MULTIPLE PRESCRIBERS IN OLDER FREQUENT OPIOID USERS – DOES IT MEAN ABUSE?

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ABSTRACT

Background
Obtaining analgesic narcotics from multiple prescribers is sometimes called 'doctor-shopping,' implying abuse. If the use of multiple prescribers can be used as an indicator for abuse, it would be a convenient way to study abuse in large populations.

Objective
To assess multiple prescribers as an indicator of abuse by relating quantity of opioids obtained by older Norwegians to number of prescribers.

Methods
Data were obtained from the Norwegian Prescription database which includes all prescriptions filled in Norwegian pharmacies. The study population consisted of people aged 70-89 who filled five or more prescriptions for weak or for strong opioids in 2008.

Results
In 2008, 4,268 persons filled five or more prescriptions for strong opioids and 19,675 for weak opioids. More than 30% had three or more prescribers. Over half of strong opioids users and 72% of weak opioid users had medication-use-periods of over 40 weeks. For strong opioids, increasing DDDs/week was found with increasing number of prescribers. When cancer/palliative care patients were excluded, the mean DDDs/week level for strong opioids was much lower, and little association with number of prescribers remained. For weak opioids, little association between mean DDDs/week and number of prescribers was found.

Conclusions
This study demonstrated that the increasing quantities of strong opioids with increasing number of prescribers are largely due to treatment of cancer/palliative care patients. While the use of multiple prescribers can be a red flag for problematic medication use, it cannot be considered synonymous with 'doctor-shopping' or abuse.

Key Words: *Analgesic opioids, doctor-shopping, multiple prescribers, population-based data, elderly, cancer/palliative care*

The use of potentially addictive medications such as narcotic analgesics continues to increase with time.[1-3] Rates of opioid use are influenced by a variety of factors. On the one hand, the increased emphasis on pain control will increase analgesic opioid use, while, on the other hand, the ever-present spectre of addiction and diversion will work to decrease it. Increased emphasis on adequate pain

control in older people has been noted in recent years. For example, the AMS Panel on Persistent Pain in Older Patients stressed that older persons should not be in pain when a treatment for that pain exists, including the use of opioids when other analgesics do not provide sufficient relief.[4] Although better pain control is to be welcomed, one always needs to be on guard for abuse and misuse of these potentially addictive medications. Because of the concerns about dependence or abuse, extra measures have been taken by the regulatory authorities of most countries. In Norway, potentially addictive drugs are classified in two prescription groups (A or B). Category A substances have to be prescribed on a special form and include the strong opioids, while category B include the weak opioids.[1] Restrictive measures at the pharmacy level include no refills and retention of the scripts in the pharmacy allowing them to be used by the health authorities for control purposes. Even with these extra measures abuse is known to occur.

Although younger people are more known for abusing opioids, it cannot be assumed that older people will not engage in drug-seeking behaviour beyond that intended by their physician. Trevisan and others working with the older population, worry that when baby boomers reach their senior year there may be an increase in opioid abuse.[5] Trevisan surmised that since baby boomers have experimented more with alcohol and illicit drugs than previous generations, they may also have more lenient attitudes about alcohol and illicit drug use than previous generations. In the USA dramatic increases in abuse of narcotics were found in older adults.[5] The burden of non-medical use of opioids on society is great and goes far beyond the mere costs of the opioids themselves. In fact, costs include not only the health care costs of the addicted persons but also the cost of their decreased productivity and the cost to society of the measures designed to prevent addiction.[6]

