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High-risk use of over-the-counter non-steroidal anti-inflammatory drugs:

a population-based cross-sectional study

Abstract

Background
The use of non-steroidal anti-inflammatory drugs (NSAIDs) is associated with serious adverse drug events (ADEs).

Aim
To determine the prevalence of over-the-counter (OTC) NSAID use in the general population and in patients with a high risk of developing a serious NSAID-related ADE.

Design and setting
Cross-sectional study in four general practices in the Netherlands.

Method
Two patient samples were selected: a random sample of adults (general population sample); and adult patients with a high risk of developing a serious ADE in case of NSAID use (high-risk sample). All included patients were sent a questionnaire regarding their use of OTC NSAIDs in the 4 weeks prior to participation.

Results
In the general population sample, 118 of 456 (26%) invited patients completed the questionnaire. Of these, 35 (30%) had used an OTC NSAID. In the high-risk sample, 264 of 713 (37%) invited patients completed the questionnaire, and of these high-risk patients 33 (13%) had used an OTC NSAID. Over 20% of OTC NSAID users in the general population sample and over 30% in the high-risk sample had used the OTC NSAID for >7 days. OTC NSAIDs were used in a dosage exceeding the recommended daily maximum by 9% and 3% of OTC NSAID users in the general population and the high-risk sample respectively.

Conclusion
OTC NSAIDs are used by almost one-third of the general population. In the high-risk patients selected, one in eight patients used an OTC NSAID. Continued efforts by health authorities and healthcare professionals to inform patients of the risks of these drugs are warranted.

Keywords
anti-inflammatory agents, non-steroidal; general practice; over-the-counter drugs; primary care.

INTRODUCTION

Non-steroidal anti-inflammatory drugs (NSAIDs) are widely prescribed because of their analgesic and anti-inflammatory properties. Their use is associated with the occurrence of serious adverse drug events (ADEs), particularly of the gastrointestinal, cardiovascular, and renal tract.[1–6] To limit the occurrence of such ADEs, guidelines have been developed and recommend avoiding the prescription of these drugs in patients with known risk factors for development of ADEs, such as old age, comorbidity, or concurrent use of interacting medication.[7–12]

In many countries NSAIDs are freely available over-the-counter (OTC). Use of OTC NSAIDs and other OTC analgesics appears to be widespread.[13,14] In general, short-term use of NSAIDs is considered relatively safe, provided it is used in OTC-doses by adults without contraindications or interacting medications.[15] However, in previous studies performed in the UK and Australia, around one-quarter of all OTC analgesic users were found to do so at a dosage exceeding the maximum dose and one-third of OTC NSAID users had a warning or contraindication for use of these drugs, or used concurrent interacting medication.[14,16]

A cross-sectional population-based study was conducted to determine the current prevalence of OTC NSAID use in the general Dutch population and in patients at a high risk of developing a serious gastrointestinal, cardiovascular, or renal NSAID-related ADE. In addition, the aim was to examine the duration and dosage of use, the reasons for use and the place of purchase, and information provision on purchase.

METHOD

Setting

A cross-sectional study was conducted in April 2012 within four GP practices in the Rotterdam region of the Netherlands, recruited from an academic network of practices associated with the Erasmus University Medical Center. In the Netherlands, all citizens are registered with one GP, who forms the first point of care for all medical complaints. The 33 593 patients registered with the four participating practices are comparable to the general population of the Netherlands with regards to age and sex (mean age 41 years, 51% female in the Dutch general

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How this fits in

Non-steroidal anti-inflammatory drugs (NSAIDs) should be used with caution as they are known to be associated with serious adverse drug events, especially in older patients and in those with relevant comorbidity or comedication. This study investigates the use of over-the-counter NSAIDs, both in these vulnerable high-risk patients and in the general population. The findings suggest that the general public are not sufficiently aware of the risks of NSAID use and therefore this has implications for both healthcare professionals and healthcare authorities.

