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Original Article

A Meta-Analysis on Misuse of Prescription/OTC Drugs: How Pharmacist Can Prevent and Manage Drug Abuse

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ABSTRACT

Background: Drug misuse is a critical issue related to both physical and psychological health associated with growing threats across the world. The role of pharmacist in preventing drug abuse is crucial to address prescription/OTC medication misuse. **Aim and Objectives:** To synthesize the research on misuse of prescription/OTC drugs, role of pharmacist in preventing and managing prescription/OTC medications induced health conditions and to provide methodological guidance for further research. **Materials and Methods:** Systematically searched epidemiological research on the topics relevant to the study through PubMed and EMBASE from 2017 to 2022 (n = 3022), studies are screened by title/abstract (n = 981) and full text articles are assessed (n = 153). The studies included for meta-analysis (n = 12) are selected by applying inclusion and exclusion criteria. STATA Version 17.0 is used to analyse the data. **Results:** Out of 12 research articles, 6 were conducted on misuse of prescription/OTC medications and another 6 were about prevention and management of the drug abuse by pharmacist. The researchers analysed data through odds ratio, 95% CI at p-value of 0.001* by plotting forest plot. The overall effect size is found to be 1.96 (1.21, 2.71) with 95% CI that shows association between drugs misuse and pharmacist role in drug abuse. Publication bias and Heterogeneity are graphically represented through Funnel plot and Galbraith plot respectively. **Conclusion:** The researchers concluded that the drug misuse is the global burden and pharmacist can endeavour to offer the management and prevention of drug abuse.

Keywords: Prescription drug misuse, OTC medication abuse, Opioid abuse, Meta-analysis.

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INTRODUCTION

Drug misuse is the term which defines as intentional use of medicinal product by inappropriately and not in accordance with the terms the marketing authorisation such as incorrect dose, taken at incorrect time, indication or schedule.[1] Drug abuse is an insistent or erratic, intentional excessive use of medicinal product, taken to get high, inflict self-harm complemented by harmful physical and psychological effects.[2] The key difference between drug misuse and drug abuse is consumer's intent as treatment versus getting high/self-harm respectively.[3] Drug misuse is a critical issue related to both physical and psychological health associated with growing threats across the world.[4] Drug misuse is accompanying with significant global morbidity, mortality, monetary expenses and community expenses.[5] The role of pharmacist in preventing drug abuse is crucial to address the prescription/OTC (Over-The-Counter) medication misuse.[6,7]

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Globally along with Asian countries drug abuse, drug misuse, drug dependence and drug addiction, including consumption of non-medical, legal, and illegal drugs is increased and became the most critical clinical issue which impact seriously on public health.[8] Around 70 million people were diagnosed with a drug use disorder throughout the world.[9] Irrational use of antibiotic due to prescription drug misuse leads to medication discrepancies like antibiotic resistance in the community.[10] Self-medication of OTC drugs leads to OTC drugs misuse and physician prescription, pharmacist lack of knowledge leads to prescription misuse.[11] Many problems confronted by a patient can be easily resolved by pharmacists, including product selection, OTC brand name confusion, appropriate product use, and when to take medications.[12] However, relatively diminutive is acknowledged about those affected individuals, particularly in relation to their management at drug dependence treatment centres.[13] Hence, Pharmacists have focused information about both prescription and OTC drugs and are trained best to communicate their potential and expected harms and benefits to patients.[14] The phenomenon involving the non-medical use and misuse of prescription and OTC medications is called as Pharming.[15]

Table 1: Characteristics of included studies.

