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Purchasing Over The Counter (OTC) Medicinal Products Containing Codeine - Easy Access, Advertising, Misuse and Perceptions of Medicinal Risk

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ABSTRACT - Purpose. Codeine containing medicines can carry a number of health risks associated with the increase in reported misuse and dependence, however they are still readily available over the counter (OTC) in many countries. The aim of this novel study was to report on the results of a survey of customers purchasing OTC codeine containing medicinal products at pharmacies in Ireland, South Africa and England; exploring use, sources of knowledge and perception of risks. **Methods.** The study design was an exploratory cross sectional survey. It involved a customer self-administered questionnaire at the point of purchase (n=1230). Relationships between categorical variables were analysed using Pearson chi-square for bivariate analysis. Continuous scale variables were analysed using one way analysis of variance. **Results.** In Ireland 6% stated they purchased codeine containing products weekly, in South Africa 13% and in England 16%. In Ireland and England women are more likely to view codeine containing products as harmful. In England older adults are more likely to perceive codeine containing products as harmful. A higher proportion of customers in South Africa opposed restricting codeine containing products to prescription only when compared with people in Ireland and England. **Conclusions.** Codeine containing products are widely purchased and used in all three jurisdictions. Whilst the majority of customers appear to have some awareness and knowledge of risks, it does not materially impact on their purchasing behaviour with a substantial minority purchasing/using such products on a weekly basis. This regularity of purchase whilst indicative of the popularity of such products, may also be a potential indicator of misuse. Future research is needed in relation to cultural and gendered differences and targeted information giving and harm reduction initiatives for safe usage of these medicinal products.

INTRODUCTION

Codeine (3-methylmorphine) is a weak opioid, widely used for its analgesic, antitussive and anti-diarrheal properties. Commonly used to manage mild to moderate pain, it is available in low dose non-prescription medicinal products in a number of countries (1-2). Over the counter (OTC) purchase of codeine based analgesic products without medical consultation occurs in many countries and even in countries where it is regulated, purchase and use is considerable (3). There is little comparative international data exploring differences in customer use, sources of information and knowledge of OTC codeine containing products between countries which allow non-prescription purchase. This paper reports on a study that aimed to address this gap through a survey of customers purchasing such products at participating community/ commercial outlet pharmacies in Ireland, South Africa and England.

Deregulation has led to increased customer access, choice, self-medication and pharmacist empowerment with regards to codeine and non-opioid analgesic dispensing (4,5,6). Consequently, the misuse of these products appears to be on the increase (2,7); with access to open purchase lessening the consumers' ability to recognise problematic use and dependency (9-10). Public perception and possibilities for opioid tolerance within a short timeframe contributing to habitual use, misuse and dependence (8). Awareness of the dangers associated with these products is somewhat mixed. Bower and colleagues found that consumers tended not to approach the use of OTC medicines with the same level of caution and care as they displayed towards prescribed medication. (11).

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Research indicates OTC analgesics and other codeine based medicinal products are frequently taken inappropriately and that consumers are generally unaware of the potential of the physical harms that can result (12-14, 4). However, there is some evidence which suggests that public awareness of harm risks is improving (15-16).

Direct to consumer advertising (DTCA) is a significant avenue through which pharmaceutical companies promote medicinal products to consumers (17-19). DTCA creates product awareness and encourages use amongst consumers. DTCA empirical research in relation to medicinal products is not extensive and tends to focus on national rather than international contexts. The available studies indicate that DTCA can be a significant source of information and is highly influential in relation to consumer choice of product, use of such products and belief in product safety (19-21); particularly if the product is regularly and widely advertised (22-25). DTCA can also be a considerable source of tension between the consumer and professional pharmacists (26), as consumers appear to trust and pay attention to DTCA messages rather than the informed opinion of pharmacists encountered at the point of purchase (25-29).

METHODS

Study Design

This study adopted an exploratory, cross sectional design, involving a self-administered questionnaire to collect data from consumers at the point of purchase with a purposive sample who, at the time of survey, purchased OTC medicinal products in pharmacies in Ireland; South Africa and England. Customers who were aged 18 or over and were able to read in English were asked to participate. Thirty-six questionnaires contained too many missing values and were therefore excluded from analysis. Hence the final sample consisted of 1230 customers across all three countries. Ethical approval was received in August 2016 from research institutions in Ireland; South Africa and England.