population versus 40 years, 51% female in the participating practices).[17] All four GP practices contribute data to the Integrated Primary Care Information (IPCI) database. This longitudinal GP electronic health record database contains the anonymised patient records of patients registered with GPs throughout the Netherlands, containing data on patient demographics, diagnoses using the International Classification for Primary Care (ICPC)[18] and journal entries, referrals, laboratory results, and hospitalisations. In addition, details of drug prescriptions using the Anatomical Therapeutic Chemical (ATC) code[19] and their dosage regimens are available. Further details of the database have been described elsewhere.[20–21]

Study population

Within the participating practices, two samples of patients were selected, using the medical records contained in the IPCI database. The first was a random sample of all adult patients aged ≥18 years (general population sample). In the second sample adult patients were specifically selected who, according to Dutch clinical prescription guidelines,[7,10–12] had at least one risk factor leading to a high risk of developing a serious NSAID-related ADE (high-risk sample). It was aimed to select at least the following number of patients from each of the following risk groups:

- 150 patients with a history of peptic ulcer or ulcer complication;
- 200 patients aged >70 years;
- 300 patients with two or more of the following minor risk factors: use of anticoagulant, use of aspirin, use of corticosteroid, use of selective serotonin reuptake inhibitor, age 60–70 years, history of severe rheumatoid arthritis, diabetes mellitus or heart failure;
- 50 patients with a history of myocardial infarction;
- 50 patients with a history of stroke;
- 100 patients with a history of heart failure; or
- 50 patients with a glomerular filtration rate (GFR) <30mL/min.

As these risk factors often overlap, patients could be selected more than once, thereby contributing to the numbers in each risk group. The diagnoses of diseases and conditions mentioned were identified based on ICPC-coding. The prescriptions of interacting medication were identified based on ATC-coding and patients were assumed to use such medication if the prescription had been issued in the 3 months prior to selection. Kidney function was determined based on the most recent laboratory measurement of GFR, performed in the 5 years prior to selection.

As the data contained within the IPCI database are anonymous, selected patients could not be approached directly. All patients have a unique identity code within the database which can only be decrypted by their GPs. The identity codes of selected patients were therefore sent to their respective GPs, who were asked to decrypt the patients' codes and to send them an information pack, thereby inviting them to participate in the study. GPs were allowed to exclude any patients they did not deem appropriate for participation.

Consent form and questionnaire

All invited patients received a consent form and a questionnaire regarding their use of OTC NSAIDs. Only participants who completed the consent form were included. The questionnaires were returned directly and contained a study code, so that they could be linked back to the participant's medical record in the IPCI database. They were developed using Teleform® (Autonomy Cardiff, Vista, CA, US), an optical character recognition system which allows the completed questionnaires to be optically read directly into a database. All questionnaires were manually checked after scanning to correct for any reading errors.

In the questionnaire, participants were asked whether they had used OTC NSAIDs in the 4 weeks prior to completion of the questionnaire. To aid them, an information leaflet containing the names and logos of all brands of available OTC NSAIDs in the

Table 1. Individual risk factors within high-risk patients in the source population and in the high-risk sample

Risk factor[a]	Number of high-risk patients: Source population *n* = 5550, *n* (%)	Number of high-risk patients: High-risk sample *n* = 819, *n* (%)
History of peptic ulcer/UGI complication	428 (8)	184 (22)
Age >70 years	3662 (66)	390 (48)
Two or more minor UGI risk factors[b]	1711 (31)	410 (50)
History of myocardial infarction	686 (12)	152 (19)
History of stroke	504 (9)	108 (13)
Heart failure	214 (4)	156 (19)
Chronic renal insufficiency (GFR <30 mL/min)	69 (1)	60 (7)

