engage in direct marketing to physicians [7,45]. The influence of pharmaceutical promotion on prescribing behavior has been well documented globally, and its impact is likely amplified in settings where regulatory oversight of promotional activities is limited.

Another systemic shortcoming in Indian hospitals is the absence of regular prescription audits and feedback systems. The Delhi study specifically stated that the high prevalence of incorrect prescribing was

probably caused by the absence of frequent audits and feedback to prescribers[10]. In institutions where prescription auditing has been implemented, significant reductions in inappropriate PPI use have been demonstrated, suggesting that systematic surveillance of prescribing practices is an effective intervention [46]. However, the infrastructure and institutional commitment required for ongoing prescription monitoring are not universally available in Indian healthcare settings, particularly in smaller hospitals and primary care facilities.

### 5.3 Patient-Level Factors

Low health literacy about the correct use and potential risks of PPIs, the expectation of getting a prescription for common gastrointestinal symptoms, and the phenomenon of rebound acid hypersecretion after discontinuing PPIs—which may encourage continued use—are patient-related factors that contribute to PPI overuse.The cross-sectional study from Kolar found that self-medicated PPI users had poor knowledge of potential adverse effects, and the most common reason for self-initiation was prior positive experience with the medication, suggesting that a cycle of use is established that persists without medical oversight [19]. The study of long-term PPI users in a general medicine outpatient department found that 32.5% of patients lacked any documented indication for their PPI therapy, and self-prescription was independently associated with inappropriate use (OR: 5.6) [20]. These findings underscore the need for patient education campaigns and regulatory measures to restrict OTC access to PPIs in India.

## 6. Counterarguments and Limitations of the Evidence

| Adverse Effect | Strength of Evidence |
|---|---|
| **CDI** | Strong |
| **CKD** | Moderate |
| **AIN** | Strong |
| **Fracture** | Moderate |
| **B12 Deficiency** | Moderate |
| **Dementia** | Weak/Conflicting |

**Table 1: Evidence Map of Adverse Effects**

While the body of evidence linking PPI overuse to adverse outcomes is substantial, it is important to acknowledge the inherent limitations of the existing literature and consider counterarguments that temper the strength of causal inference. The majority of studies examining the association between PPI use and adverse effects are observational in design, including cohort studies, case-control studies, and cross-sectional analyses, which are inherently susceptible to confounding by indication, selection bias, and unmeasured confounders [41].

Confounding by indication is a particularly important consideration in the PPI literature, as the conditions for which PPIs are legitimately prescribed, such as GERD and PUD, may themselves be associated with the adverse outcomes attributed to PPIs. For example, patients with GERD may have comorbidities such as obesity, smoking, and alcohol use that independently increase the risk of cardiovascular events and fractures, making it difficult to disentangle the effect of the PPI from the effect of the underlying condition and its associated risk factors [41].

Over a median follow-up of three years, Moayyedi et al. (2019) found no significant increase in fracture risk, cardiovascular events, or other serious adverse events among PPI users in their seminal randomized controlled trial comparing pantoprazole to placebo in patients receiving rivaroxaban or aspirin [47]. This trial provides important evidence that PPIs may be safer than observational studies suggest, at least in the

short to medium term. However, the trial population was selected and may not be representative of the broader patient population receiving PPIs in routine clinical practice, particularly elderly patients with multiple comorbidities who are at the highest risk of adverse effects.

Additionally, it is still uncertain if PPI use and dementia are related. Although previous meta-analyses indicated marginally positive correlations [42], a 2024 meta-analysis found no substantial elevated risk of dementia among PPI users [43].This discrepancy might be caused by variations in study populations, follow-up times, confounding adjustments, and PPI exposure assessment methods. Some commentators have noted that the weak and non-causal relationships reported in many studies are frequently portrayed to be conclusive evidence of harm in press coverage [41]. The media's amplification of observational study findings linking PPIs to serious adverse outcomes has been criticized for causing disproportionate public anxiety.

