Alimentary Pharmacology & Therapeutics

Changing perceptions and practices regarding aspirin, nonsteroidal anti-inflammatory drugs, and cyclooxygenase-2 selective nonsteroidal anti-inflammatory drugs among US primary care providers

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SUMMARY

Background
Our understanding of the benefits and risks of aspirin non steroidal anti-inflammatory drugs (NSAIDs), cyclooxygenase-2 (COX-2) selective NSAIDs and gastro-protective agents (GPAs) continues to expand.

Aim
To assess the perceptions and practices of US primary care physicians (PCPs) regarding the use of aspirin, NSAIDs, COX-2 selective NSAIDs and GPA.

Methods
A 34-question survey was administered to 1000 US PCPs via the internet. Questions addressed issues involving aspirin, NSAIDs, COX-2 selective NSAIDs, and GPAs. Around 491 of 1000 PCPs had participated in a similar survey conducted in 2003.

Results
Eighty-five per cent of PCPs reported that >25% of their patients were taking aspirin for preventive reasons. Nineteen per cent performed a risk calculation when deciding whether to start aspirin for cardioprotection. Fifty-four per cent recommended a proton pump inhibitor (PPI) for a patient with a recently healed ulcer who required ongoing aspirin. Thirty-one per cent reported prescribing NSAIDs more often and 52% were more likely to recommend a GPA with an NSAID than in 2003. Although PCPs were less likely to recommend a COX-2 selective NSAID compared to 2003, only 41% felt that rofecoxib increased cardiovascular risk. One-third felt that celecoxib and traditional NSAIDs were associated with increased cardiac risk.

Conclusion
This survey identified several areas of ongoing confusion regarding aspirin, NSAIDs, COX-2 selective NSAIDs and GPAs, which should help direct future educational efforts regarding the benefits, risks and appropriate use of these agents.

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INTRODUCTION

Nonsteroidal anti-inflammatory drugs (NSAIDs) including aspirin are the most widely used drugs in the world. Prescribed by physicians and purchased by consumers over the counter, it is estimated that millions of people take these drugs on a daily basis.[1] In addition to NSAID use for pain control, aspirin is commonly used for cardioprotection,[2, 3] as well as chemoprophylaxis for a number of malignancies.[4–6] Serious adverse events, ranging from dyspepsia to upper and lower gastrointestinal (GI) bleeding, perforation and obstruction, have been attributed to NSAID or aspirin use.[7–12] Cyclooxygenase-2 (COX-2) specific inhibitors (COX-2 selective NSAIDs) provide an alternative to nonselective NSAIDs that confer a reduced risk for serious GI toxicity.[13–16] However, the withdrawal of two COX-2 selective NSAIDs from the US market and failure to approve two others primarily for reasons of cardiovascular (CV) safety,[17–20] have negatively impacted the prescription of COX-2 selective NSAIDs and have drawn attention to the use of gastroprotection concomitant with NSAID use.[21]

Primary care physicians (PCPs) are responsible for the largest proportion of NSAID prescriptions. However, incorporation of new information by healthcare providers in this area, which is undergoing rapid data accrual, can be slow and is subject to influence from promotional efforts of the pharmaceutical industry, which not only target prescribers, but aggressively market directly to consumers. The recognition of adverse CV events associated with COX-2 selective NSAIDs has led to confusion regarding the use of these medications in patients with increased GI and/or CV risk. Uncertainty also remains regarding the appropriate use of low dose aspirin and NSAIDs.

There has been a rapid evolution of information addressing the use of aspirin, NSAIDs, COX-2 selective NSAIDs and gastroprotective agents (GPAs). As such, it is important to identify those areas in which PCPs need further education. In 2003, we surveyed 1000 US PCPs to assess their perceptions and prescribing habits as they pertain to these agents.[22] That survey identified multiple areas of misinformation regarding the risk-benefit of NSAIDs and aspirin as well as appropriate utilization of gastroprotective strategies. For example, a majority of PCPs felt that enteric coating reduced the risk of adverse GI events. In addition, at the time of our original survey, PCPs recommended a COX-2 selective NSAID in a patient requiring an NSAID over 40% of the time. There was confusion about the interaction between aspirin and COX-2 selective NSAIDs and the use of gastroprotection in patients at increased risk for GI adverse events who required ongoing treatment with an NSAID or aspirin.

