Contextualizing National Policies Regulating Access to Low-Dose Aspirin in America and Europe Using the Full Report of a Transatlantic Patient Survey of Aspirin in Preventive Cardiology

Alan P. Jacobsen, MB, BCh, BAO; Zi Lun Lim, MB, BCh, BAO; Blair Chang, BA; Kaleb D. Lambeth, MD; Thomas M. Das, MD; Colin Gorry, MB, BCh, BAO; Michael McCague, MSc; Faisal Sharif, MB, BCh, BAO, PhD; Darren Mylotte, MB, BCh, BAO, PhD; William Wijns, MD, PhD; Patrick W. J. C. Serruys, MD, PhD; Roger S. Blumenthal, MD; Seth S. Martin, MD, MHS; John W. McEvoy, MB, BCh, BAO, MHS

BACKGROUND: Aspirin is widely administered to prevent cardiovascular disease (CVD). However, appropriate use of aspirin depends on patient understanding of its risks, benefits, and indications, especially where aspirin is available over the counter (OTC).

METHODS AND RESULTS: We did a survey of patient-reported 10-year cardiovascular risk; aspirin therapy status; form of aspirin access (OTC versus prescription); and knowledge of the risks, benefits, and role of aspirin in CVD prevention. Consecutive adults aged ≥50 years with ≥1 cardiovascular risk factor attending outpatient clinics in America and Europe were recruited. We also systematically reviewed national policies regulating access to low-dose aspirin for CVD prevention. At each site, 150 responses were obtained (300 total). Mean±SD age was 65±10 years, 40% were women, and 41% were secondary prevention patients. More than half of the participants at both sites did not know (1) their own level of 10-year CVD risk, (2) the expected magnitude of reduction in CVD risk with aspirin, or (3) aspirin’s bleeding risks. Only 62% of all participants reported that aspirin was routinely indicated for secondary prevention, whereas 47% believed it was routinely indicated for primary prevention (P=0.048). In America, 83.5% participants obtained aspirin OTC compared with 2.5% in Europe (P<0.001). Finally, our review of European national policies found only 2 countries where low-dose aspirin was available OTC.

CONCLUSIONS: Many patients have poor insight into their objectively calculated 10-year cardiovascular risk and do not know the risks, benefits, and role of aspirin in CVD prevention. Aspirin is mainly obtained OTC in America in contrast to Europe, where most countries restrict access to low-dose aspirin.

Key Words: aspirin ■ cardiovascular disease prevention ■ guidelines ■ patient understanding ■ regional variation

In contrast to its generally accepted benefit in secondary prevention,1 the role of aspirin in the primary prevention of cardiovascular disease (CVD) is more controversial.2,3 An updated 2019 meta-analysis found that primary prevention aspirin was associated with a small-to-modest benefit in the composite cardiovascular outcome (number needed to treat, 241) driven by a reduction in no-fatal CVD events, which was largely counterbalanced by an increased risk of major bleeding (number needed to harm, 210).4,5
**CLINICAL PERSPECTIVE**

**What Is New?**
- Participants in the United States and Europe lacked insight into both their cardiovascular risk and the indications for aspirin in cardiovascular prevention.
- Greater numbers of primary prevention participants were taking aspirin in the United States than Europe, and most US participants obtained their aspirin over the counter.
- Most countries in Europe require a prescription or pharmacist input to access aspirin.

**What Are the Clinical Implications?**
- If low-dose aspirin for cardiovascular disease prevention is to be continued as an over-the-counter option, greater efforts need be made to better educate both patients and physicians on the role of aspirin in primary and secondary cardiovascular disease prevention; messaging and dissemination of guideline recommendations also need to be clearer and consistent to avoid confusion.
- Primary and secondary prevention patients should be encouraged to discuss their plans to take over-the-counter aspirin with their physician and should also be made aware of their objective cardiovascular risk such that they can make an informed decision.
- Alternatively, consideration could be given in the United States to move to a European model, where access to low-dose aspirin for cardiovascular disease prevention is not over the counter and requires input from a health care professional.

**Nonstandard Abbreviation and Acronym**

**OTC** over the counter

Reflecting the inconclusive evidence base, guideline recommendations on primary prevention aspirin have historically differed on either side of the Atlantic. The 2016 European Society of Cardiology CVD prevention guideline recommended against the use of aspirin for primary prevention (Class 3, harm). The 2019 American College of Cardiology/American Heart Association guideline provided a weak Class IIb endorsement of aspirin for select high-risk primary prevention adults aged 40 to 70 years who are not at high risk for bleeding. Guidelines on both sides of the Atlantic continue to recommend aspirin for secondary prevention. Because of the conflicting evidence and guideline recommendations, patients may have heard mixed messages about aspirin use in primary prevention and, even more concerning, may now be uncertain as to its benefits in secondary CVD prevention.

We conducted a transatlantic survey of patient-reported access to and understanding of aspirin in contemporary preventive cardiology. In a recently published research letter, we reported limited top-line results from this survey. In this full report of the study, we now present the complete baseline demographic and clinical characteristics of the survey sample; more detailed data on participants’ aspirin use; and new results describing patient-reported understanding of the risks, benefits, and indications for aspirin in CVD prevention in addition to patient-reported factors that motivate aspirin use. For the present study, we also added a systematic audit of the various national policies regulating access to low-dose aspirin in Europe.

**METHODS**

**Survey Design, Participants, and Setting**

The data used for this study may be made available upon reasonable request to the corresponding author. We surveyed men and women aged ≥50 years who had ≥1 cardiovascular risk factors. Non-English-speaking and incarcerated individuals were excluded. Taking a convenience sample approach, consecutive eligible participants attending hospital-based cardiology or internal medicine outpatient clinics at 2 sites were invited to participate. No financial incentives were offered to complete the survey. This anonymous survey was administered at a tertiary care academic center in the United States (Johns Hopkins Hospital) and in Europe (National University of Ireland, Galway). The Johns Hopkins School of Medicine Institutional Review Board reviewed the protocol and determined the study to be exempt from ethical approval as responses were anonymized (approval date November 12, 2019; protocol number IRB00220110). For the same reasons, ethics review was waived at the European site.