Questionnaire development

The questionnaire, based on previously published literature, was assessed for content validity by the research team (academic researchers and experts in pharmacology, addiction and pharmacovigilance). Pilot testing was conducted in three outlets to test the survey form. Following on from this pilot, some items were changed and the overall number of items reduced.

The final 18 item questionnaire consisted of closed-, open-ended and Likert scale response items covering demographics; use of OTC codeine containing medicines; purchasing patterns of such products; views on their safety and availability. The survey was anonymous and no individuals could be identified through their responses.

DATA ANALYSIS

The statistical package SPSS v.22 was used for analyses. To examine relationships with other study variables, the demographic variables of gender; marital status; age; education and employment status were treated as categorical data. Variables relating to the use of OTC codeine containing products and knowledge pertaining to where to purchase such medicines were also treated as categorical data. Relationships between these variables were analysed using standard statistical methods for categorical data – Pearson chi-square for bivariate analysis.

The questionnaire's final section contained 5 closed-ended statements, measured on a Likert scale. The data was treated as continuous and each category was recoded to indicate positive or negative agreement with each of the statements. This produced a scale of +2 to -2 where +2 showed the strongest agreement and -2 indicated the strongest disagreement. Neutral responses were scored as 0. Consequently, the data was analysed mainly using parametric methods. Adjoining categories within these items were collapsed; strongly agree and agree were combined; neutral was treated as a separate category and finally, disagree and strongly disagree were also merged. The percentage agreement and frequencies were then presented as an indication of the overall level of agreement with the statements. Additionally, these variables were subsequently treated as categorical and were analysed by Pearson chi-square and the results were then compared.

RESULTS

Profile of respondents

Demographics for each country are presented in Table 1.

Use of Codeine containing products medicine

The majority of respondents took codeine containing medicines to treat pain; however 2% in Ireland and 0.5% in England took these medicines to help them to relax, compared to 6% in South Africa (Fig. 1).

In both Ireland and England the proportion of males (77%, 70%) who had taken codeine containing medicines was not significantly different to females (81%, 80%). However, a difference was seen in

South Africa, where 74% of males took these medicinal products compared to 79% of females and there was a significant association between gender and use of Codeine containing products medicine ($\chi^2(2, n=665) = 6.40, p=0.04, phi=0.10$).

Nineteen percent and 15% of respondents in Ireland and England indicated they did not read the information leaflet, whereas in South Africa this figure was roughly a third at 29% (Table 2). Chi-square test for independence indicated a significant association between country and reading advice ($\chi^2(4, n=1027) = 25.60, p=0.00, phi=0.16$). There were no statistically significant results in terms of gender and reading advice; however in all three countries the proportion of females reading the advice was always higher than for males.

A significantly higher proportion of English respondents (94%) stated they consumed combination codeine containing analgesics ($\chi^2(4, n=1020) = 94.81, p=0.00, phi=0.31$). Furthermore,

English respondents (80%) seemed more aware of the warnings associated with paracetamol packaging ($\chi^2(2, n=297) = 16.28, p=0.00, phi=0.23$).

The majority of Irish respondents (42%) took codeine containing products less than once a month (Fig. 2). In South Africa, 17% took such products a couple of times a week and 17% stated less than once a month. In England, 26% of respondents stated they consumed these products less than once a month but this was followed closely by 22% who stated at least a couple of times a week.

In all three countries, respondents stated constipation, drowsiness and nausea among the unpleasant side effects. In South Africa, these also included dizziness and dependence. In England side effects included dizziness and headache. All three countries were very similar in relation to the proportion that had experienced these unpleasant side effects (12% in Ireland, 14% in South Africa and 16% in the U.K.).