A simple-to-use indicator of opioid abuse would be a very useful tool in monitoring opioid abuse at all ages including the older population. Since it has been shown that for older people at the stage of seeking treatment for opioid addiction, their largest source of opioids was from prescriptions received from physicians[7], an important source of information on potential abuse of analgesic narcotics would be prescription data bases. One approach to obtaining opioids for non-medical use is called 'doctor shopping'. 'Doctor-shopping' can be defined as the use of multiple prescribers to obtain higher amounts of opioids than therapeutically indicated.[8,9] Individuals will actively seek out other physicians to obtain more of analgesic opioids, either by embellishing the severity of their pain, or by not informing physicians of opioids already received. Previous studies have used various methodologies for assessing the extent of 'doctor-shopping' in drug data bases: such as comparing number of prescribers for three addictive drugs with that of three non-addictive drugs[10]; calculating a doctor shopping index based on measuring the overlap of prescriptions from different prescribers[9]; or examining number of prescribers and number of pharmacies used.[11,12] However, there are also studies that simply assume that obtaining opioids from multiple prescribers means 'doctor shopping'.[13,14] If number of prescribers can be used as an indicator of abuse, this would present a convenient means of monitoring potential abuse using population-based data bases. However, this needs to be validated. Since the aim in 'doctor-shopping' is to increase the amount of opioids obtained, relating the quantities of opioids obtained by patients to number of prescribers used should provide a clue as to whether the use of multiple prescribers points to a potential for abuse. Therefore, the objective of this study is to relate the quantities of prescribed opioids obtained by older patients to number of prescribers in order to examine to what extent the use of multiple prescribers can be related to, or equated, with 'doctor shopping' or drug seeking behaviour.

METHODS

The study population was derived from the Norwegian Prescription Database (NorPD) which registers all prescriptions filled at any pharmacy in Norway. Medications are coded using the anatomical, therapeutic, chemical (ATC) classification which allows the selection of specific medications.[15] For this study, medications were limited to the opioids from the ATC N02A category. Data on each prescription include prescription identification (id), user id, sex, year of birth, prescriber id, ATC code. Also included are administrative reimbursement codes which indicate

whether the patient is receiving palliative care or treatment for cancer. Patients with at least one code related to cancer treatment or palliative care in 2008 were identified as cancer/palliative care patients. The quantity of medication prescribed expressed as defined daily dose (DDD).[16,17] DDD is a quantitative unit of measurement defined as the assumed average maintenance dose per day for the medication's main indication for adults. Norwegian population statistics were obtained from Statistics Norway (statbank.ssb.no/statistikkbanken/).

The age of the study population selected was 70-89 in 2008, and consisted of two groups: 1) persons filling at least five prescriptions for weak opioids, to be called frequent weak opioid users, or 2) persons filling at least five prescriptions for strong opioids, to be called frequent strong opioid users. The reason for limiting the study population to persons using at least five prescriptions in 2008 is that in order to use multiple prescribers a corresponding number of prescriptions needed to be filled. Five prescriptions still allowed for sufficient numbers in the study population while larger numbers decreased the size of the study population without much change in pattern of use. Weak opioids include tramadol and combination drugs with codeine or dextropropoxyphene (ATC N02AA59, N02AC54, and N02AX02). Strong opioids include morphine, oxycodone, fentanyl and buprenorphine (ATC N02AA01, N02AA05, N02AB03, and N02AE01). ATC codes with fewer than a thousand prescriptions in 2008 were excluded for analysis. Use of opioids in hospitals or nursing homes or opioids sold as supplies to physicians' offices are not included in the NorPD at an individual level and could therefore not be included in this study. Excluded were all those who died in 2008 since they would be exposed to opioids only up to the time of deaths and thus not the whole year. Another issue is that many patients will be admitted to hospital or live in nursing homes, in shorter or longer periods, in the end stage of life and this would further limit the time of opioid exposure that can be measured in our study.

Analysis

For statistical analysis, SAS version 9.2 (SAS Institute, Cary, NC, USA) was used. The unit used for comparing medication use was mean DDDs/week which was derived by dividing the total DDD over 2008 by the medication period for each person, i.e., Mean DDDs/week=total DDD/medication period. Medication periods were estimated from the weeks (numbered from 1 to 52 in 2008) in which the first and last prescriptions in 2008 were filled, i.e., Medication period = (last week - first week) + 2 weeks.

The two weeks at the end were added to account for use of the final prescription. Mean DDDs/week was calculated per person and for strong opioids and weak opioids separately.