**Survey Development**

Using cloud-based software, the survey was developed and optimized with 4 objectives in mind: first, to collect sufficient demographic and clinical information to calculate the estimated 10-year risk of future CVD among respondents; second, to collect information on their use of and access to aspirin; third, to assess participants’ understanding of the risks and benefits of aspirin in preventive cardiology; and fourth, to determine patient motivations for aspirin use.

The choice of candidate survey questions pertaining to cardiovascular risk and the risk–benefit profile of aspirin was informed by review of the literature.
The survey was piloted with 10 patients, and questions were refined to improve participant comprehension and to ensure the survey could be completed in <7 minutes. The full survey is available in Data S1.

Survey Data Collection
The survey was administered between November 2019 and September 2020. After approximately one third of the planned responses had been collected from in-person visits, in March 2020 we began completing the survey by phone in conjunction with a widespread shift towards telemedicine at both study centers in response to COVID-19.12 The survey was hosted online (http://www.qualtrics.com; Qualtrics, Provo, Utah) using a secure institutional account.

Review of National Policies Regulating Access to Low-Dose Aspirin in Europe
We conducted an analysis of national policies regulating access to low-dose aspirin in Europe by reviewing the Summary of Product Characteristics of low-dose aspirin from each European country.13 Access to this data was obtained from the national register of authorized medicines for each country, sourced from the European Medicine Agency (Data S2).14,15 Low-dose aspirin was defined as <150 mg daily.

Statistical Analysis
For our sample size estimate (assuming χ² testing at an α level of 0.05 and β of 0.2), we calculated that 300 patients would be needed to determine a >15% difference in the primary outcome. Specifically, the proportion of participants at both sites who answered “yes—routine use of aspirin for CVD prevention is guideline recommended” was compared between question stems that described a primary versus secondary CVD prevention scenario. As we were enrolling half of the participants in the United States where aspirin in primary prevention is common and has historically been endorsed in guidelines and the other half in Europe where aspirin in primary prevention is uncommon and has not been historically endorsed in guidelines, we predicted that ≈50% would respond in the affirmative for aspirin in primary prevention. A conservative estimate of 15% difference for secondary prevention was chosen based on prior studies from similar settings where patient understanding of CVD prevention medications was assessed.16 Demographics and other baseline variables were compared among respondents in the United States versus Europe using the Student t test for normally distributed continuous variables and the Fisher exact test for categorical variables. CIs were estimated using a Wald interval. In the case of non-normal distributions, nonparametric testing was used.

Estimated 10-year CVD risk was calculated using the QRISK3 score.11 QRISK3 has been shown to be comparable with the American College of Cardiology/American Heart Association pooled cohort equation in predicting cardiovascular events17 and, importantly, allowed the CVD risk calculation to be completed using only patient-reported data. This is in contrast to the pooled cohort equation, which requires entry of measured blood pressure and lipid values, which we anticipated many patients would be unable to accurately self-report.18 All patients who reported a history of CVD were allocated a 10-year CVD risk of 20% in continuous analyses or were allocated to the CVD risk ≥10% category in categorical analyses of this data set.19 Although this survey was designed to be descriptive in nature, we did a post hoc analysis to test whether differences in baseline characteristics by study site influenced the following 2 key outcomes of interest: (1) aspirin use (yes/no) among primary prevention participants and (2) form of access (over the counter [OTC] versus prescription) among all participants taking aspirin. To this end we estimated relative risks (RRs) using adjusted robust Poisson regression models. The model testing aspirin use among primary prevention adults was adjusted for age (continuous), sex (binary), education level (categorical), race (categorical), smoking status (categorical), 10-year risk of CVD (QRISK3 score—continuous), diabetes status (binary), stomach acid medication use (binary), oral anticoagulation use (binary), and nonaspirin antiplatelet medicine use (binary). The model testing forms of access among all participants taking aspirin was adjusted for age (continuous), sex (binary), education level (categorical), race (categorical), smoking status (categorical), secondary CVD prevention status (binary yes/no), diabetes status (binary), stomach acid medication use (binary), oral anticoagulation use (binary), and nonaspirin antiplatelet medicine use (binary). Analyses were conducted using R version 4.0.2, and a 2-sided P value of <0.05 was chosen as the cutoff for statistical significance.

RESULTS
Survey Sample Demographics and Baseline Clinical Data
Among all eligible adults who were invited to participate, 25% in the United States and 32% in Europe agreed to complete the survey. In total, 300 complete survey responses were obtained; 150 at each site. Men comprised 60% of the overall sample, and the mean±SD age of the cohort overall was 65±10 years. The mean age of the US group was 68 years and 63 years in the European group. Almost all of the European participants (97%) reported being White race, whereas 39% of US participants reported being Black race (Table 1).
Almost half of the European cohort reported a personal history of CVD compared with 32.7% of the US cohort \((P=0.005)\); however, a greater proportion of the US group reported a personal history of diabetes (36% versus 16%; \(P<0.001\)).

Despite these differences, the mean±SD 10-year CVD risk of the entire sample (ie, both the primary and secondary prevention groups) was 20±9%, and there was no significant difference between US and European participants (US 21% versus Europe 16% \([\text{IQR}, 7–27]; P=0.06\)).