Table 1. Demographic profile of respondents

N=1230	Ireland ^a		South Africa ^a		England ^a (N=237)	
	n	%	n	%	n	%
Gender						
Male	80	25	266	42	95	41
Female	243	75	374	58	139	59
Age						
Over 18	26	8	44	7	8	3
21-30	86	27	141	21	57	24
31-40	77	24	164	25	40	17
41-50	66	20	141	21	44	19
51-60	44	14	92	14	40	17
61-70	21	6	47	7	27	12
71 and over	5	1	31	5	19	8
Marital status						
Married/living with partner	174	54	359	56	137	59
Never married	107	33	163	25	45	19
Divorced / Separated	21	7	78	12	32	14
Widowed	19	6	43	7	18	8
Education						
Primary School	10	3	16	2	4	2
Secondary / High School	105	32	360	55	109	47
College	209	65	279	43	120	51
Employment status						
Employed	231	71	483	73	141	60
Unemployed	21	6	48	7	30	13
Homemaker	29	9	36	6	14	6
Student	20	6	29	5	7	3
Unable to work due to a chronic condition	7	2	8	1	4	2
Retired	18	6	55	8	39	16

^a Some percentages calculated using denominator less than stated total due to missing data

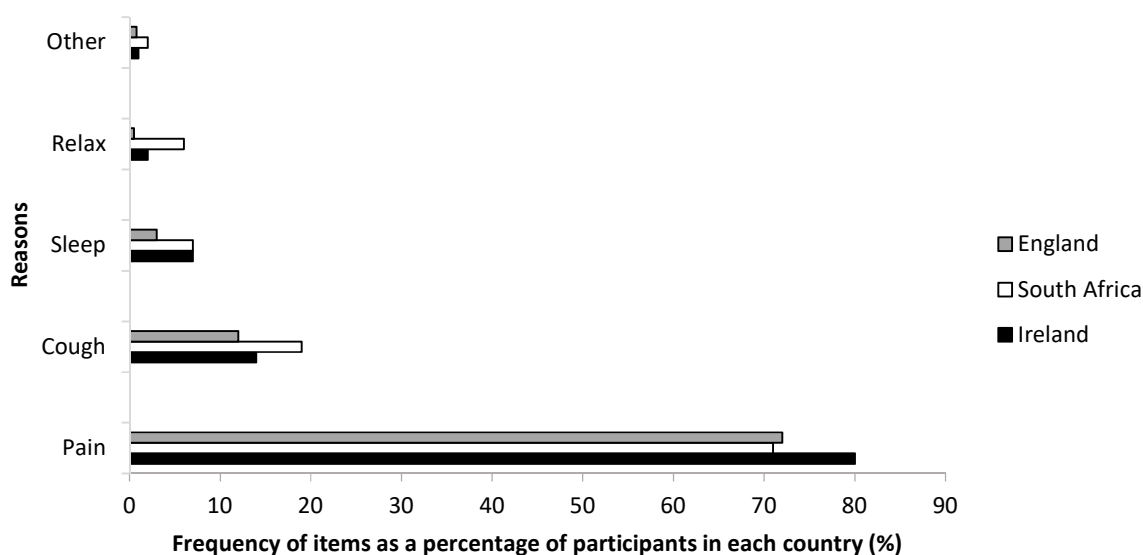


Figure 1. Reasons cited for taking codeine containing products

Table 2. Advice and warnings

N=1027	Ireland		South Africa		England	
	n	%	n	%	n	%
Read advice***						
Yes	216	78	390	69	150	80
No	54	19	161	29	27	15
Don't know	7	3	11	2	11	5
Used combination analgesic***						
Yes	173	64	306	55	176	94
No	58	21	164	29	5	2
Don't know	41	15	90	16	7	4
Notice paracetamol warning***						
Yes	99	65	—	—	116	80
No	41	27	—	—	13	9
Don't know	12	8	—	—	16	11

*** $p < 0.001$

In relation to the purchase of Codeine containing products, in Ireland, 65% stated that they purchased these products in the local pharmacy; a higher percentage (73%) stated the same in South Africa. However, in England the percentage was only 45% (Table 3). In Ireland and England, 1% and 2% respectively stated they purchased these products every day; however in South Africa this was 5%. In Ireland 6% stated they purchased weekly, in South Africa 13% and in England 16%. Medicines purchased most frequently in Ireland included Nurofen Plus[®], Solpadeine[®] and Feminex[®]. Medicines purchased most frequently in South Africa

included Adcodol[®] and Benylin[®]. Medicines purchased regularly in England included Codamol[®], Nurofen[®] and Solpadeine[®].