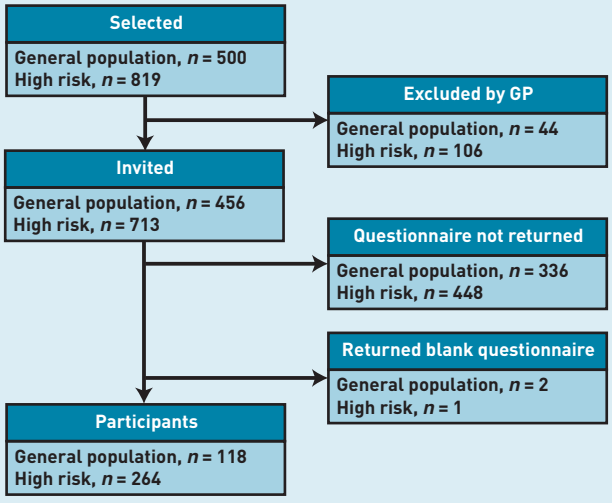
GFR: glomerular filtration rate. UGI = upper gastrointestinal. [a]Risk factors can overlap. [b]Two or more of the following minor risk factors: use of anticoagulant, use of aspirin, use of corticosteroid, use of selective serotonin reuptake inhibitor, age 60–70 years, history of severe rheumatoid arthritis, diabetes mellitus, or heart failure.

Netherlands was provided. Those patients who had used OTC NSAIDs were asked to also answer questions regarding:

- the type(s) of OTC NSAIDs used;
- the number of days of use;
- the average number of tablets used per day;
- the dosage per tablet used;
- the reason(s) for use;
- the place of purchase; and
- the provision of information on purchase.

If participants had used more than two NSAIDs, they were asked to complete these follow-up questions for the two most frequently used only. To determine whether any participants had used an OTC NSAID in a dosage exceeding the daily maximum, the average daily dosage used was calculated per NSAID by multiplying the average number of tablets used per day by the dosage per tablet used.

Figure 1. Flow chart of participants.



Characteristics of participants

To compare participants who had used an OTC NSAID to those who had not, some additional characteristics were determined from their medical records. GP prescriptions of an NSAID or proton pump inhibitor (PPI) in the 6 months prior to selection were identified based on ATC-coding. Diagnoses of musculoskeletal complaints, headache, or menstrual pain in the 6 months prior to selection were identified based on ICPC-coding.

Statistical analyses

Characteristics were compared between participants and non-participants and between those who had used OTC NSAIDs and those who had not, using a χ^2 test for dichotomous variables and independent *t*-test for age as a continuous variable. Information provision on purchase was compared per place of purchase using a χ^2 test or Fisher's exact test. All analyses were performed using SPSS (version 20).

RESULTS

Response and patient characteristics

Five hundred patients from the general population were initially selected. In the high-risk sample, sampling from each risk group as described in the methods section led to a selection of 819 high-risk patients. Table 1 shows the individual risk factors within this high-risk sample and within high-risk patients in the source population. The participating GPs excluded a total of 44 patients from the general population sample and 106 high-risk patients (Figure 1). The most common reasons for exclusion given were language barriers, cognitive impairment, and severe comorbidity. When compared to included patients, excluded patients in the general population sample were significantly older (mean age 59 years versus 49 years, $P = 0.004$) and significantly more likely to have a high gastrointestinal risk (46% versus 19% of patients, *P*-value <0.001) or high cardiovascular risk (14% versus 4% of patients, $P = 0.016$). In the high-risk sample, no statistically significant differences between excluded and included patients were found for gastrointestinal risk, but excluded patients were older (mean age 78 years versus 68 years, $P<0.001$), more likely to be female (65% versus 48%

Table 2. Characteristics of participants and non-participants in the two study samples