### Aspirin Use

Of the 300 participants overall, 57% reported aspirin use, a proportion that was not significantly different between the US and European cohorts (Table 2). Although a greater percentage of the US primary prevention subgroup was taking aspirin compared with the European primary prevention subgroup (46.5% versus 26.3%; difference 20% \([95\% \text{ CI}, 6\%–34\%]; P=0.008\)), the proportion of individuals who were taking aspirin for secondary prevention at both sites (90% versus 81%;
difference 9% [95% CI, −4% to 21%]; \(P=0.214\) was not statistically significantly different. In regression models among primary prevention participants, aspirin use was less common in Europe versus the United States, but this difference was no longer statistically significant after adjustment for model variables that differed by study site (RR, 0.79 [95% CI, 0.47– 1.34]; \(P=0.39\)).

Participants at both sites were primarily taking low-dose aspirin (75 mg or 81 mg/day). However, 84% of the US group obtained aspirin as an OTC medication. By contrast, almost all of the European group reported obtaining aspirin with a prescription. In regression models among all participants taking aspirin, access to aspirin by prescription was far higher in Europe versus the United States even after adjustment for model variables that differed by study site (RR, 10.57 [95% CI, 6.04–18.51]; \(P<0.001\)). Although 13% of the US group reported a nonstandard dosing regimen, most of the European group were taking aspirin once daily. Almost all of the patients taking aspirin (99%) reported that their primary care physician was aware that they were taking the medication, and most (87.1%) reported that the reason for their aspirin use was to prevent CVD.

### Understanding of CVD Risk

In terms of perceived risk, many participants (54%) self-reported that they did not know or were unsure of their CVD risk for 10 years, with more Europeans (63%) being unsure than Americans (44%); \(P=0.004\). Taking respondents who did self-identify into a perceived CVD risk category, only 19.3% of the entire sample perceived their 10-year CVD risk as ≥10% (noting that 85.7% of the sample were calculated to have actual...
10-year CVD risks ≥10%). Similar findings were seen when stratified into primary and secondary prevention groups (Table 3).

**Aspirin Understanding and Perception**

A significant proportion of the study participants in both the United States and Europe were uncertain about the relative magnitude of benefits (61% unsure) and risks (69% unsure) from taking aspirin for CVD prevention (Table 3). A larger percentage of European participants were unsure than US participants. Of those who felt that they knew the relative magnitude of benefit for aspirin (n=118, 39%), most tended to overestimate the benefits of taking aspirin. Specifically, 77 of the 118 participants (65%) responded that aspirin can lower CVD by more than half, but only 41 participants (35%) reported the more accurate relative reduction in CVD of less than half with aspirin use (noting that meta-analyses report a RR reduction for CVD of ≈10% with aspirin in primary prevention and 15% in secondary prevention).

Furthermore, the majority of participants also either did not know or underestimated the bleeding risks of aspirin. Of those who felt that they knew the relative magnitude of risk for aspirin (n=93, 31%), only 36 (39%) reported the more accurate relative increase in bleeding of more than half with aspirin use (noting that meta-analyses report a RR increase for major bleeding of ≈45%–55% with aspirin).

Among the study sample overall, 47% incorrectly responded that, yes, aspirin was routinely recommended in guidelines for the primary prevention of CVD. Surprisingly, a greater proportion of the US group than the European group (17% versus 9%) answered this correctly by responding “no” to this question. Despite an overall better appreciation for the role of aspirin in secondary prevention, only 62% of all participants reported correctly that aspirin was routinely indicated for secondary prevention, and the vast majority of other responses were “don’t know/not sure.” These results did not differ by location. Finally, the greatest motivation for aspirin use among the majority of participants

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**Table 3. Understanding of Cardiovascular Disease Risk in the Sample, Compared by Location**

|                      | Entire sample | Johns Hopkins Hospital, n=150 | National University of Ireland, Galway, n=150 | P value |
|----------------------|---------------|-------------------------------|---------------------------------------------|---------|
| Actual 10-y CVD risk |                |                               |                                             |         |
| <1 in 10 (<10%)     | 43 (14.3)     | 18 (12.0)                     | 25 (17.7)                                   | 0.323   |
| >1 in 10 (≥10%)     | 257 (85.7)    | 132 (88.0)                    | 125 (83.3)                                  |         |
| Perceived 10-y CVD risk |            |                               |                                             |         |
| <1 in 10 (<10%)     | 81 (27.0)     | 49 (32.7)                     | 32 (21.3)                                   | 0.004   |
| >1 in 10 (≥10%)     | 58 (19.3)     | 35 (23.3)                     | 23 (15.3)                                   |         |
| Don’t know/not sure | 161 (53.7)   | 66 (44.0)*                    | 95 (63.3)*                                  |         |
| Secondary prevention subsample |                |                               |                                             |         |
| Actual 10-y CVD risk |                |                               |                                             |         |
| <1 in 10 (<10%)     | 0 (0.0)       | 0 (0.0)                       | 0 (0.0)                                     | 1.000   |
| >1 in 10 (≥10%)     | 123 (100.0)   | 49 (100.0)                    | 74 (100.0)                                  |         |
| Perceived 10-y CVD risk |            |                               |                                             |         |
| <1 in 10 (<10%)     | 31 (25.2)     | 15 (50.6)                     | 16 (21.6)                                   | 0.043   |
| >1 in 10 (≥10%)     | 23 (18.7)     | 13 (26.5)                     | 10 (13.5)                                   |         |
| Don’t know/not sure | 69 (56.1)     | 21 (42.9)                     | 48 (64.9)                                   |         |
| Primary prevention subsample |                |                               |                                             |         |
| Actual 10-y CVD risk |                |                               |                                             |         |
| <1 in 10 (<10%)     | 43 (24.3)     | 18 (17.8)                     | 25 (32.9)                                   | 0.023   |
| >1 in 10 (≥10%)     | 134 (75.7)    | 83 (82.2)                     | 51 (67.1)                                   |         |
| Perceived 10-y CVD risk |            |                               |                                             |         |
| <1 in 10 (<10%)     | 50 (28.2)     | 34 (33.7)                     | 16 (21.1)                                   | 0.069   |
| >1 in 10 (≥10%)     | 35 (19.8)     | 22 (21.8)                     | 13 (17.1)                                   |         |
| Don’t know/not sure | 92 (52.0)     | 45 (44.6)                     | 47 (61.8)                                   |         |

Data are provided as frequency (percentage). P values are for differences comparing both study sites. CVD indicates cardiovascular disease.