In light of changes in COX-2 selective NSAID availability in the US and new data on indications and the safety of aspirin and NSAIDs, we conducted a follow-up survey to assess current perceptions on the safety and appropriate use of these drugs.

METHODS

A 34 question survey was independently developed by a group of academic physicians and was administered via the internet to US PCPs. PCPs who participated in the 2003 survey[22] were first targeted for enrolment in this survey. Of the original 1000 participants, 491 PCPs enrolled in the 2006 survey. An additional 509 PCPs were recruited to achieve a final sample of 1000. Roughly half of the questions were present on both surveys.

Study population

To be eligible to participate in the study, participants must have been a general practitioner, family practitioner or internist in the US for at least two but no more than 35 years. Physicians who spent more than 50% of their time in a teaching capacity were not eligible for participation. The PCPs were accessed via a panel provided by a professional Internet survey research organization (Ziment, New York, NY, USA). A fee of $25 was offered for completing the survey. Funding for the services provided by the survey research organization and participant honoraria were provided by TAP Pharmaceuticals (Chicago, IL, USA), who otherwise played no role in the design, interpretation or reporting of the results.

Survey administration

The specific survey questions are available in an Supporting information. Participants had to complete each question in sequence before proceeding to the next. Once a question was completed and participants proceeded to the next question, they could not go back and change an answer to a previous question. Participants were neither encouraged nor discouraged to use reference materials when completing the survey.

Questionnaire content

Aspirin related-issues. Questions investigated the attitudes of PCPs regarding the use of aspirin as a primary and secondary cardioprotective agent. The PCPs were queried on how often and at which dose they recommend aspirin for cardioprotection. We asked whether they felt that buffering or enteric coating of aspirin reduced the risk of serious adverse GI outcomes. We attempted to understand how they weighed the risks and benefits of low dose aspirin when considering such therapy in an individual patient. We further attempted to gauge how often they recommend a GPA in patients taking low dose aspirin with or without a traditional NSAID or COX-2 selective NSAID. We also questioned them on the negative effects of some traditional NSAIDs on the antiplatelet effects of aspirin and the impact of aspirin therapy on the GI safety benefits of the COX-2 selective NSAIDs.

NSAIDs/COX-2 selective NSAIDs. We asked participants how often they recommended traditional NSAIDs and COX-2 selective NSAIDs. In addition, we assessed their use of GPAs including PPIs, histamine H_2-receptor antagonists (H_2RAs) and misoprostol in patients using these agents. We assessed whether they felt that COX-2 selective NSAIDs as a class, specific COX-2 selective NSAIDs or traditional NSAIDs were associated with an increased risk of myocardial infarction. We questioned about the potential interaction between *Helicobacter pylori* infection and NSAIDs. We also queried whether they felt that traditional NSAIDs were associated with an increased risk of lower GI bleeding. We assessed their perceptions regarding the comparative risk of adverse GI outcomes in patients using traditional NSAIDs vs. COX-2 selective NSAIDs.

Hypothetical patient scenarios. We presented participants with a series of hypothetical patient scenarios as outlined below:

A patient with a history of an ulcer-related upper GI bleed who needs to be on antiplatelet therapy for secondary prevention of coronary artery disease (CAD).

A patient with an acute *H. pylori*-negative, NSAID-associated gastric or duodenal ulcer.

A patient with a recently healed *H. pylori*-negative, NSAID-associated ulcer, who requires an NSAID for joint pain.