Knowledge of codeine containing products

Respondents were asked to state their main sources of information in relation to medicine containing codeine. In all three countries, the most frequent answer was from the physician or pharmacist (Fig. 3). However, this was followed by advice from family and friends in both Ireland (23%) and South Africa (26%). In England, 27% stated they sourced their information from the packaging or leaflet.

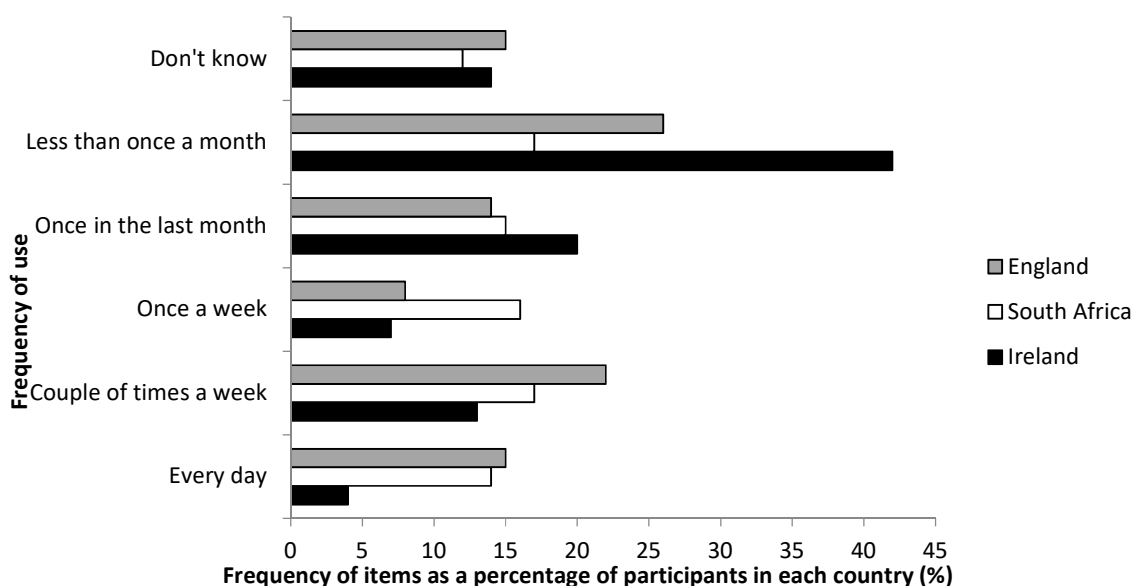


Figure 2. Frequency of use in the last year

To a statement concerning effectiveness, the majority in all three countries agreed that it is effective (Table 4; 79% v 73% v 80%). Only, 34% of respondents in Ireland, 43% in South Africa and 25% in England disagreed with the statement that codeine containing medicines should be prescription only. In Ireland and England a similar proportion agreed that these medicines were harmful and addictive. However, in South Africa the proportion was lower. A one-way between-groups analysis of variance and a chi-square test were conducted and revealed a statistically significant difference between countries ($p=0.00$), post hoc analysis indicated that South Africa was significantly different to both Ireland and England for both statements.

An independent-samples T-Test was used to compare gender against areas of knowledge. In Ireland, this was statistically significant for prolonged use of such products is harmful ($p=0.000$) and medicine containing codeine is addictive ($p=0.000$). In both of these areas females agreed to a greater extent with the statements compared with males. In England, females appeared to agree more strongly than males that prolonged use of codeine containing products is harmful ($p=0.026$) and that such products are addictive ($p=0.022$). However, when a Chi-square test for independence was run using the categorical data from England, no significant association was identified.