RESULTS

The almost 20,000 persons, aged 70-89, who filled at least five prescriptions for weak opioids, and the 4,268 persons for strong opioids in Norway in 2008 (table 1) were defined as frequent users of weak opioids and strong opioids, respectively, for this study. These figures represent 4.3% (frequent weak opioid users) and 0.9% (frequent strong opioids users) of the Norwegian population of this age group in 2008 (not shown in the table). The number of female frequent opioid users is almost three times that of male frequent opioid users for both weak opioids and twice that for strong opioid use. While the majority of frequent opioid users had only one or two prescribers, more than 30% had three or more prescribers. Almost 5% of frequent strong opioid users and 6.6% of frequent weak opioid users received prescriptions from five or more prescribers in 2008. The maximum number of prescribers was well over 15 (not shown in the table). More than half of the frequent opioid users had medication periods of more than 40 weeks in 2008. The cancer/palliative care patients made up only 6% of frequent weak opioid users but 41% of frequent strong opioids users.

Table 2 shows logistic regression models with a dichotomous dependent variable of 5 or more, mean DDDs/week, versus less. The models are stratified for strong and weak opioids and for cancer/palliative care patients and non-cancer/palliative care patients. The cancer/palliative care patients subgroup showed the greatest increase in strong opioid use with number of prescribers. Smaller increases were seen for the non-cancer/palliative care groups and for weak opioids.

Adjusting for age and sex does not significantly alter the results. Nor does using the variable mean DDD per week as continuous variable for dependent variable (not shown in table) alter the results. In a figure with continuous distribution of mean DDDs/week along the y-axis, strong opioid users showed greater increasing trends of mean DDDs/week with increasing number of prescribers than did weak opioid users (figure 1). When the populations of frequent opioid users were stratified for cancer/palliative care, the cancer/palliative care patients showed a much greater use of strong opioids than the remainder of the population. Cancer/palliative care patients accounted for nearly the entire increase in amount of strong opioid with number of prescribers (figure 1).

TABLE 1 Frequent* opioid users among Norwegians, aged 70-89, by demographic and medication-related variables, 2008

		weak opioids users		strong opioids users	
		N	%	N	%
Total		19,675		4,268	
Sex	males	5,436	27.6	1,341	31.4
	females	14,239	72.4	2,927	68.6
Age	70-74	5,465	27.8	919	21.5
	75-79	5,620	28.6	1,112	26.1
	80-84	4,989	25.4	1,217	28.5
	85-89	3,601	18.3	1,020	23.9
Number of prescribers	1	6,397	32.5	1,540	36.1
	2	6,348	32.3	1,388	32.5
	3-4	5,630	28.6	1,135	26.6
	5-6	1,074	5.5	166	3.9
	7+	226	1.1	39	0.9
Length of medication episode in weeks	<20	1,117	5.7	692	16.2
	20-29	1,388	7.1	562	13.2
	30-39	2,922	14.9	686	16.1
	40-46	5,506	28.0	941	22.0
	47-53	8,742	44.4	1,387	32.5
DDDs/week over the medication episode	<2	2,662	13.5	1,397	32.7
	2	3,588	18.2	707	16.6
	3	3,717	18.9	490	11.5
	4	2,716	13.8	362	8.5
	5-6	3,513	17.9	405	9.5
	7-8	1,710	8.7	266	6.2
	9-12	1,219	6.2	261	6.1
	13+	550	2.8	380	8.9
Cancer/palliative care patients	yes	1,175	6.0	1,749	41.0
	no	18,500	94.0	2,519	59.0

*Frequent opioid use: at least 5 prescriptions for weak opioids or at least 5 prescriptions of strong opioids in 2008 or strong opioids in 2008.
DDD-Defined Daily Dose

TABLE 2 Logistic regression models of frequent* opioid users among Norwegians, aged 70-89, by number of prescribers, adjusted and unadjusted for age and sex. Dependent variable: 5+DDDs\week versus less.