	General population sample			High-risk sample		
	Non-participants (*n* = 338), *n* (%)	Participants (*n* = 118), *n* (%)	*P*-value[a]	Non-participants (*n* = 449), *n* (%)	Participants (*n* = 264), *n* (%)	*P*-value[a]
Age, years (mean ± SD)	47 (±17)	55 (±15)	<0.001	67 (±14)	69 (±10)	0.106
Age category, years						
18–40	138 (41)	23 (19)	<0.001	24 (5)	3 (1)	0.004
41–60	122 (36)	45 (38)	0.692	98 (22)	44 (17)	0.096
61–80	72 (21)	48 (41)	<0.001	250 (56)	178 (67)	0.002
>80	6 (2)	2 (2)	0.954	77 (17)	39 (15)	0.406
Female	176 (52)	71 (60)	0.022	215 (48)	128 (49)	0.877
High gastrointestinal risk	55 (16)	31 (26)	0.017	413 (92)	249 (94)	0.242
History of peptic ulcer/ UGI complication	4 (1)	3 (3)	0.301	117 (26)	46 (17)	0.008
Age >70 years	42 (12)	22 (19)	0.094	199 (44)	110 (42)	0.490
Two or more minor risk factors[b]	14 (4)	9 (8)	0.136	212 (47)	149 (56)	0.017
High cardiovascular risk	14 (4)	5 (4)	0.964	190 (42)	115 (44)	0.746
History of myocardial infarction	10 (3)	3 (3)	0.815	83 (18)	48 (18)	0.919
History of stroke	5 (1)	1 (1)	0.604	51 (11)	38 (14)	0.236
Heart failure	2 (1)	1 (1)	0.767	80 (18)	37 (14)	0.186
High renal risk: chronic renal insufficiency	0 (0)	0 (0)	NA	29 (7)	8 (3)	0.046

UGI = upper gastrointestinal. NA = non applicable. [a]Participants versus non-participants, χ^2 test for dichotomous variables and independent t-test for age as a continuous variable. [b]Two or more of the following minor risk factors: use of anticoagulant, use of aspirin, use of corticosteroid, use of selective serotonin reuptake inhibitor, age 60–70 years, history of severe rheumatoid arthritis, diabetes mellitus, or heart failure.

of patients, $P = 0.002$) and more likely to have a high cardiovascular risk (58% versus 43% of patients, $P = 0.004$) or high renal risk (22% versus 5%, $P<0.001$) when compared to included patients.

In the general population sample, 118 of the 456 invited patients (26%) and in the high-risk sample 264 of the 713 invited patients (37%) completed the questionnaire. Two patients in the general population sample and one patient in the high-risk sample did complete a consent form but did not answer any of the questions in the questionnaire. These patients were considered non-participants. The mean duration between selection of the patient and completion of the questionnaire was 30 days.

Table 2 shows the characteristics of participants and non-participants in each study population. In the general population sample, participants were significantly older than non-participants and were significantly more likely to be female. In the high-risk sample the mean age and sex of participants did not differ significantly from non-participants.

Table 3. Use of OTC NSAIDs in the two study samples

	General population sample (*n* =118)	High-risk sample (*n* = 264)
OTC NSAID used, *n* (% of total sample)		
Yes	35 (30)	33 (13)
No	83 (70)	231 (88)
Number of OTC NSAIDs used, *n* (% of OTC NSAID users)		
1	24 (69)	27 (82)
2	7 (20)	5 (15)
>2	4 (11)	1 (3)
Duration (days) of OTC NSAID use, *n* (% of OTC NSAID users)		
1–7	27 (77)	19 (58)
8–14	5 (14)	7 (21)
15–21	1 (3)	2 (6)
22–28	2 (6)	2 (6)
Missing	0 (0)	3 (3)
Daily dosage, *n* (% of OTC NSAID users)		
Within daily maximum	31 (89)	32 (97)
Exceeding daily maximum	3 (9)	1 (3)
Missing	1 (3)	0 (0)

NSAID = non-steroidal anti-inflammatory drug. OTC = over-the-counter.

Use of OTC NSAIDs

In the general population sample, 35 of the 118 participants (30%) reported use of an OTC NSAID in the 4 weeks prior to completion of the questionnaire (Table 3). Of these 35 OTC NSAID users, 11 (31%) had used two or more NSAIDs and eight (23%) had used the NSAID for >7 days. Nine per cent of the OTC NSAID users in the general population sample were found to have used the NSAID in a daily dosage exceeding the recommended daily maximum.