*Estimation of difference in 2 proportions is 19% using normal approximation with 95% CI (8%–30%).
Findings of the Review of National Policies Regulating Access to Low-Dose Aspirin

Policies regulating access to low-dose aspirin in Europe were reviewed, and the vast majority of European countries were using the 100-mg dose of aspirin as their standard low dose. A prescription was required to obtain low-dose aspirin in 10 countries, including Ireland, Denmark, Italy, and Spain (Figure). In 18 of the 20 European countries that allowed patients to access low-dose aspirin without a prescription, the medication was only available from behind the pharmacy counter after a discussion with a pharmacist. This policy was seen in the United Kingdom, Germany, France, and Belgium. Of the 30 countries in Europe reviewed, only Hungary and the Czech Republic had OTC low-dose aspirin access policies similar to those in the United States.

DISCUSSION

In this full reporting of a patient survey conducted in the United States and Europe, we further characterize patient-reported perspectives on their own level of CVD risk and on their use of aspirin for CVD prevention. Some potentially important new findings are noted. A significant proportion of survey participants were unable to correctly identify whether aspirin was indicated by clinical practice guidelines for primary or secondary prevention, with more than a third (38%) not knowing that aspirin was routinely indicated for secondary prevention. Despite most

Table 4. Aspirin Understanding and Perception

| Variable | Overall, n=300 | Johns Hopkins Hospital, n=150 | National University of Ireland, Galway, n=150 | P value |
|----------|----------------|--------------------------------|-----------------------------------------------|---------|
| Aspirin is predicted to reduce risk of myocardial infarction/stroke by | | | | 0.005 |
| More than half | 77 (25.7) | 37 (24.7) | 40 (26.7) | |
| Less than half | 41 (13.7) | 30 (20.0) | 11 (7.3) | |
| Don’t know/not sure | 182 (60.7) | 83 (55.3) | 99 (66.0) | |
| Aspirin is predicted to increase risk of bleeding by | | | | 0.016 |
| More than half | 36 (12.0) | 22 (14.7) | 14 (9.3) | |
| Less than half | 57 (19.0) | 36 (24.0) | 21 (14.0) | |
| Don’t know/not sure | 207 (69.0) | 92 (61.3) | 115 (76.7) | |
| Aspirin is routinely recommended in guidelines for primary CVD prevention | | | | 0.026 |
| Yes | 141 (47.0) | 73 (48.7) | 68 (45.3) | |
| No | 39 (13.0) | 26 (17.3) | 13 (8.7) | |
| Not sure/don’t know | 120 (40.0) | 51 (34.0) | 69 (46.0) | |
| Aspirin is routinely recommended in guidelines for secondary CVD prevention | | | | 0.958 |
| Yes | 186 (62.0) | 93 (62.0) | 93 (62.0) | |
| No | 13 (4.3) | 7 (4.7) | 6 (4.0) | |
| Not sure/don’t know | 101 (33.7) | 50 (33.3) | 51 (34.0) | |
| Factors that motivate aspirin use | | | | 0.218 |
| Prior history of a heart attack or stroke | 47 (15.7) | 19 (12.7) | 28 (18.7) | |
| Family history heart attack or stroke | 41 (13.7) | 16 (10.7) | 25 (16.7) | |
| Risk factors such as smoking, high blood pressure, high cholesterol | 29 (9.7) | 14 (9.3) | 15 (10.0) | |
| Your primary care/general practitioner’s recommendation | 172 (57.3) | 95 (63.3) | 77 (51.3) | |
| Guidelines for the prevention of heart disease | 11 (3.7) | 6 (4.0) | 5 (3.3) | |

Data are provided as frequency (percentage). P values are for differences comparing both study sites. CVD indicates cardiovascular disease.

*Estimation of difference in 2 proportions is 11% using normal approximation with 95% CI (1%–22%).
†Estimation of difference in 2 proportions is 15% using normal approximation with 95% CI (5%–26%).
‡Estimation of difference in 2 proportions is 9% using normal approximation with 95% CI (1%–16%).

(57%) was based on their clinician’s recommendation rather than a guideline recommendation or history of CVD risk factors.
Figure. Access to low-dose aspirin in America compared with Europe.
A, Widespread access to aspirin over the counter in the United States. B, European countries that require a prescription or discussion with a pharmacist before accessing aspirin and those that allow over-the-counter access. A list with specific country names and access policies is available in Data S2.
participants (86%) being at a high-level of calculated CVD risk, only 19% appeared to be aware of this, and more than half (54%) were unable to quantify their CVD risk at all. Intriguingly, this inability to quantify personal CVD risk did not differ by primary (52%) versus secondary prevention (56%) status, which is remarkable when one considers that the latter group had suffered a CVD event in the past. Furthermore, approximately 3 out of every 5 participants were unable to comment on the relative magnitude of potential risks or benefits that can be expected from taking aspirin. Perhaps most interesting, in contrast to commonly accessing aspirin OTC in the United States (84%), the finding from our patient-reported survey that very few Irish patients obtain aspirin OTC was seen to align closely with our systematic review of European national policies regulating access to low-dose aspirin (specifically, only 2 of the 30 European countries reviewed allow access to low-dose aspirin for CVD prevention as an OTC medication).