A person with a history of previous myocardial infarction, but no previous or current GI problems, who requires low-dose aspirin for cardioprotection and an NSAID for arthritis-related pain.

A patient with a history of an ulcer-related upper GI bleed who requires low dose aspirin for a history of CAD and an NSAID for joint pain.

For each patient scenario, study participants were presented with a series of clinical choices, which varied based upon the specific case characteristics. The specific case scenarios and potential answers can be found in the Supporting information.

Statistical analysis

Descriptive statistics were employed to characterize the survey responses. Comparisons between subgroups of the study sample (gender-, age- and region-based comparisons) were performed using the chi-squared test (QUANTUM software; SPSS, Chicago, IL, USA). In situations where answers to a question created a continuous variable, a Student's *t*-test was utilized. A *P*-value of <0.05 defined a statistically significant difference between groups. When present, significant differences in the data based on the gender, age and region of residence are mentioned in the results section.

RESULTS

Survey participant demographics

A geographically diverse cohort of 1000 PCPs completed the on-line survey anonymously from 9 October through 17 October, 2006. Demographics of PCPs were similar in both surveys. Over 70% of participants were between the ages of 35 and 54 years. Approximately 80% of the survey sample was male (Table 1). The geographic distribution of our sample was diverse with representation from 40 of the 50 states of the US. Sixty-three per cent of PCPs reported that they were part of a group practice, 28% were in solo private practice, and 9% were in partnerships. Thirty-four per cent of PCPs practiced in communities of 100–500 K. Another 25% practiced in metropolitan areas of >500 K. When asked about payer mix, mean responses were as follows: 23% HMO, 22% PPO, 10% POS, 26% Medicare, 8% Medicaid, 6% Other insurance and 5% No insurance.

We initially analysed answers from PCPs who participated in the 2003 and current surveys separately

Table 1. Primary care physician demographic information

	2003 Participants	2006 Participants
General practitioner	54	35
Family practitioner	465	485
Internist	481	480
Gender		
Male	80%	81%
Female	20%	19%
Physician age		
<35	10%	2%
35–44	35%	33%
45–54	38%	42%
55–64	14%	23%
>65	1%	1%

from PCPs who only participated in the current survey. However, because the answers between the two groups of respondents were statistically similar, we have chosen to present data for the pooled population of 1000 PCPs.

Questionnaire results

Aspirin related-issues. Eighty-five per cent of PCPs felt that more than a quarter of their patients were taking aspirin for prevention of CAD, stroke or other indications such as prevention of colon cancer. Forty-one per cent reported that more than half of their patients were taking aspirin to prevent these conditions. When asked how often they recommended aspirin as primary preventive therapy for myocardial infarction in persons over 60 years, 42% of PCPs responded 'always' while 46% responded 'most (>50%) of the time'. This represented a change from 2003 when 66% PCPs stated that they 'always' recommended aspirin for the same type of patient. We found that despite national guidelines to the contrary, 81% of PCPs do not perform a formal CV risk calculation prior to initiating aspirin therapy (Figure 1). We noted some improvement in the understanding of the risks associated with aspirin and strategies to reduce that risk. In 2003, 69% recommended 81 mg of aspirin as the preferred dosage; this increased to 82% in the current survey. Fifteen per cent of PCPs continued to recommend 325 mg of aspirin per day for cardioprotection (Figure 2). Forty-six per cent of PCPs felt that less than a quarter of their patients taking aspirin were also taking a GPA. An additional 39% of PCPs

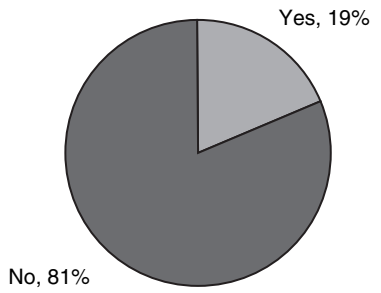

Figure 1. Response to the question: 'When you are deciding whether a patient needs aspirin for primary prevention of coronary artery disease, do you perform a formal 'risk calculation' – for example, as available on the internet?'.