a. Weak opioid users

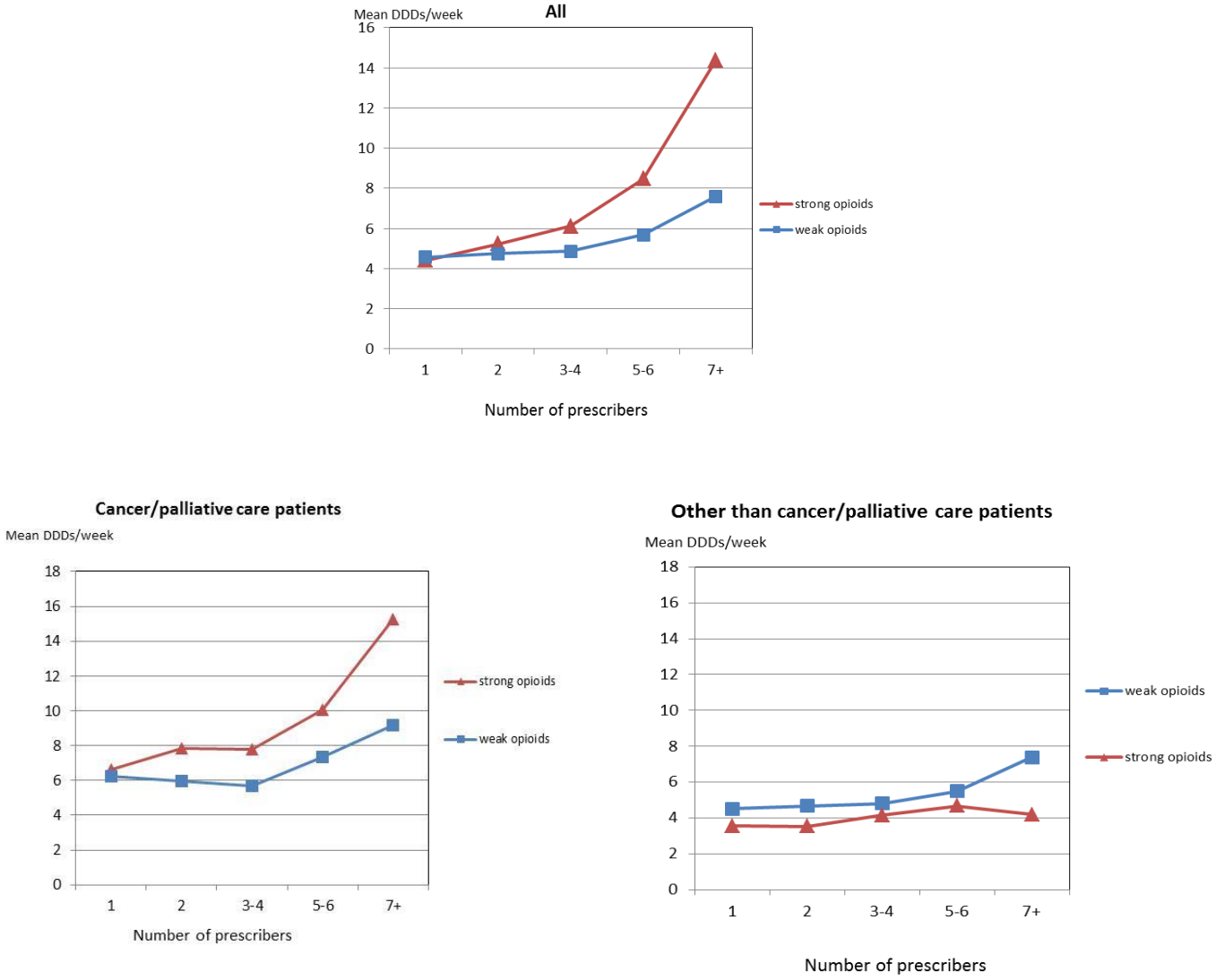
		Cancer /palliative care patients							
		yes (N=1,175)				no (N=18,500)			
		adjusted		unadj.		adjusted		unadj.	
		OR	C.I.	OR	C.I.	OR	C.I.	OR	C.I.
males		1.1	0.8-1.4	-		0.9	0.9-1.0	-	
age		1.0	1.0-1.0	-		1.0	1.0-1.0	-	
Number of prescribers in 2008	1	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0
	2	0.9	0.6-1.2	0.9	0.6-1.2	1.2	1.0-1.2	1.2	1.0-1.2
	3-4	0.8	0.6-1.1	0.9	0.6-1.2	1.3	1.1-1.3	1.3	1.1-1.3
	5-6	1.4	0.9-2.3	1.4	0.9-2.3	1.8	1.3-1.7	1.9	1.3-1.8
	7 +	2.2	1.2-8.2	2.3	1.2-8.3	3.2	2.1-3.9	3.3	2.1-4.0