We believe that our data generate a compelling argument for further education of both patients and physicians on the updated role of aspirin in CVD prevention. A greater understanding of the role of aspirin in primary prevention may prompt a patient to engage in discussion with their primary care provider on the topic before taking this medication OTC. Such education may also equip primary care providers with the knowledge to safely deprescribe or discontinue inappropriate aspirin use. Equally, an informed primary care physician may initiate aspirin therapy for those who may benefit such as primary prevention adults with especially high-risk of CVD (eg, elevated coronary calcium scores) and low bleeding risks. Indeed, education of patients and providers should also extend to the use of aspirin in secondary prevention. For example, recent guidelines on aspirin use in primary prevention have received a lot of attention in the lay press, but often the messaging is regarding “aspirin in heart disease” rather than aspirin in primary prevention, and it is possible that some secondary prevention patients taking aspirin OTC may inappropriately stop this medication as a result of confusion.

A number of CVD prevention guideline documents have shifted to recommending shared decision making. Although shared decision making has many strengths in empowering patients to help them make decisions pertaining to their health, the current study highlights the importance of ensuring that patients are well informed. This applies in particular to therapies where equipoise exists, such as for aspirin in primary CVD prevention. The relatively high rate of aspirin use in the primary prevention subgroup of this survey sample (37% overall and up to 48% in the United States) may reflect the inclusion of older adults attending hospital-based outpatient clinics (who are expected to be higher risk than the general population) and also the inclusion of greater numbers of patients recruited from cardiovascular clinics rather than the primary care setting. Nonetheless, despite the inherent possibility of selection bias in patient surveys such as ours, the prevalence of primary prevention aspirin use in the current study is generally consistent with other reports. Primary prevention aspirin use in the United States had a similar prevalence reported in both the 2017 National Health Interview Survey and in the nationally representative US-based BRFSS (Behavioral Risk Factor Surveillance) study. For example, the latter reported that 45.6% of adults aged ≥70 years are taking aspirin for primary prevention of CVD.

Although almost all patients in the United States reported that their primary care provider was aware of their OTC aspirin use, some of these clinicians may actually be unaware of the patient’s aspirin use or have forgotten about it (both because aspirin will not be listed in the electronic health record under the medications prescribed by that physician and because an ever-expanding list of electronic health record practice advisories commands their attention). The 2017 National Health Interview Survey reported that 22.8% of US adults who take aspirin did so without a clinician’s recommendation. This is important because, unlike in Europe, low-dose aspirin can be obtained OTC in the United States. From a regulatory perspective, the Durham–Humphrey and Kefauver–Harris Amendments define 4 criteria that were used by the US Food and Drug Administration to evaluate whether drugs should be available OTC. These criteria comprise the following 4 elements: first, can the patient recognize the condition specified in the proposed indication; second, when reading the product label, can the patient extract the key information necessary to use the drug correctly; third, will the drug be effective; and fourth, is the drug safe to use as instructed.

The summation of trial data thus far calls into question the third and fourth criteria, whether aspirin is of net benefit when used for the primary prevention of CVD. The US Food and Drug Administration drug label does not provide instructions for the use of aspirin for CVD prevention, which entirely invalidates the second criterion. Our results, documenting that many patients do not know their CVD risk, nor the magnitude of risks and benefits that can be expected with aspirin, nor the difference between primary and secondary prevention of CVD (or if aspirin is indicated in either case), contest the first criterion, whether the patient can recognize and diagnose the condition specified in the proposed indication. Thus, our findings support the US Food and Drug Administration’s decision to have not approved aspirin for the primary prevention.
of CVD and challenge the availability of low-dose aspirin OTC in the United States for CVD prevention (while also supporting tighter access policies such as those in Europe). Although some of the Durham–Humphrey and Kefauver–Harris Amendments may be fulfilled for aspirin OTC use in the secondary prevention of CVD, the fact that patients in our survey often did not understand their own CVD risk, nor were they aware of the differences in aspirin efficacy between primary versus secondary prevention, suggest that the more conservative approach, like in Europe, to regulating access to low-dose aspirin might represent a safer option.

Several limitations of this study should be considered. First, all data were self-reported. Second, although our participation rate is typical for such patient-reported surveys, a relatively high rate of the individuals approached refused to participate in the study. In Europe, because of the general data protection regulation, we could not collect and store data on people who did not consent to initial study enrollment, and so we cannot comment on differences in response rates by subgroups or modality (in-person versus phone). This low response rate may have resulted in a sample of patients who are more interested in their health and more informed about aspirin (although if anything this would only serve to further highlight the poor awareness of patients regarding their own levels of CVD risk and the recommended indications for aspirin). Third, the survey was limited to a convenience sample at single centers in the United States and in Europe. Fourth, participants were primarily recruited from cardiovascular clinics, which may have resulted in a higher risk cohort. Each of these factors may limit the external validity of the study. Reassuringly, Johns Hopkins represents the typical practice in urban academic US medical centers (indeed, as outlined previously, our data match those from reported from similarly aged participants in the nationally representative National Health Interview Survey and BRFSS of US adults). Data from the EuroASPIRE (European Action on Secondary Prevention Through Intervention to Reduce Events) surveys have also shown that the use of aspirin and preventive cardiology care provided to patients enrolled in Galway and Ireland is broadly representative of European patients in general. Fifth, some of the questions may have reached the limits of participant understanding. However, a “don’t know/not sure” option was provided for all questions to avoid participant guessing. Finally, although our study focused on policies regulating access to low-dose aspirin for CVD prevention in Europe, we note that short courses of full-dose aspirin can be obtained OTC for analgesic purposes in many European countries. This may be a source of confusion for some patients and might explain why 2.5% of our Ireland-based European sample reported OTC aspirin use even though a prescription is required in Ireland to obtain low-dose aspirin for CVD prevention.