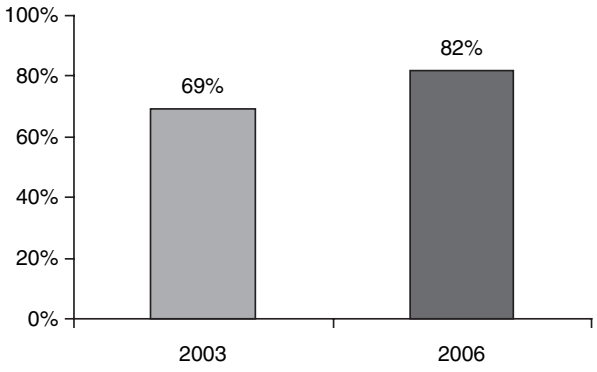

Figure 2. Percentage of primary care physicians recommending 81 mg vs. 325 mg ASA for cardioprotection.

felt that between 25% and 49% of their patients taking aspirin were taking a GPA. When the scenario was changed to a patient taking both aspirin and an NSAID, PCPs were more inclined to recommend gastroprotection. In fact, only 11.5% felt that less than a quarter were taking gastroprotection while 55% felt that more than half of their patients taking aspirin and an NSAID were using a concomitant GPA. Sixty-one per cent of PCPs surveyed believe that enteric coating or buffering of aspirin reduces the risk of developing a serious upper GI bleeding event compared to uncoated and un-buffered aspirin. This result remained virtually unchanged from 2003 when 59% of PCPs responded in kind to the same question.

The current survey also addressed PCPs' perceptions regarding the potentially disruptive effect of specific NSAIDs on the antiplatelet effect of aspirin. Eighty-eight per cent were aware that some NSAIDs can

interfere with the antiplatelet effect of aspirin. Among NSAIDs, PCPs were most concerned with ibuprofen's impact on the antiplatelet effect of aspirin. Sixty-two per cent of respondents recognized this important drug interaction. Despite evidence to the contrary, 53% and 33% of PCPs felt that naproxen and celecoxib also interfered with the antiplatelet effect of aspirin. Eight per cent of respondents felt that none of these agents interfered with aspirin and 15% responded that they did not know whether such an interaction existed.

Regarding the potential impact of aspirin on the GI safety benefits of the COX-2 selective NSAIDs, 65% were aware that concurrent aspirin use reduced the GI safety benefit of the COX-2 selective NSAIDs. This was very similar to 2003 when 69% of PCPs were aware of this drug interaction. Twenty-five per cent and 23% of respondents in 2003 and in the current survey respectively felt that concurrent aspirin therapy had no effect on the GI safety benefit of the COX-2 selective NSAIDs.

NSAIDs/COX-2 selective NSAIDs. Thirty-one per cent of PCPs reported that they prescribe NSAIDs more commonly now than in 2003, while 21% felt they prescribed NSAIDs less commonly. Fifty-four per cent felt that different traditional NSAIDs were associated with differences in the likelihood of causing ulcers and complications such as bleeding while 40% of respondents that all traditional NSAIDs carried the same risk of ulcers and bleeding. Fifty-two per cent reported that they were more likely to recommend a GPA in patients taking an NSAID. Ninety per cent of PCPs felt that COX-2 selective NSAIDs offered improved GI safety compared to traditional NSAIDs. In fact, PCPs most commonly identified the potential GI safety benefits offered by a COX-2 selective NSAID as the most important reason they chose such an agent over a traditional NSAID. Fifty-nine per cent of PCPs reported that they prescribed COX-2 selective NSAIDs less frequently than in the 2003. In the 2003 survey, COX-2 selective NSAIDs accounted for 43% of all NSAID recommendations, whereas in the current survey, COX-2 selective NSAIDs accounted for only 25% of NSAID recommendations (Figure 3).