In terms of the data specific to India, it is crucial to remember that the majority of research are cross-sectional, single-center assessments with rather small sample sizes, which restricts their applicability to the larger Indian population. It is difficult to compare prevalence estimates across contexts due to the variation in improper prescribing definitions across research, with some adopting NICE guidelines, some using American College of Gastroenterology recommendations, and still others using institutional criteria[11]. Additionally, the economic analyses are limited to individual institution-level data and do not capture the national-level economic burden of PPI overuse.Despite these drawbacks, the finding that a significant portion of PPI prescriptions are inappropriate in a variety of Indian settings and the mechanistic plausibility of side effects from prolonged acid suppression support the conclusion that PPI overuse constitutes a serious public health issue in India that requires systematic intervention.

## 7. **Strategies for Rationalization**

### 7.1 **International Guidelines and Deprescribing Recommendations**

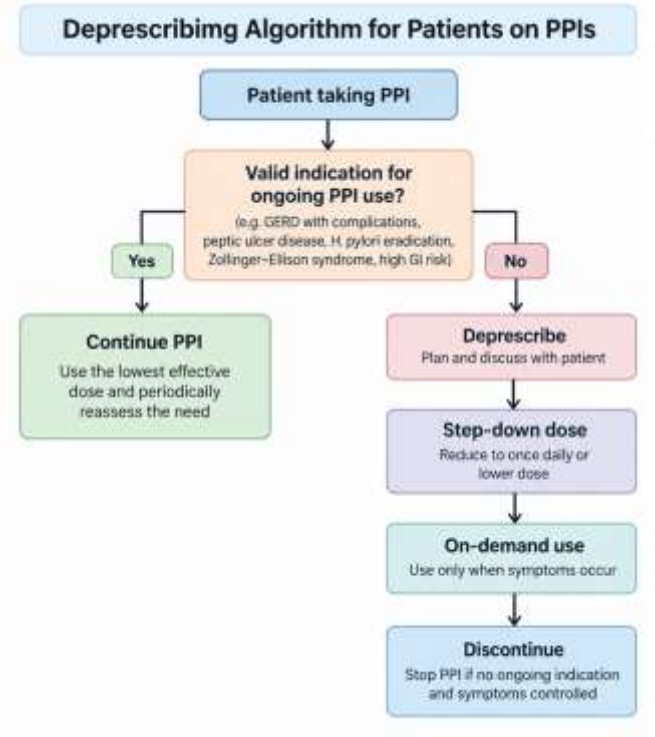


**Figure 7. Deprescribing Algorithm**

The proper usage and deprescribing of PPIs are currently covered by a number of regional and international recommendations. In 2022, the American Gastroenterological Association (AGA) released a clinical practice update on deprescribing PPIs, offering clinicians best practice recommendations. Key recommendations include: (1) all patients taking PPIs should have a regular review of the ongoing indication for use; (2) patients without a definitive indication for chronic PPI therapy should be considered for a trial of deprescribing; (3) most patients on twice-daily dosing should be considered for step-down to once-daily dosing; and (4) patients with complicated GERD, Barrett's esophagus, eosinophilic esophagitis, or idiopathic pulmonary fibrosis should generally not be considered for deprescribing [48].

A 2026 Southeast Asian consensus on rationalizing PPI use was created by an expert working group comprising Malaysia, Thailand, Singapore, Vietnam, the Philippines, and Indonesia. The consensus included 20 recommendation statements that addressed indication-based prescribing, deprescribing strategies specific to Southeast Asia, and the extent and impact of inappropriate PPI use[49].Given the shared characteristics in South and Southeast Asian healthcare systems, prescription practices, and regulatory frameworks, this consensus's recommendations are quite applicable to the Indian context, even though India was not a participant nation.The consensus emphasized the importance of education, electronic prescribing support, and periodic prescription review as pillars of PPI stewardship [49].

Randomized controlled trials have assessed deprescribing strategies at the clinical practice level. Fournier et al. (2026) evaluated a patient- and general practitioner-facing intervention in primary care through a cluster randomized clinical trial and showed that it was successful in lowering the use of inappropriate PPIs [50]. A systematic review of PPI deprescribing interventions in primary care concluded that these interventions are feasible and potentially effective, particularly low-cost educational strategies based on shared decision-making [51]. These findings provide an evidence base for implementing deprescribing programs in the Indian primary care context.