b. Strong opioid users

		Cancer /palliative care patients							
		yes (N=1,749)				no (N=2,519)			
		adjusted		unadj.		adjusted		unadj.	
		OR	C.I.	OR	C.I.	OR	CI	OR	C.I.
males		1.3	1.1-1.6	-		1.4	1.1-1.7	-	
age		0.8	0.7-0.8	-		0.9	0.8-0.9	-	
Number of prescribers in 2008	1	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0
	2	1.2	0.9-1.5	1.2	0.9-1.5	1.0	0.8-1.3	1.0	0.8-1.3
	3-4	1.4	1.1-1.8	1.5	1.2-2.0	1.3	1.0-1.6	1.7	1.0-1.6
	5-6	2.0	1.3-3.0	2.4	1.6-3.7	1.6	0.9-3.1	2.2	0.9-3.3
	7 +	6.7	2.7-16.6	7.8	3.2-19.1	2.0	0.2-22.6	2.2	0.2-24.0

*Frequent opioid users: at least 5 prescriptions of weak or at least 5 prescriptions of strong opioids in 2008
DDD - Defined Daily Dose

FIG. 1 Mean DDDs/week by number of prescribers for frequent weak or strong opioid users: all and stratified for cancer/palliative care, Norway 2008



DISCUSSION

At first glance, the mean DDDs/week for strong opioid use seemed to increase dramatically with rising numbers of prescribers (figure 1a), apparently confirming the 'doctor-shopping' found in other studies.[9-11] However, when strong opioid use was stratified for cancer/palliative care patients, it was seen that the cancer/palliative care patients were the ones who received the very large amounts with increasing numbers of prescribers. The remaining strong opioid users received lower amounts and showed much smaller increases in mean DDDs/week with increasing prescribers. The implication is that most of the people receiving large doses of strong opioids did so for justified medical reasons.

As with all studies, there are strengths and limitations to the data used. Strengths include the accuracy of the data and their availability for the entire Norwegian population, for the entire year.

Strengths also include the information available on each prescription, such as prescriber id, age, sex, as well as ATC codes and number of DDDs for each medication prescribed. Since it was possible to convert the prescription-based data into person-based data, the amount of opioids received could be accumulated both for number of prescriptions and for total DDD over the year 2008 for each person. A population of frequent users could be selected in which a potential association of number of prescribers and amount of opioid received could be studied. A concern is the lack of information on people living in institutions since their medications are not recorded in the NorPD even though they are still included in the general population, i.e., the denominator, which may lead to an underestimation of rates. Since institutionalizing increases with age, the study population was truncated at age 89.

Another issue to be considered is the use of DDDs to quantify consumption. The recommended dose ranges for opioids are wide and assigning comparable DDD for the various opioids and formulations is a challenge, and, thus, DDD for the various opioids cannot always be considered to be equipotent doses.[15] However, we have used the number of DDDs as a measure for comparing different user groups (cancer/palliative care patients versus non-cancer patients) separately for strong and weak opioids in 2008 and thus, the problem of using DDDs for measuring changes in therapy and doses over time is not relevant in our study.

Not knowing the prescribed daily dose necessitated developing a methodology which could be used to infer the amount of analgesic opioids consumed over time from the available data. The time unit developed was the medication period measured in weeks based on time elapsed between dates of first and last prescription in 2008 adding two weeks for use of the last prescription. Rate of use was then calculated by dividing the accumulated amount in number of DDDs of opioids by the medication period length, providing a unit of mean DDDs/week. For regular use over a specific amount of time, the mean DDDs/week provides a reliable estimate of use. Irregular use would result in a lower mean DDDs/week which for our purposes of estimating increasing amounts available for use in relation to numbers of prescribers is a useful way of dealing with this issue. An overestimate of the rate may result when large amounts are prescribed intended for longer periods of use in which case the two weeks added at the end of the formula may be too short. However, since strong opioids are medications with restricted use and are to be sold in small quantities only this should not be an important concern. Another problem is the fact that use of opioids during short time stay in hospitals or nursing homes would not be included in our data, which is a likely occurrence for the cancer/palliative care patients, and the oldest age groups. Thus, the rates determined in our study may be underestimates especially for the cancer/palliative care patients, and the oldest age groups.