Regarding COX-2 selective NSAIDs, NSAIDs and CV safety, we found that 41% of PCPs felt that rofecoxib was associated with a higher risk of MI compared with not taking an NSAID, while 41% felt that there was no increased risk of MI and 18% responded 'don't know'. For celecoxib, 32% felt there was an increased risk of MI compared to not taking an NSAID, while 53% felt there was no increased risk of MI and 15% did not know. Despite the fact that more than half of PCPs felt there was no increased CV risk with celecoxib, 57% reported that concerns regarding CV risk influence their willingness to prescribe celecoxib. Thirty-five per cent of PCPs felt that traditional NSAIDs were associated with increased CV risk, while 49% did not believe this to be so and 16% did not know.

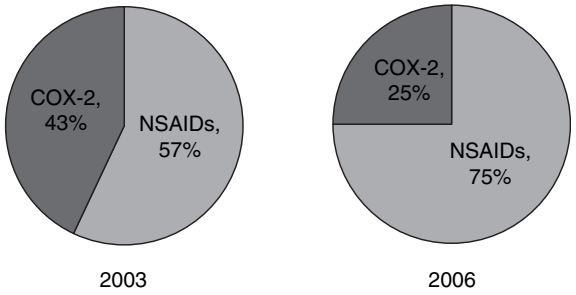

Figure 3. Response to the question: 'What percent of the NSAID prescriptions that you prescribe are traditional NSAIDs and what percent are COX-2 selective agents?' $P = 0.005$, comparison of COX-2 selective nonsteroidal anti-inflammatory drug between 2003 and 2006.

Seventy-one per cent of PCPs were aware that *H. pylori* infection increases the risk of developing an ulcer in patients taking an NSAID. This was similar to 2003 when 78% of PCPs reported being aware of the additive ulcer risk of *H. pylori* infection and NSAID use. Eighty per cent of PCPs rarely or never tested their patients for *H. pylori* before starting an NSAID. Seventy-eight per cent rarely or never tested their patients already taking an NSAID for *H. pylori*. Both values were virtually identical to responses offered to the same questions in the 2003 survey.

Seventy-five per cent of PCPs felt that NSAIDs increased the risk of lower GI bleeding. In 2003, 76% were aware of this fact. Similar to 2003, roughly a third of PCPs continued to feel that most patients with an NSAID-associated ulcer bleed experienced antecedent dyspeptic symptoms.

Hypothetical patient scenarios. A patient with a history of an ulcer-related upper GI bleed who needs to be on antiplatelet therapy for secondary prevention of CAD.

Fifty-four per cent of PCPs chose to initiate gastroprotective therapy with an over the counter (OTC) (23%) or prescription (31%) PPI in this patient. Twenty-six per cent chose to replace aspirin with clopidogrel, while another 12% chose to use enteric-coated aspirin alone. Less than 5% chose co-therapy with an H_2RA or misoprostol.

A patient with an acute *H. pylori*-negative, NSAID-associated gastric or duodenal ulcer.

For this patient, 95% of PCPs chose to use an OTC PPI (12%) or prescription PPI q.d.s. (58%) or b.d. (24%).

A patient with a recently healed *H. pylori*-negative, NSAID-associated ulcer, who requires an NSAID for joint pain.

Eighty-eight per cent of PCPs chose gastroprotective therapy with an OTC (22%) or prescription (q.d.s. = 55%, b.d. = 11%) PPI. Eight per cent chose to start this patient on an H_2RA or misoprostol and 2% recommended no gastroprotective therapy.

A person with a history of previous myocardial infarction, but no previous or current GI problems, who requires low dose aspirin for cardioprotection and an NSAID for arthritis related pain.