**7.2 Region-Specific Initiatives**

Expert panels in India have examined global guidelines and offered suggestions tailored to India about the prudent use of PPIs, which have been published in the Journal of the Association of Physicians of India [21]. These recommendations, while not yet widely adopted, represent an important step toward context-sensitive guidance for Indian prescribers. The Central Drugs Standard Control Organisation (CDSCO) has issued drug safety alerts regarding PPI-associated adverse effects, including kidney injury, through the Pharmacovigilance Programme of India (PvPI), which has identified India-specific safety signals and issued alerts to healthcare professionals [33,52].

Since 2013, the Indian Council of Medical Research (ICMR) has funded antimicrobial resistance surveillance networks. The development of PPI stewardship programs can benefit from the lessons learned from these programs about implementation science, surveillance techniques, and stewardship infrastructure[53]. However, dedicated PPI stewardship or medication stewardship programs remain rare in Indian healthcare institutions, representing a significant gap in the system's capacity to address medication overuse.

### 7.3 Proposed Framework for India

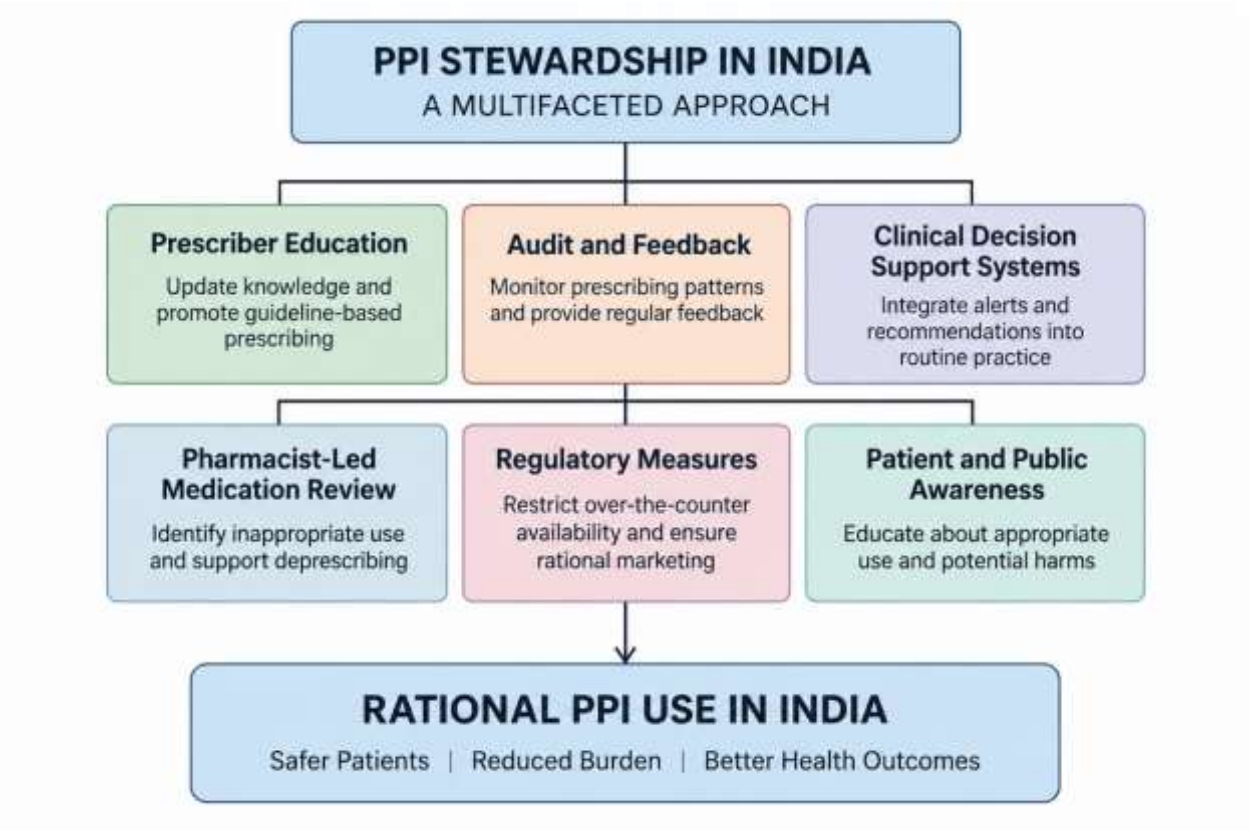


**Figure 8. Proposed Indian PPI Stewardship Framework**

Based on the evidence reviewed, a comprehensive, multi-pronged framework for addressing PPI overuse in India should encompass the following elements. First, at the prescriber education level, specific educational interventions with a focus on evidence-based PPI indications, appropriate dosing and duration, recognition of adverse effects, and deprescribing principles should be incorporated into undergraduate and graduate medical curricula, continuing medical education programs, and hospital induction procedures.Second, hospitals should mandate prescription indications for all PPI orders at the institutional level. Electronic clinical decision support systems should be used to encourage prescribers to record the indication, offer evidence-based substitutes in the absence of a clear indication, and identify patients who are taking PPIs for longer than recommended periods of time for medication review.

Third, pharmacist-led drug review systems ought to be created, utilizing clinical pharmacists' knowledge to spot PPI prescriptions that aren't suitable at the point of dispensing and advise prescribers to deprescribe. Fourth, structured deprescribing protocols should be developed and implemented, incorporating the AGA best practice advice and the Southeast Asia consensus recommendations, adapted to the Indian clinical context. These protocols should include stepwise dose reduction, on-demand therapy as an alternative to continuous therapy, and scheduled reassessment of the ongoing need for treatment.