The objective of this study was to examine the relation between multiple prescribers and 'doctor shopping.' by relating quantities of prescription opioid received to the number of prescribers used. The results found that 35% of frequent weak opioid users and 31% of frequent strong opioid users received prescriptions from three or more prescribers, and 6.6% and 4.8%, respectively, for five and more prescribers. Strong opioid users showed considerable increase in total amount of opioid received when multiple prescribers were used, far more than for weak opioid users. Adjusting for age and sex made only a small difference but stratifying for cancer/palliative care showed that a large part of the association between strong opioid use and multiple prescribers could be explained by their use in cancer/palliative care patients. It may be concluded that a large part of the increases in amounts of strong opioids with number of prescribers were due to severity of pain in patients treated and cannot automatically be attributed to the type of drug-seeking behaviour associated with addiction. These results emphasise the need for great caution when considering number of prescribers as a measure of 'doctor shopping.' The results will not come as a surprise to many since older cancer patients not only are known to suffer from severe pain but also are more likely to visit multiple prescribers due to different care settings such as primary care physicians, various specialists, outpatient clinics. We cannot exclude the possibility that some among the frequent opioid users sought to obtain larger amounts of opioid than intended by their physicians but the mere use of multiple prescribers cannot be considered an indicator for

abuse. The use of weak opioids showed much less association with number of prescribers. Weak opioids users also showed a decrease in mean DDDs/week level when cancer/palliative care patients were removed but not to the same extent.

The associations of number of prescribers in the non-cancer/palliative care patients were shown to be stronger for weak opioids than for strong opioids. That smaller associations between opioid use and number of prescribers were seen for non-cancer use is not that surprising. Numbers of prescribers are most likely associated with severity of disease or the number of conditions to be treated. This will result in an increasing need for visiting different physicians including specialists which in turn present opportunities for refill of pain medications.

Although multiple prescribers as such cannot be considered a reliable indicator of opioid abuse, there are other concerns with receiving opioids from multiple prescribers. Even when the larger amounts are medically warranted, one may still worry whether use of multiple prescribers allows for adequate supervision of the medication use. Lack of oversight may lead to poor supervision of medication use leading to poor dosing, or inadequate therapeutic benefit or more than necessary side effects such as frequent nausea and constipation.[18] It is likely that many patients such as the cancer /palliative care patients will also be receiving many other medications and this would also be more difficult to control with many prescribers. Thus, poor oversight would also worsen the adverse effects of polypharmacy.

CONCLUSION

The objective of this study was to relate level of opioid use to number of prescribers in an older population of frequent opioid users on the assumption that such an increase may be indicative of 'doctor shopping.' While increases in quantities of strong opioids were associated with increasing number of prescribers, it was found that such increases could be explained by the large proportion of cancer/palliative care patients receiving strong opioids. With these removed, the association disappeared. This does not mean that none of these older patients were abusing opioids, whether cancer/palliative care patients or not. However, it does mean that one cannot consider multiple prescribers and 'doctor shopping' as synonyms. This finding needs to be confirmed for other age groups since this older population would contain a larger proportion of cancer patients than younger populations. In any case, measures taken to decrease strong opioid use should be motivated more by a concern for quality of health care and for quality of life for the older, than by a concern to detect the small proportion of potential abusers.

Key Points

- The increasing use of prescription analgesic opioids particularly in the older population with its potential for abuse is a public health concern. Although abuse is better known to occur in younger persons, one cannot assume that the older do not engage in drug seeking behaviour.
- 'Doctor shopping' can be defined as the use of multiple prescribers to obtain higher doses of opioids than therapeutically indicated. If 'doctor shopping' occurs in this population of older Norwegians, one would expect that higher amounts of opioids would be obtained by patients with multiple prescribers
- The results showed a steep rise of amount of opioids with increasing number of prescribers but this increase was shown to be almost entirely limited to cancer/palliative care patients.
- Cancer/palliative patients comprise a population needing large amounts of opioids and varied medical care including many able to prescribe opioids as needed.
- In conclusion, use of multiple prescribers cannot be equated with 'doctor shopping.'

Competing Interests and Author Contributions

None of the authors have any conflict of interest, financial or otherwise. All of the authors participated in the data analysis and writing of this article and all have read and approved the final version of the article. The work has been funded by the Norwegian Institute of Public Health.

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