CONCLUSIONS

This survey demonstrated that a significant proportion of patients continue to take aspirin for primary prevention, particularly in the United States where aspirin is obtained OTC more often than in Europe. Many patients did not know the difference between aspirin recommendations for primary and secondary prevention, misunderstood the risks and benefits of aspirin, and lacked insight into their own level of CVD risk. These findings support greater education of both physicians and patients on the role of aspirin in cardiovascular prevention and also question the widespread and unfettered availability of OTC aspirin for CVD prevention in the United States, particularly when compared with the situation in Europe, where access to low-dose aspirin almost always requires involvement of a health care professional.

ARTICLE INFORMATION

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Affiliations

Ciccarone Center for the Prevention of Cardiovascular Disease, Division of Cardiology, Department of Medicine, Johns Hopkins Medical Institutions, Baltimore, MD (A.P.J., B.C., K.D.L., T.M.D., R.S.B., S.S.M., J.W.M.); National Institute for Prevention and Cardiovascular Health, National University of Ireland Galway School of Medicine, Galway, Ireland (Z.L.L., O.G., J.W.M.); and Clinical Research Facility (M.M.) and School of Medicine (F.S., D.M., W.W., P.W.S.), National University of Ireland Galway, Galway, Ireland.

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Supplemental Material

Data S1–S2

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SUPPLEMENTAL MATERIAL
SURVEY QUESTIONS

Start of Block: Demographics

Q1.1 What is your sex?

- Male (1)
- Female (2)
- Other (4)

Q1.2 What is your date of birth?

Please Select: (1)

| Month              | Day      | Year          |
|--------------------|----------|---------------|
| ▼ January (1 ...   | ▼ 1 (1 ... 31 (31) | ▼ 1900 (1 ... 2049 (150) |
| December (12)      |          |               |

Q1.3 What is the highest level of formal education you have received?

- No school (1)
- Some school, no college/university (3)
- Some college/university (4)
- College/university graduate (5)
Q1.4 What is your race?

- White (1)
- Black/African/ African American (2)
- Chinese (15)
- Other Asian (8)
- Indian (6)
- Pakistani (10)
- Bangladeshi (11)
- Black Caribbean (12)
- Other (16)

End of Block: Demographics

Start of Block: Past medical history and risk factors for cardiovascular disease

Q2.1 Have you ever had stents placed in your heart (coronary artery stent) or undergone a cardiac bypass surgery (coronary artery bypass graft, CABG)

- Yes (1)
- Don't know/not sure (2)
- No (3)
Q2.2 Regarding cigarette smoking, which describes you best?

- Current smoker (1)
- Former smoker (2)
- Never smoker (3)

Display This Question:
If Regarding cigarette smoking, which describes you best? = Current smoker

Q2.3 How many cigarettes do you smoke per day?

- <10 (2)
- 10-19 (3)
- 20 or more (4)

Q2.4 Do you know of any first-degree relatives (mother, father, brother, sister, children) who were diagnosed with a heart attack or had chest pain with exercise before the age of 60?

- Yes (1)
- Don't know/not sure (2)
- No (3)
Q2.5 Have you ever been diagnosed with or told that you had any of the following disorders which could increase your risk of heart attack or stroke?

- [ ] Heart attack (1)
- [ ] Stroke or TIA (transient ischemia attack) (2)
- [ ] Blood vessel disease involving narrowing/blockage in your legs (3)
- [ ] High blood pressure (4)
- [ ] Diabetes (type 1) (5)
- [ ] Diabetes (type 2) (6)
- [ ] Atrial fibrillation (an irregular heartbeat) (7)
- [ ] Migraine (8)
- [ ] Systemic lupus erythematosus (SLE) (9)
- [ ] Chronic kidney disease (poor kidney function) (10)
- [ ] Severe mental illness (11)
- [ ] Rheumatoid arthritis (12)
- [ ] High cholesterol (13)
- [ ] Erectile dysfunction (14)
- [ ⊗ ] None of the above (15)
Q2.6 Which of the following medications are you currently taking

☐ A statin or cholesterol medication (2)
☐ A blood pressure medication (3)
☐ An atypical antipsychotic (1)
☐ A PPI (proton pump inhibitor) or stomach acid lowering medication (4)
☐ None of the above (11)

End of Block: Past medical history and risk factors for cardiovascular disease

Start of Block: Past medical history and risk factors for bleeding

Q3.1 Please select from the medications below any medications which you take daily.

☐ Steroids, for example prednisone (1)
☐ Blood thinning medications such as warfarin, apixaban, rivaroxaban, dabigatran, edoxaban (3)
☐ Blood thinning medications such as clopidogrel, ticagrelor, prasugrel (4)
☐ None of the above (5)

Q3.2 Have you ever been diagnosed with or told that you had a bleed in the upper part of the bowel (upper gastrointestinal bleed) or peptic ulcer disease (seen on endoscopy/camera test to look at the inside of your bowel)?

☐ Yes (1)
☐ Don't know/not sure (2)
☐ No (3)
Q3.3 Have you ever been diagnosed with or told that you had poor blood clotting ability (coagulopathy) or told that you had low numbers of cells called platelets which help with blood clotting (thrombocytopenia)?

- Yes (1)
- Don’t know/not sure (2)
- No (3)

End of Block: Past medical history and risk factors for bleeding

Start of Block: Aspirin use

Q4.1 Do you take aspirin?

- Yes (1)
- No (2)
- Don’t know/not sure (3)

Display This Question:

If Do you take aspirin? = Yes

Q4.2 How often do you take aspirin?

- Every day (1)
- Every other day (2)
- Two times a week (3)
- Other (4)
- Don’t know/not sure (5)
Q4.3 How do you obtain aspirin?

- Receive aspirin as a prescription medication (1)
- Take aspirin as an over the counter medication (2)
- Don't know/not sure (3)

Q4.4 What dose of aspirin do you take?