Sl. No	Authors, years	Study Design	Sample size	Country	Gender (F=Female; M=Male)	Age (years)	Study conducted year	Follow up in years	Outcome
1.	Vi T. Le, *et al*. 2017	Cross sectional survey	939	U.S.A.	F: 561 M: 361 Missed: 17	18-19: 223 20-21: 275 >22: 433 Missed: 8	2011	N/A	OTC misuse has greater odds than prescription drug misuse.
2.	T.Tran *et al*. 2017	Interventional study	661	Australia	F: 561 M: 361 Missed: 17	Not mentioned	-	0.3	Decrease of oxycodone prescription and median of dose from 100mg per patient to 50mg per patient after post-intervention.
3.	Saul Shiffman *et al*. 2018	Cross sectional survey	14481	U.S.A.	Not mentioned	Not mentioned	2011	5	Odds of misuse of Paracetamol has greater than OTC/Prescription drugs misuse in prescribed days.
4.	Penelope wood *et al*. 2018	Cross sectional survey	904	Australia	Not mentioned	<30: 242 30-39: 288 40-49: 151 50<: 223	March 2016- June 2017	1	Pharmacist had assessed the clinical tool via The Pharmacy guild, myCPD website, online PDF version to evaluating inappropriate use of OTC combination analgesics containing codeine.
5.	Scholz Irene et.al. 2019	Cohort study	904	Switzerland	F: 126 M: 218	16-36: 166 36-56: 147 >56: 30	2012-2017	5	Misuse of more 1 Prescription/OTC drugs or additional illicit drugs co-use had greater odds than misuse of Ethanol co-use.
6.	Richard H et.al. 2019	Interventional study	4630	U.S.A.	F: 126 M: 218	Mean: 60.65	2011-13 to 2014-16	3	Analgesics use for pain management service has greater odds than opioid misuse.
7.	Desmond cariveau et.al. 2019	Cohort study	234	U.S.A.	F: 153 M: 81	Mean: 60.65	2016	1	The percentage of naloxone prescribing increased from 3.4% for high-risk patients treated with chronic opioid therapy for pain.
8.	Wui Ling Chan et.al. 2020	Cross sectional survey	999	Singapore	F: 498 M: 500 Transgender: 1	Median= 35	2015	N/A	Prescription drug misuse associated with lifetime and past year misuse in this study.
9.	Abubaker *et al*. 2020	Cross sectional survey	98	Nigeria	F: 31 M: 64	<30: 31 31-40: 34 41-50: 16 51<: 15	2019	-	Community pharmacist's confidence in dispensing antibiotics without prescription is the main reason for prescription antibiotic misuse.

Sl. No	Authors, years	Study Design	Sample size	Country	Gender (F=Female; M=Male)	Age (years)	Study conducted year	Follow up in years	Outcome
10.	Anette De Santigo *et al.* 2021	Cross sectional survey	11	U.S.A.	Not mentioned	Not mentioned	Dec 2019-Jan 2020	N/A	Pharmacist role in preventing OTC misuse had greater odds than preventing opioids abuse.
11.	Shu-wei liu *et al.* 2021	Cross sectional survey	2126	India	F: 1078 M: 1048	15-24: 301 25-44: 745 45-64: 728 >65: 352	2020	N/A	Higher suicidal ideation has greater odds with prescription drug use.
12.	Kotwani. A, Joshi. J., *et al.* 2021	Cross sectional survey	72	India	F: 31 M: 41	15-25: 15 26-34: 16 35-45: 14 46-55: 14 >55: 13	2020	N/A	Antibiotic misuse has greater odds than OTC misuse.

Training programmes increase the knowledge of pharmacist about pharming.[16,17]

Meta-analysis provides more robust results that can help researchers better understand the magnitude of an effect.[18] A meta-analysis can make available of a single summary statistic of the strength of an association across a huge number of studies and can assess connects of effect size.[19,20] Drug misuse is associated with both prescription and OTC drugs that results in many severe medical conditions, increased casualty visits, overdose deaths and admissions for addiction treatment. The impact of pharmacy directed management services and prevention programme are essential to prevent the drug abuse.[21] In this study, the researchers conduct a statistical analysis of misuse of drugs and how pharmacist prevent and manage the drug abuse in which the results of several studies are combined and then analysed.

The aims of present study are to statistically summarize the misuse of prescription/OTC drugs with the role of pharmacist in preventing and managing the prescription/OTC medications induced health conditions; and to provide methodological guidance for further research.

MATERIALS AND METHODS

Primary study inclusion

The researchers applied inclusion criteria for the process of literature search includes studies must be published in English language, it should be scientific peer reviewed article which published in the period of 2017-2022, the reason for restricting the search period illuminates how knowledge has changed within the field and time as every year a new drug therapy is introduced and prescribed. Also, as it is a Meta-analysis it represents a novel approach for further drug therapy design therefore newer cases needed to be analysed in this study. The study population aged 15 years and above, the study must be Epidemiological study.