In the high-risk sample, 33 of the 264 participants (13%) reported having used an OTC NSAID. Of those, six (18%) reported

Table 4. Use of OTC NSAIDs per risk group within the high-risk sample

	Total invited, *n*	Total participants *n* (% of invited)	OTC NSAID used *n* (% of participants)
Total number of patients[a]	713	264 (37)	33 (13)
High gastrointestinal risk	662	249 (38)	31[b] (12)
History of peptic ulcer/UGI complication	163	46 (28)	7 (15)
Age >70 years	309	110 (36)	8 (7)
Two or more minor risk factors	361	149 (41)	18 (12)
Use of anticoagulant	72	31 (43)	1 (3)
Use of aspirin	288	118 (41)	11 (9)
Use of corticosteroid	57	21 (37)	3 (14)
Use of SSRI	49	13 (27)	1 (8)
Age 60–70 years	254	117 (46)	16 (14)
Severe rheumatoid arthritis	14	5 (36)	0 (0)
Heart failure	117	37 (32)	6 (16)
Diabetes mellitus	122	45 (37)	8 (18)
High cardiovascular risk	305	115 (38)	14 (12)
History of myocardial infarction	131	48 (37)	5 (10)
History of stroke	89	38 (43)	5 (13)
Heart failure	117	37 (32)	6 (16)
High renal risk: chronic renal insufficiency	37	8 (22)	2 (25)

UGI = upper gastrointestinal. NSAID = non-steroidal anti-inflammatory drug. OTC = over-the-counter. SSRI = selective serotonin reuptake inhibitor. [a]Each patient can potentially have more than one risk factor. [b]Of which 5 (16.1%) had been prescribed a proton pump inhibitor in 3 months prior to selection.

having used two or more NSAIDs and 11 (33%) had used the OTC NSAID for >7 days. In this population, only one of the OTC NSAID users (3%) had used the NSAID in a high dose. Table 4 shows the percentage of OTC NSAID use per risk group within the high-risk sample. As most participants had more than one risk factor, these risk groups overlap.

Types of NSAIDs used, reasons for use and place of purchase

In the general population sample, ibuprofen was the most commonly used NSAID, followed by high-dose acetylsalicylic acid, naproxen, and diclofenac (respectively 54%, 28%, 9%, and 9% of all OTC NSAIDs used). The most common reasons for use in this population were headache, musculoskeletal complaints, and menstrual pain (respectively 42%, 31%, and 16% of all given reasons for use). In the high-risk sample, musculoskeletal complaints and headache formed the most common reasons for use (respectively 51% and 38% of all given reasons for use). In this population, high-dosed acetylsalicylic acid was the most popular, followed by ibuprofen, diclofenac, and naproxen (respectively 53%, 29%, 11%, and 8% of all OTC NSAIDs used in this group).

In both the general population and the high-risk sample, participants were most likely to purchase the NSAID at drugstores (respectively 58% and 62% of all OTC NSAIDs), followed by pharmacies (respectively 23% and 21%) and supermarkets (15% in both populations). Drugstores in the Netherlands differ from pharmacies in that they are not staffed by certified pharmacists or qualified pharmacy assistants. High-risk OTC NSAID users were more likely to receive information on purchase at a pharmacy than at a drugstore or supermarket (88% versus 50% and 33% respectively). In the general population sample, this trend was not observed, as OTC NSAID users were most likely to receive information at the drugstore, followed by the pharmacy and supermarket (47%, 33%, and 25% respectively).

Characteristics of OTC NSAID users versus non-users

In both the general population and the high-risk sample, OTC NSAID users were younger than non-users (Table 5). In the

Table 5. Characteristics of OTC NSAID users versus non-users

	General population sample			High-risk sample		
	Non-users (*n* = 83), *n* (%)	OTC NSAID Users (*n* = 35), *n* (%)	*P*-value[a]	Non-users (*n* = 231), *n* (%)	OTC NSAID Users (*n* = 33), *n* (%)	*P*-value[a]
Age, years (mean ± SD)	58 (± 15)	49 (±15)	0.004	69 (± 10)	65 (± 12)	0.022
Female	48 (58)	23 (66)	0.424	109 (47)	19 (58)	0.264
NSAID prescribed in 6 months prior	14 (17)	9 (26)	0.268	24 (10)	6 (18)	0.235
PPI prescribed in 6 months prior	18 (22)	4 (11)	0.191	110 (48)	10 (30)	0.062
GP diagnosis in 6 months prior of:						
Musculoskeletal complaint	33 (40)	14 (40)	0.981	79 (34)	19 (58)	0.009
Headache	3 (4)	0 (0)	0.554	4 (2)	3 (9)	0.014
Menstrual pain	0 (0)	1 (3)	0.297	1 (0)	0 (0)	1.000