Impact of age was explored on knowledge of codeine containing products. In England, there was a statistically significant difference in relation to the statements that prolonged use of codeine containing products is harmful ($p=0.001$) and that medicine containing codeine is addictive ($p=0.000$). The 41-50 ($p<0.00$) and 61-70 ($p<0.05$) age groups agreed more strongly with the first statement compared to the 21-30 age group. Similarly, the 41-50 ($p<0.00$) and 51-60 ($p<0.01$) age groups agreed with the second statement more than the 21-30 age group.

Level of education was compared against areas of knowledge of medicinal products containing codeine. In Ireland, this was statistically significant for prolonged use of codeine containing products is harmful ($p=0.01$) and medicine containing codeine is addictive ($p=0.04$). Those with college or a technical background agreed to a greater extent with the statements compared with those who completed secondary school ($p<0.01$ and $p<0.05$). In South Africa, those educated to college level appeared to agree more strongly, compared to those who had completed secondary level education, that medicine containing codeine should be available on prescription only ($p=0.02$); that prolonged use of codeine containing products is harmful ($p=0.01$) and that medicine containing codeine is addictive ($p=0.05$).

Table 3. Purchase of medicine containing codeine containing products

	Ireland ^a (N=328)		South Africa ^a (N=665)		England (N=237) ^a	
	n	%	n	%	n	%
Purchased in the last year						
Yes	202	63	471	74	115	48
No	84	26	163	26	101	43
Don't know	34	11	0	0	21	9
Where do you purchase						
Local pharmacy	212	65	487	73	107	45
Supermarket	16	5	---	---	29	12
The internet	1	0.3	3	0.5	0	0
Other	0	0	9	1	0	0
Frequency of purchase						
Every day	2	1	27	5	2	2
Weekly	13	6	65	13	20	16
Monthly	52	23	158	32	27	22
Very occasionally	136	63	206	41	68	56
Never buy it	6	3	6	1	3	3
Don't know	8	4	37	8	2	1

^a Some percentages calculated using denominator less than stated total due to missing data