Thirty-nine per cent of PCPs recommended no gastroprotective therapy for this patient. Twenty-seven per cent chose to start this patient on an OTC or prescription PPI while 8% chose co-therapy with an H_2RA. Interestingly, despite aspirin's deleterious effects on the GI safety benefits associated with a COX-2 selective NSAID, 26% of PCPs chose to replace the traditional NSAID with a COX-2 selective NSAID either without (16%) or with (10%) a PPI.

A patient with a history of an ulcer-related upper GI bleed who requires low dose aspirin for a history of CAD and an NSAID for joint pain.

For this very high-risk patient, 44% of PCPs recommended gastroprotective therapy with a PPI (OTC = 15%, prescription = 28%). Forty-one per cent chose to give a PPI and COX-2 selective NSAID in place of the traditional NSAID. Six per cent and 4% chose an H_2RA or misoprotol for this patient, respectively. Five per cent stated that they would treat with aspirin and a traditional NSAID alone.

DISCUSSION

Our survey of US PCPs identified a number of areas of improving knowledge regarding the use of aspirin, traditional NSAIDs, COX-2 selective NSAIDs and gastroprotective strategies. For example, we were encouraged that a substantial proportion of PCPs are recommending aspirin for cardioprotection. We were also pleased to find that a significantly larger percentage of PCPs in the current survey were recommending 81 mg vs. 325 mg of aspirin for cardioprotection when compared to 2003. A recent systematic review found that higher doses of aspirin did not provide improved cardioprotection compared to 70–85 mg/day, but were associated with a higher incidence of GI adverse events.[23] Further, most PCPs correctly identified that NSAIDs and *H. pylori* are independent risk factors for peptic ulcer disease (PUD)[24] and that NSAIDs could cause lower GI as well as upper GI bleeding.[25] We were pleased that a majority of PCPs were aware of the potential drug interactions between aspirin and COX-2 selective NSAIDs. As the CLASS (Celecoxib Long Term Arthritis Safety Study) trial originally taught us and subsequent studies have confirmed, concomitant aspirin therapy reduces or eliminates the GI safety benefits of COX-2 selective NSAIDs.[15, 26] We were also impressed that most PCPs were aware of the potentially deleterious effects of ibuprofen on the antiplatelet effect of aspirin.[27, 28]

At the same time, our survey clearly identified a number of areas of confusion regarding the use of these agents. While it is encouraging that the vast majority of PCPs reported using the lower dose of aspirin for cardioprotection, it is noteworthy that one in seven PCPs continue to recommend 325 mg of aspirin for this indication. It is also important to note that more than 80% of PCPs surveyed continue to prescribe aspirin for primary prophylaxis of CAD without any formal risk calculation (Figure 2). While the benefits of aspirin clearly outweigh the risks for secondary prevention of CAD,[3, 29] the determination of risk-benefit for aspirin in the setting of primary prevention is more complicated. National guidelines from the American Heart Association have recommend aspirin for those with a 10 years event risk of >10% for primary prevention, while the US Preventive Services Task Force is less conservative, recommending cardioprotection in individuals with a 10 year event risk exceeding 6%.[2, 3] Formal risk calculation helps clinicians balance the CV benefits with the increased risk of significant GI bleeding and haemorrhagic stroke that can complicate therapy with low-dose aspirin.[30–34] The lack of a formal risk calculation before recommending aspirin makes it likely that a substantial number of patients are being exposed to the risks of aspirin in exchange for only a low likelihood of benefit.

Another area of considerable concern pertaining to aspirin concerns the scenario in which a patient with a history of previous ulcer bleeding required low dose aspirin for cardioprotection. We were surprised that only 54% of PCP respondents recommended gastroprotection with a PPI for this patient at high risk for an adverse GI outcome. On the other hand, almost 90% of PCPs recommended gastroprotection in a patient with a recently healed ulcer who needed aspirin for cardioprotection and an NSAID for joint pain. Presumably, the disparity in results yielded by the two scenarios reflects less concern when treating with only low dose aspirin. It is important to realize that patients with a history of ulcer bleeding have a remarkably increased risk of ulcer recurrence and rebleeding in the face of ongoing aspirin therapy without gastroprotective therapy.[35] In a randomized, controlled trial, Lai *et al.*[36] reported a 15% risk of recurrent ulcer bleeding at 1 year in patients with a history of ulcer bleeding who were replaced on aspirin and placebo vs. <2% for patients randomized to aspirin and lansoprazole 30 mg/day. Our results provide some of the first such data from the US and confirm a recent study from Manitoba, Canada which found that gastroprotective PPI therapy was prescribed in only 56% of patients with a history of an upper GI complication taking aspirin.[37]