NSAID = non-steroidal anti-inflammatory drug. OTC = over-the-counter. PPI = proton pump inhibitor. [a]OTC NSAID users versus non-users, χ^2 test or Fisher's exact test.

high-risk sample, 58% of OTC NSAID users had been diagnosed with a musculoskeletal complaint by their GP in the 6 months prior to consultation, versus only 34% of non-users ($P<0.05$). OTC NSAID users in this population were also more likely than non-users to have consulted their GP because of headache (9% of OTC NSAID users versus 2% of non-users, $P<0.05$).

DISCUSSION

Summary

In this cross-sectional study, one in eight patients selected because of their high gastrointestinal, cardiovascular, or renal risk used OTC NSAIDs. The percentage of use was at least 10% in the majority of the separate risk groups investigated. In addition, almost one-third of the general population sample were found to use OTC NSAIDs. Although most people in this general population have no contraindications for use, there is still potential for inappropriate use. Almost one-third of OTC NSAID users in this population had used more than one NSAID and two users had used NSAIDs on a daily basis over the previous 4 weeks. In addition, 9% of OTC NSAID users in this population were found to do so in a dosage exceeding the daily maximum. Considering the widespread use of OTC NSAIDs in particularly the general population, this would result in at least 333 000 Dutch adults using OTC NSAIDs in a dosage exceeding the maximum at any given time.

Strengths and limitations

The strength of this study is that it had access to participants' electronic medical records and hence the ability to accurately identify patients at a high risk of developing an ADE in case of NSAID use. There are, however, several limitations that should be considered when reviewing the results. First, the fact that patients from specific risk groups were oversampled in the high-risk sample, means that the overall result in this sample cannot be extrapolated directly to the total population of high-risk patients in the Netherlands. However, the results per individual risk group, such as patients with a history of peptic ulcer, myocardial infarction, stroke, heart failure, or chronic renal insufficiency, are representative, and the percentage of use was at least 10% in the majority of the risk groups investigated. Secondly, the participating GPs excluded patients who they deemed inappropriate for participation, which limits to some degree the generalisability of the results and may have led to a slight overestimation of actual OTC NSAID use, as excluded patients were older and more likely to have a high risk than included patients. Thirdly, the response rate was low in both groups, which may have led to an under- or overestimation of OTC NSAID use. However, even in the unlikely event that none of the non-participants used an OTC NSAID, OTC NSAID use in the high-risk sample would still be at least 5%. Finally, it has been suggested that >60% of people cannot identify the active ingredient in their brand of analgesic.[22] If this is the case, the use of OTC NSAID may have been underreported by participants in this study. The risk of participants under- or overreporting the use of OTC NSAIDs was minimised, by supplying an overview of all brands of NSAIDs available OTC in the Netherlands, including pictures of the brand logos, and by asking participants to tick the box next to the OTC NSAID they had used.

Comparison with existing literature

The prevalence of use of OTC NSAIDs in patients with a contraindication for use has been examined in one previous Dutch study in 2005.[23] This previous study did not examine OTC NSAID use in the general population and did not include ischaemic cardiovascular disease as a contraindication for NSAID use. Nonetheless, at 14% the prevalence of OTC NSAID use among high-risk patients found in this previous study is similar to the current finding of 13%. NSAIDs are available OTC in many other countries, including the US, UK, and Australia. A US survey conducted in 1997 found that 12% of adults had used OTC NSAIDs on at least two occasions in the past 12 months for at least 5 consecutive days at a time.[24] In a later survey performed in the same country in 2002, 83% of individuals interviewed reported OTC analgesic use in the past year, and 37% of those interviewed reported using them daily or several times a week.[24] In the current study, the use of OTC NSAIDs in the past month was examined only, which makes it difficult to compare the current findings among the general population with those in the US. A UK study did investigate the same time period and found that 68% of individuals interviewed had used an OTC NSAID in the past month.[14] This high prevalence may be explained by the fact that the study was performed among University students instead of the general population, but may also reflect differences between countries. In Australia, for instance, the use of OTC NSAIDs was found to be much lower than in the current study. In two surveys performed there in