- 75mg (1)
- 81mg (2)
- 150mg (3)
- 300mg (4)
- 325mg (5)
- Other (6)
- Don't know/not sure (7)
Q4.5 Why do you take aspirin?

- Pain relief (1)
- Prevention of heart disease (2)
- Other (3)
- Not sure/don't know (4)

Display This Question:

If What is your location? = Baltimore
And Do you take aspirin? = Yes

Q4.6 Is your primary care physician aware that you take aspirin?

- Yes (1)
- Not sure/don't know (2)
- No (3)

Display This Question:

If What is your location? = Galway
And Do you take aspirin? = Yes

Q4.7 Is your general practitioner aware that you take aspirin?

- Yes (1)
- Not sure/don't know (2)
- No (3)

End of Block: Aspirin use

Start of Block: Awareness of cardiovascular disease and benefits and risks of aspirin use
Q5.1 Based on your risk factors for heart disease the risk of you having a heart attack or stroke in the next 10 years is?

- Less than one in ten (1)
- More than one in ten (>10%) (2)
- Don’t know/not sure (3)

Q5.2 By taking a daily aspirin you could reduce your risk of heart attack or stroke by?

- More than half (1)
- Less than half (2)
- Don’t know/not sure (3)

Q5.3 By taking a daily aspirin you could increase your risk of bleeding in the bowel or brain by?

- More than half (1)
- Less than half (2)
- Don’t know/not sure (3)

End of Block: Awareness of cardiovascular disease and benefits and risks of aspirin use

Start of Block: Awareness of guidelines and factors influencing patient use of aspirin

Display This Question:

If What is your location? = Baltimore

Q6.1 Primary prevention of cardiovascular disease aims to prevent the first heart attack or stroke among adults who have never before been diagnosed with cardiovascular disease. In the
last 5 years, have there have been changes to primary prevention American guidelines for aspirin use?

- Yes (1)
- Not sure/don’t know (2)
- No (3)

Display This Question:
If What is your location? = Baltimore

Q6.2 Secondary prevention of cardiovascular disease aims to prevent another subsequent heart attack or stroke among adults who have previously suffered a heart attack or stroke and therefore have already been diagnosed with cardiovascular disease. In the last 5 years, have there have been changes to secondary prevention American guidelines for aspirin use?

- Yes (1)
- Not sure/don’t know (2)
- No (3)

Display This Question:
If What is your location? = Galway

Q6.3 Primary prevention of cardiovascular disease aims to prevent the first heart attack or stroke among adults who have never before been diagnosed with cardiovascular disease. In the last 5 years, have there have been changes to primary prevention European guidelines for aspirin use?

- Yes (1)
- Not sure/don’t know (2)
- No (3)
Q6.4 Secondary prevention of cardiovascular disease aims to prevent another subsequent heart attack or stroke among adults who have previously suffered a heart attack or stroke and therefore have already been diagnosed with cardiovascular disease. In the last 5 years, have there been changes to secondary prevention European guidelines for aspirin use?

- Yes (1)
- Not sure/don't know (2)
- No (3)

Q6.5 Do the guidelines recommend that you take aspirin to prevent cardiovascular disease?

- Yes (1)
- Not sure/don't know (2)
- No (3)

Q6.6 Which of the following most influences you to take aspirin if you take it already (or would influence you to take aspirin if you were considering starting)?

- Prior history of a heart attack or stroke (1)
- Family history heart attack or stroke (2)
- Risk factors such as smoking, high blood pressure, high cholesterol (3)
- Your doctors recommendation (4)
- American guidelines for the prevention of heart disease (5)
Q6.7 Which of the following most influences you to take aspirin if you take it already (or would influence you to take aspirin if you were considering starting)?

- Prior history of a heart attack or stroke (1)
- Family history heart attack or stroke (2)
- Risk factors such as smoking, high blood pressure, high cholesterol (3)
- Your doctors recommendation (4)
- European guidelines for the prevention of heart disease (5)

End of Block: Awareness of guidelines and factors influencing patient use of aspirin
Data S2.

ACCESS TO LOW-DOSE ASPIRIN IN EUROPEAN COUNTRIES

| Country                | Low-dose aspirin requires a prescription | Low-dose aspirin only available from a pharmacist |
|------------------------|-----------------------------------------|--------------------------------------------------|
| Denmark                | YES                                     | -                                                |
| Ireland                | YES                                     | -                                                |
| Italy                  | YES                                     | -                                                |
| The Netherlands        | YES                                     | -                                                |
| Norway                 | YES                                     | -                                                |
| Portugal               | YES                                     | -                                                |
| Slovenia               | YES                                     | -                                                |
| Spain                  | YES                                     | -                                                |
| Sweden                 | YES                                     | -                                                |
| Switzerland            | YES                                     | -                                                |
| Austria                | NO                                      | YES                                              |
| Belgium                | NO                                      | YES                                              |
| Bulgaria               | NO                                      | YES                                              |
| Croatia                | NO                                      | YES                                              |
| Cyprus                 | NO                                      | YES                                              |
| Estonia                | NO                                      | YES                                              |
| Finland                | NO                                      | YES                                              |
| France                 | NO                                      | YES                                              |
| Germany                | NO                                      | YES                                              |
| Greece                 | NO                                      | YES                                              |
| Latvia                 | NO                                      | YES                                              |
| Lithuania              | NO                                      | YES                                              |
| Luxembourg             | NO                                      | YES                                              |
| Malta                  | NO                                      | YES                                              |
| Poland                 | NO                                      | YES                                              |
| Romania                | NO                                      | YES                                              |
| Slovakia               | NO                                      | YES                                              |
| The United Kingdom     | NO                                      | YES                                              |
| The Czech Republic     | NO                                      | NO                                               |
| Hungary                | NO                                      | NO                                               |

Low-dose aspirin is defined as <150mg daily consistent with contemporary studies.
The vast majority of European countries use the 100mg dose of aspirin as the low dose of aspirin.
The availability of over-the-counter low-dose aspirin was determined by reviewing online national registers of authorized medicines. Where this did not provide the information, a need for a prescription was identified by reviewing online pharmacies located in each country.
The availability of medications from non-pharmacy outlets was provided from a 2021 review by Oleszkiewicz et al.15
A non-pharmacy outlet is defined here as a retail outlet which does not have the input of a trained pharmacist or pharmaceutical technician.