Fifth, regulatory measures should be strengthened to restrict OTC access to PPIs, reclassify all PPI formulations as Schedule H1 or Schedule X drugs to ensure mandatory prescription requirements, and enhance enforcement at the retail pharmacy level. Sixth, public awareness programs should be created to inform people on the proper use of PPIs, the possible dangers of prolonged use, and the significance of seeking medical advice before starting or continuing PPI therapy. In order to provide the data required for

continuous monitoring and assessment of stewardship initiatives, national-level surveillance of PPI prescribing trends and adverse outcomes should be implemented, building on the current PvPI infrastructure.

## 8. Conclusion and Future Directions

The increasing amount of information showing that PPI usage is a serious public health issue in India has been summarized in this narrative review. Inappropriate PPI prescribing rates, which range from 33% to 91%, are regularly reported in hospital-based studies. These rates are caused by a combination of prescriber, system, patient, and regulatory factors. Although there are the limitations of the evidence base that call for cautious interpretation, observational evidence and mechanistic plausibility strongly support the clinical consequences of unjustified PPI exposure, such as increased risks of enteric infections, renal injury, bone fractures, and nutritional deficiencies.PPI misuse has a significant economic impact; in Indian hospital settings, these drugs can account for up to 20% of outpatient prescribed medication costs, a significant portion which can be attributable to misuse of these medications.

A coordinated, multi-stakeholder strategy that incorporates prescriber education, institutional stewardship initiatives, regulatory reform, patient involvement, and national surveillance is necessary for the future. The Southeast Asia consensus on PPI rationalization, which was just released, offers a useful model that can be modified and extended for the Indian setting. Large-scale, multi-center epidemiological studies to measure the national prevalence of PPI overuse across various healthcare settings, pragmatic randomized trials of deprescribing interventions adapted to the Indian healthcare context, pharmacoeconomic analyses to measure the complete economic impact of PPI overuse at the national level, and implementation science research to determine the best ways to incorporate evidence-based prescribing recommendations into routine clinical practice in India should all be priorities for future research.

The ultimate objective is to ensure that the significant therapeutic benefits of PPIs are realized in a way that minimizes avoidable harm and optimizes the allocation of limited healthcare resources, rather than to deny patients access to effective and frequently necessary therapy for legitimate acid-related disorders. In addition to offering a significant chance to fortify the culture of rational prescription within the Indian healthcare system, achieving this balance will want persistent dedication from physicians, educators, legislators, regulators, and patients alike.

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