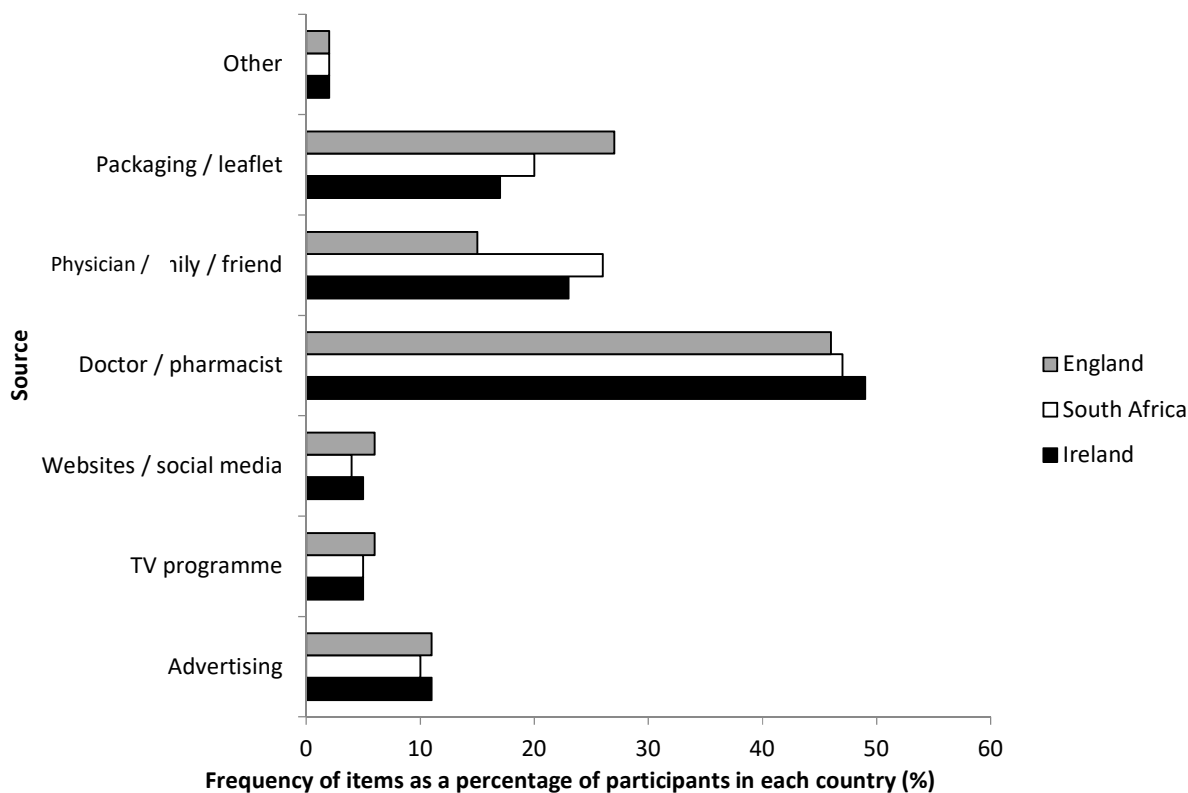


Figure 3. Sources of Information

Table 4. Knowledge relating to codeine containing products

Statements	Ireland ^a (N=328)	South Africa ^a (N=665)	England ^a (N=237)
	Mean (±SD) n (%)	Mean (±SD) n (%)	Mean (±SD) n (%)
Medicine containing codeine is effective	1.12 (0.84) 251 (79)	0.97 (0.97) 437 (73)	0.96 (0.71) 177 (80)
Medicine containing codeine is safe to use	0.53 (0.90) 177 (58)	0.52 (1.0) 310 (52)	0.51 (0.90) 114 (54)
Medicine containing codeine should be available on prescription only	0.02 (1.16) 99 (32)	-0.21 (1.30) 180 (30)	0.21 (1.11) 84 (39)
Prolonged use of medicine containing codeine is harmful	0.98 (0.96) 210 (67)	0.57 (1.11) 271 (45) ***	0.82 (0.92) 133 (62)
Medicine containing codeine is addictive	0.91 (0.97) 195 (63)	0.39 (1.05) 315 (52) ***	0.80 (0.96) 127 (60)

*** $p < 0.001$ ^a Some percentages calculated using denominator less than stated total due to missing data

DISCUSSION

The literature indicates that patients develop an iatrogenic codeine dependence as a result of initially taking this medication to manage pain; the literature also indicates that others commence using it to manage stress, anxiety or help them sleep (1-2). Thus, minorities in this survey in each country admitted to use of codeine containing products for relaxant effects.

The management of family centred stresses tends to fall upon women (30) and non-prescription codeine containing products provide an accessible distress intervention. This can be seen in the two most popular products consumed by South Africans which were Adco Dol[®], a product used to manage 'general body pain' with an associated sedative effect and Benylin[®] which has a sedative effect. Less support in South Africa for prescription only may reflect the fact that more daily use of these products when combined with having to obtain prescription from a physician (31), was perceived as adding an unacceptable expense to a product perceived as relatively benign.

Availability and easy access to codeine containing medicine greatly reinforces perceptions of harmlessness and willingness to seek out and use the product regularly (4-6). The majority of respondents said they purchased these products in local pharmacies. However, it should be noted that as the survey was conducted in community pharmacy outlets this sample may be likely to state that they

purchased these products in the pharmacy and not elsewhere (e.g. online).

In terms of level of regular use, the results of the survey were ambiguous; particularly for South Africa and England where differences between those who took such products regularly on a weekly basis and those who used the product less than once a month were evenly split. Whilst those using it weekly were worryingly high, it is perhaps the higher comparative figure for England that is a surprise (bearing in mind the socio-economic position of the South Africa population is considerably less favourable than in England). These results suggest that comparative cultural aspects of OTC use need to be further examined. This is further reinforced considering the substantial difference between England, South Africa and Ireland in using combination analgesics, with 94% of English respondents using these analgesics compared to 64% and 55% in Ireland and South Africa respectively.

In all three countries the most commonly bought products are amongst those with a high brand recognition. These results would appear to give some credence to the limited evidence that branding plays an important role in consumer choice of medicine (22-25). However, what is striking is that research on the relationship between advertising and use of OTC products such as Solpadeine is limited. It needs to be further examined within the context of people developing dependency.