Austria
https://aspregister.basg.gv.at/aspregister/faces/aspregister.jspx?_afrLoop=541919893416061&_afrWindowMode=0&_adf.ctrl-state=8q34680vi_9
https://www.shop-apotheke.at/arzneimittel/A3504847/aspirin-protect-100-mg-tabletten.htm?query=aspirin&queryID=f915807101d40f42eb0a4fec31e5d115&objectIDs=[A3504847]&position=4&eventName=click%20on%20product%20in%20suggest&eventType=click

Belgium: 80 and 100 doses not subject to prescription
https://banquededonneesmedicaments.afmps-fagg.be/#

Bulgaria
https://mypharmacy.bg/lekarstva-i-zdrave/srdechno-sdovi-zabolyavaniya/aspirin-protekt-za-srceto-tabletki-100mg-h-40.html

Croatia https://www.halmed.hr/Lijekovi/Baza-lijeкова/#rezultati

Cyprus https://www.phs.moh.gov.cy/web/guest/drug-search

Czech Republic www.sukl.eu/modules/medication/search.php?lang=2

Denmark https://laegemiddelstyrelsen.dk/en/pharmacies/over-the-counter-medicines/

Estonia https://ravimiregister.ee/?pv=PublicSearchResult

Finland https://www.fimea.fi/laakehaut_ja_luettelot/laakehaku

France: Does not need prescription http://agence-prd.anms.sante.fr
(Interestingly the Bayer aspirin does require a prescription to be dispensed however Aspirine Arrow does not, and per its spc it is indicated only for secondary cardiovascular prevention)

Germany: https://www.shop-apotheke.com/arzneimittel/6706155/aspirin-protect-100-mg-tabletten.htm?eventName=click%20on%20product%20list%20item&eventType=click&objectIDs=[06706155]&position=4&query=aspirin&queryID=a0968727a58937cb4b4e734239af7f1a
Greece https://www.eof.gr/web/guest/search

Hungary https://ogyei.gov.hu/gyogyszeradatbazis&action=show_details&item=16107
https://www.ogyei.gov.hu/generalt_listak/gyk_lista.csv

Ireland: https://www.medicines.ie/medicines/nunseals-75-33174/doc-history

Italy: farmaci.agenziafarmaco.gov.it/bancadatifarmaci/ “This medicine has been prescribed for you”
https://farmamare.com/#/dfclassic/query=aspirin&query_name=match_and
https://store.farmaciaflorio.com/catalogsearch/result/?q=aspirin

Latvia
https://www.zva.gov.lv/zvais/zalu-registrs/en/?iss=1&q=Aspirin+Cardio&IK-1=1&IK-2=2&NAC=on&SAT=on&DEC=on&ESC=on&ESI=on&PIM=on&RNE=on

Lithuania
https://vapris.vvkt.lt/vvkt-web/public/medications/view/20057

Luxembourg
https://www.pharmaglobe.lu/aspirine-100-mg-comp-30.html

Malta
http://www.medicinesauthority.gov.mt/search-medicine-results?modSearch=adv

Norway
https://www.felleskatalogen.no/medisin/pasierter/pil-acetylsalisylsyre-actavis-574532;jsessionid=w7wGB-fJqRLkq8T7jleVqxP1MWRE8cseTjYFc2Ss.fkweb-live-web-cluster-fkweb-live-1

The Netherlands https://www.apotheek.nl/medicijnen/acetylsaliclyzuur-bij-pijn-of-ontsteking#heb-ik-een-recept-nodig

Poland https://www.doz.pl/apteka/szukaj?search=aspirin

Portugal https://extranet.infarmed.pt/INFOMED-fo/detalhes-medicamento.xhtml
Dispensing classification: MSRM: Medicinal product subject to medical prescription

Romania
https://www.anm.ro/nomenclator/medicamente

Slovakia
https://www.sukl.sk/ hlavna-stranka/slovenska-verzia/databazy-a-servis/vyhladavanie-liekov-zdravotnickych-pomocok-a-zmien-v-liekovej-databaze/vyhladavanie-v-databaze-registrovanych-liekov?page_id=242&lie_nazov=Aspirin&atc_nazov=&lie_kod=&atc_kod=&lie_rc=&drz_kod=&vyd_kod=F

Slovenia
http://www.cbz.si/cbz/bazazdr2.nsf/o/115D8FFCD33E79C1C12579EC001FFAB6?open document

Spain http://cima.aemps.es/cima/publico/lista.html
https://www.farmaciadelsol.es/store-search-result.php?keywords=aspirin
https://www.farmaciacampoamor.com/en/search?controller=search&search_query=aspirin+81&search=&tipo_search=0

Sweden https://www.lakemedelsverket.se/48f5c3/globalassets/dokument/handel-medlakemedel/otc---substansrapporter/acetylsalicylsyra-otc-2016-06-10.pdf
https://www.meds.se/acetylsalicylsyra-g-l-pharma-75-mg-100-tablett-er-tablett

Switzerland
https://en.adlershop.ch/p/8149/aspirin-cardio-100-filmtabletten-100mg-98-stueck
https://www.swissmedicinfo.ch/?Lang=EN
B means repeat prescription

The United Kingdom: https://www.medicines.org.uk/emc/product/2614/pil