2001 and 2009, respectively 7.5% and 14% of adults reported regular NSAID use (at least once a month). The authors suggest that the increase found may be due to the fact that ibuprofen received a general sales status in 2004, making it more widely available.[16]

Implications for research and practice

In the Netherlands, high-dose NSAIDs and large package sizes can only be purchased in pharmacies, while lower doses in smaller package sizes are freely available in drugstores and, in the case of ibuprofen 200 mg, in supermarkets.[25] The majority of OTC NSAID users in this study purchased their NSAID at a drugstore. It has been suggested that changing the legal status of all NSAIDs to 'pharmacy only' may reduce the use of OTC NSAIDs by high-risk patients, as pharmacists can often identify such patients.[12] In this study, high-risk patients did appear to receive information on purchase more frequently at a pharmacy than at a drugstore or supermarket. The question remains whether the information they received was sufficient, as they did proceed to purchase the NSAID. In addition, this study provides no information on the number of high-risk patients who intended to purchase OTC NSAIDs, but refrained from purchasing them after being warned against such use. Further studies are needed to assess whether changing the legal status of all NSAIDs (including low doses) to 'pharmacy only' will encourage safer use of OTC NSAIDs.

GPs can also play an important role in encouraging safer use of OTC NSAIDs, by informing patients of the risks of these drugs, for instance when a new diagnosis is made or medication is prescribed that alters the patient's risk profile. Compared to non-users, OTC NSAID users in the high-risk sample were far more likely to have been diagnosed with a musculoskeletal complaint or headache by their GP in the 6 months prior to participation. At least 58% of OTC NSAID users in this population had consulted their GP because of one or both of these complaints. The true percentage is likely to be even higher, as ICPC-coded diagnoses were examined only and GPs do not always apply this coding. Therefore, these consultations provide an additional opportunity to inform patients of their risk of developing ADEs in case of NSAID use. It is possible that GPs also play a role in the high percentage of OTC NSAID use found in the general population. In the Netherlands, for many patients the use of OTC NSAIDs may be cheaper than using NSAIDs on prescription. It is possible that GPs recommend OTC NSAID use in such patients. If this is the case, it is important that sufficient warnings are given regarding the dosage and duration of use.

Within the high-risk sample, the use of OTC NSAIDs was particularly low in patients using anticoagulants. This may be explained by the fact that these patients are monitored at anticoagulant clinics, where they are frequently seen and receive extensive advice regarding interacting medication. This suggests that providing more structural advice regarding NSAIDs for patients using aspirin, corticosteroids or SSRIs, may encourage safer use in these risk groups. Larger scale studies are needed to further explore these findings and to investigate interventions aimed at improved informing of specific groups of high-risk patients.

In conclusion, the use of OTC NSAIDs is widespread, not only in the general population but also in patients in whom such use may lead to a high risk of developing serious ADEs. Future studies should focus on specific risk groups and interventions aimed at encouraging safer use of OTC NSAIDs. Continued efforts by health authorities and healthcare professionals to inform patients of the risks of these drugs are warranted.

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Ethical approval

The study was approved by the Medical Ethics Review Committee of the Erasmus Medical Centre and by the Board of Directors of the IPCI database.

Provenance

Freely submitted; externally peer reviewed.

Competing interests

Vera E Valkhoff conducted research for AstraZeneca in the past as an employee of the Erasmus MC University Medical Center. Miriam CJM Sturkenboom coordinates a research group that occasionally performs research for pharmaceutical industries; none of the grants were related to the current article. All other authors declare no competing interests.

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