Another point worthy of discussion has to do with PCP perceptions of reducing the risk of GI adverse events through the use of enteric-coated or buffered aspirin. Similar to results obtained in our previous 2003 survey, we found that 66% of PCPs felt that enteric-coated or buffered aspirin decreased the risk of upper GI bleeding compared to plain aspirin. In fact, for the scenario in which a patient with previous ulcer bleeding required ongoing aspirin therapy for cardioprotection, 12% of PCPs chose to replace plain aspirin with enteric-coated aspirin rather than provide one of the more evidence-based gastroprotective strategies. The literature has shown that the risk of upper GI bleeding associated with enteric-coated or buffered aspirin is similar to that of plain aspirin.[38–40]

In the current survey, it was uncommon for PCPs to recommend gastroprotection in patients without a previous history of ulcer bleeding. For example, in a patient who required both aspirin and an NSAID, only a quarter of PCPs recommended gastroprotection with a PPI. This practice does not reflect recent studies, which have shown that the addition of aspirin to an NSAID significantly increases the risk of GI toxicity.[14, 30, 38, 41, 42]

In contrast, for a patient with a previous history of ulcer bleeding who needed both aspirin for cardioprotection and an NSAID for joint pain, a higher proportion of physicians recommended gastroprotection with a PPI. In the corresponding case scenario, 85% of PCPs said they would add a PPI to aspirin and an NSAID. It is noteworthy that within this group, approximately half of the PCPs stated that they would actually switch the patient from a traditional NSAID to a COX-2 selective NSAID in addition to recommending a PPI (Figure 4). It was interesting that such a large proportion of PCPs still recommended a COX-2 selective NSAID in a patient who needed aspirin for cardioprotection, given that COX-2 selective NSAIDs have been strongly associated with dose related increased CV risk.[18, 19, 43]

We found that perceptions of COX-2 selective NSAIDs have changed since 2003. Fifty-nine per cent of

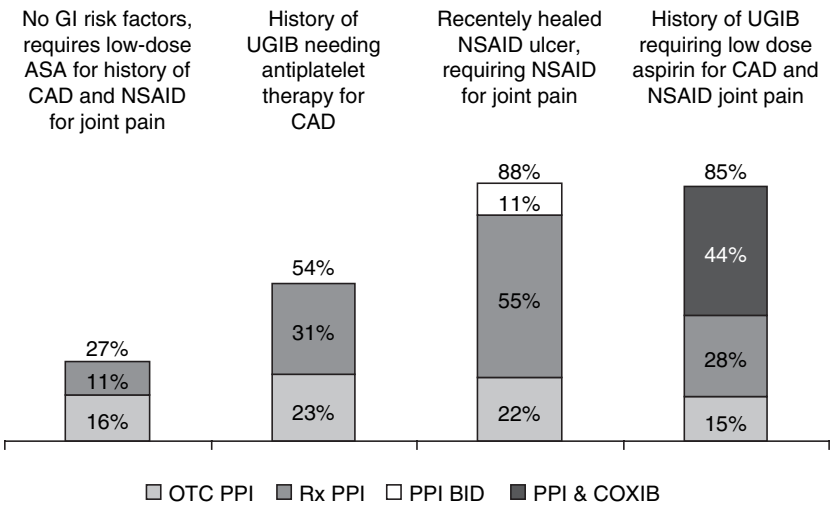

Figure 4. Percentage of primary care physicians recommending proton pump inhibitor for various scenarios. ASA, aspirin; CAD, coronary artery disease; UGIB, upper gastrointestinal bleed.