Insert leaflets are often not consulted by consumers and advertising's role is considerable in

terms of information reception (19-21). Whilst the overall results would not necessarily run counter to this finding (see Table 2), the survey did indicate that this is more nuanced than the literature suggests. Thus, for example, women in all three countries were more likely to read the insert leaflet than men (though not statistically significant).

There were differences between countries in terms of sources of information, with more people in England stating they got information from the leaflet; whereas more people in South Africa and Ireland said they got information from family and friends (perhaps reflecting a cultural difference in the strength and proximity of family relationships). The majority in all three countries indicated that they relied on medical professionals and pharmacists for advice and information.

The literature indicates that highly educated people are more aware of OTC medicine risks than those less educated (4). The survey results appear to support this conclusion for Ireland and South Africa. However, people in England seem more aware of warnings about dangers of codeine containing products and that was a statistically significant difference. One possible reason for this, other than differences in package design in different jurisdictions (which would not account for the difference with Ireland), might be the way products are displayed or again cultural factors as to how different societies are socialised to recognise and internalise signs of risk/ warnings.

Just over half of all those surveyed in the three countries viewed codeine containing products as a safe medication. In Ireland, women were more likely to view such products as harmful though this was not statistically significant in England and South Africa. In England there was an age difference, with older people (those over 40) more likely to perceive codeine containing products as harmful. This was not the case, however, in Ireland and South Africa. These results would appear broadly reflective of the literature which indicates that people in general do not perceive codeine containing products as harmful, even though they are aware of their potential dangers (4, 13-14, 32).

Finally, with regards to our samples' views on whether or not to make codeine containing products a prescription only medicine there was a considerable number of people in Ireland and England who were not against this proposition and even in South Africa there was majority support. Again, within this context a number of features should be noted, including that in Ireland and South Africa, the higher respondents' education the more likely they were to support this proposition (it should be noted that people in England had the highest level of agreement

that codeine containing products should be a prescription only drug, with level of education not being a significant factor). The level of disagreement with the proposition in South Africa (43%) can be seen as aligned with the fact that South Africans were the least likely of the three samples to view such products as harmful. Overall, the challenge lies in ensuring availability of codeine containing medicines for therapeutic use whilst preventing dependence and related harms. Best practices and innovations have been identified which focus on the products retail lifecycle from manufacture to community pharmacy practitioner (33). These innovations warrant further consideration and inclusion in regulatory and policy debate in each country in order to reduce misuse, dependence and related health harms.

Limitations of the study

This study has several limitations and hence interpretations should be treated with some caution. A disadvantage of implementing questionnaires, which being anonymous and self-reporting reduce bias and facilitates honest responses, is that it is difficult to establish cause-and-effect conclusions. Therefore, demographics outlined in the study may not be the proximal reason for some of the chosen answers and the results remain descriptive in nature. With regards analysis, the decision was taken to use parametric tests at times, as these tests furnish additional information in relation to the data. In order to support this further, chi-square analysis was also conducted using the same variables and where only the parametric tests were significant, this was highlighted. The inability statistically to generalise findings due to the sampling method selected is recognised as a limitation, although as the study was exploratory in nature, it was deemed as the most appropriate choice. However, the sample size in each of the three sites was of a relatively large size and therefore the data being gathered possess a better description of the relative characteristics of the general population involved in the study.

CONCLUSION

This study aimed to explore comparatively customer use, sources of information and knowledge of OTC codeine containing medicinal products in three countries. In this context, the survey indicates two important factors which should be examined in further research. The first relates to cultural differences in perceptions, knowledge seeking and communicating with regard harms and harm reduction. It is an issue that one might argue is pressing, from a public health perspective. The

second area is the issue of gender differences. This survey would indicate that women are more likely to engage with insert patient leaflets on codeine containing products and its potential harms. Bearing in mind the significance of women within a family context this is an area worth examining in terms of how to disseminate information to reduce harms more effectively than the literature indicates is presently the case.

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