PCPs reported that they prescribe COX-2 selective NSAIDs less frequently when compared to 2003. In addition, COX-2 selective NSAIDs which accounted for over 40% of NSAID recommendations in 2003 accounted for only 25% in the current survey. We presume that this change in utilization was largely driven by increased concerns regarding the CV safety of these agents and/or fear of litigation resulting from recommending a COX-2 selective NSAID. In fact, over 40% of PCPs felt that rofecoxib was associated with an increased risk of MI. However, despite an ever growing body of literature supporting this association,[19, 44] we were surprised to find that over 40% of PCPs did not feel that rofecoxib was associated with an increased risk of MI compared with not using an NSAID. Reflecting the confusion in the available literature,[19, 44] over 50% of PCPs did not feel that that celecoxib was associated with an increased risk of MI. This result was similar to the percentage of PCPs who were aware of recent literature suggesting that some traditional NSAIDs may be associated with an increased risk of cardiac events.[19, 45]

Whether the increased risk of adverse CV events with COX-2 selective NSAIDs and traditional NSAIDs is drug-specific or represents a class effect remains controversial. On the basis of meta-analyses, naproxen appears to be differentiated from other traditional NSAIDs across the CV risk spectrum.[20] Part of the mechanism of adverse events may be related to blockade of aspirin's access to the platelet COX enzyme sterically by certain NSAIDs, but not COX-2 selective NSAIDs. This information appeared to be poorly understood by our survey respondents, as 53% and 33% felt that naproxen and celecoxib respectively interfered with the antiplatelet effects of aspirin.

One of the main strengths of our study was the large, geographically diverse group of PCPs who participated in the survey. The fact that roughly half of the questions we asked were the same as in our previous study and that nearly half of the study cohort also participated in our previous survey, allowed us to perform meaningful comparisons in practice patterns at two points in time. However, as with any survey, there were a number of limitations. First, the PCPs were recruited via e-mail which probably increased the likelihood of recruiting younger physicians. For example, only 1% of our participants in both surveys were above 65 years old but, according to the American Medical Association, 18% of physicians are above 65 years old. Because of recently imposed recertification standards, which preferentially affect younger physicians, we speculate that younger physicians are more likely to be aware of recently published medical literature. Another limitation is that we do not have demographic information about PCPs who chose not to participate in our study. The construct of the survey did not allow participants to return to a question to change an answer once completed. We feel that this limited the influence of questions appearing later in the survey on answers to questions appearing earlier in the survey. However, the use of reference materials when answering survey questions was neither encouraged or discouraged in the participant instructions. That being said, the use of reference materials by participants would be expected to have inflated the proportion of 'correct' answers to our questions.

In conclusion, our survey identified a number of areas of improving knowledge regarding PCP knowledge and use of aspirin, traditional NSAIDs, COX-2 selective NSAIDs and GPAs. In addition, our survey identified a number of areas in need of further education regarding the use of these agents. In particular, ongoing education regarding CV risk calculation when deciding upon the need for low dose aspirin therapy, the hazards associated with low dose aspirin therapy in patients at increased risk for adverse GI outcomes and a better understanding of GI risk stratification and the appropriate use of risk reduction strategies in patients using NSAIDs and COX-2 selective NSAIDs appears to be warranted.

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Pharmaceuticals. The authors take full responsibility for writing and editing this manuscript.

SUPPORTING INFORMATION

Additional Supporting Information may be found in the online version of this article:

Appendix S1. Nonsteroidal anti-inflammatory drug usage analysis study main questionnaire

Please note: Wiley-Blackwell are not responsible for the content or functionality of any supporting materials supplied by the authors. Any queries (other than missing material) should be directed to the corresponding author for the article.

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