Literature search and search strategy

The researchers used to search scientific literature through database sources like EMBASE, PubMed and Google Scholar. Search strategy includes the searching terms "Misuse of drugs", "Misuse of prescriptions drugs", "Misuse of OTC and prescription drugs", "Prevention of misuse of drugs", "Preventing misuse of prescription drugs", "Preventing prescription drug abuse", "Role of Pharmacist in misuse of prescription and OTC drugs", "Role clinical pharmacist in preventing drug abuse", "Preventing drug abuse", The researchers collected the studies which shown under these searching terms and screened by applying inclusion and exclusion criteria.

Criteria for inclusion and exclusion

The researchers design the inclusion criteria which classifies literatures into cross-sectional study, cohort study or case-control studies. The study conducted on the misuse of OTC or prescription

drug and about the role of pharmacist in drug abuse. The effects of drug misuse occurred in only human. The Study outcome must represent the report of Prescription/OTC misuse and role of pharmacist in drug abuse. The exclusion criteria determine that the study which are published only as an Abstract, Review literature, which contains not enough data, Case studies, sample size less than 10, used inappropriate statistics.

Data Extraction

Data abstraction is conducted through Microsoft Excel Version: 1808. The researchers extract the data by using headings such as author names, years of published, study design, sample size, country names, gender, age in years, study conducted year, follow up in years, outcome, source of outcome, and calculated odds ratio (95% CI) with respect to the outcome (Table 1).

Statistical Analysis

The researchers calculated the Odds ratio (95% CI), heterogeneity by applying Random-effect Der Simonian- laird model. Because of the heterogeneity in the included studies, the researchers applied random effect model. If the study results Homogeneity, then the researchers can apply fixed effect model. Heterogeneity was identified by using I^2. I^2 is reported that from 0% to 40% represents might not be significant heterogeneity; from 30% to 60% might represent reasonable heterogeneity; from 50% to 90% might represent substantial heterogeneity; from 75% to 100% shows significant heterogeneity at the *p*-value <0.001*, the researchers used to test publication bias by plotting Funnel plot. The Statistical analysis of included studies is conducted through the Statistical software STATA Version 17.0.

RESULTS

The researchers identified 12 studies out of 3024 studies which can be included for the meta-analysis, that consists of 25,499 individuals with drug misuse and the included population were assessed about the role of pharmacist in preventing managing drug abuse. The selection criteria were reported through PRISMA flow diagram (Figure 1).

Characteristics of included studies

The (Table 1) descriptions of involved studies were extracted and presented in which there are 6 studies showing outcome as prescription/OTC drugs misuse,[22-27] and other 6 studies reports the role of pharmacist in preventing and managing drug abuse.[28-33] The 5 studies were conducted at U.S.A. (n=20, 295, 79.59%),[26-28,30,32] 2 studies from Australia (*n* = 1565, 6.14%),[31,33] 1 each studies were conducted at Taiwan (*n*=2126, 8.34%)[22], Singapore (*n*=999, 3.92%),[24] Switzerland (*n* = 344, 1.35%),[25] Nigeria (*n* = 98, 0.38%),[29] and India (*n*=72, 0.28%).[23] The 10 studies were Cross-sectional studies and 2 were Cohort Studies. The Commonly misused class of drugs are graphically presented in the (Figure 2) in that The researchers presented through Bar graph of number of studies mentioned about the class of drugs misuse in which Pain medications misuse are most mentioned in the included studies.[34]

Data and analysis

The researchers represent the data analysis of this meta-analysis through forest plot (Figure 3), Galbraith plot (Figure 4), Funnel plot (Figure 5).

Forest plot (Figure 3) is the graph, individual study resembles to square indicates effect size and weightage of study centred at the point with horizontal line (whiskers) represents effect size at Confidence interval. The green diamond estimates the complete effect size with horizontal lines on both sides of overall CI.

Heterogeneity

It is a natural for effect sizes of studies collected in meta-analysis, shows variations between studies of sampling variability. In this study, the heterogeneity measures I^2=74.12%, H^2=3.86, τ^2=0.98 and homogeneity shows Q statistic of 42.5. There are several strategies to address the heterogeneity such as subgroup analysis, Meta-regression, performing random effect analysis, exclude studies. The researchers consider random effect meta-analysis that shows the result (Figure 3). There are no significant changes with the subgroup analysis. Henceforth, the researchers excluded 3 studies due to large sample size and other 3 studies due to variance in the outcome. Then, the researchers found the Heterogeneity

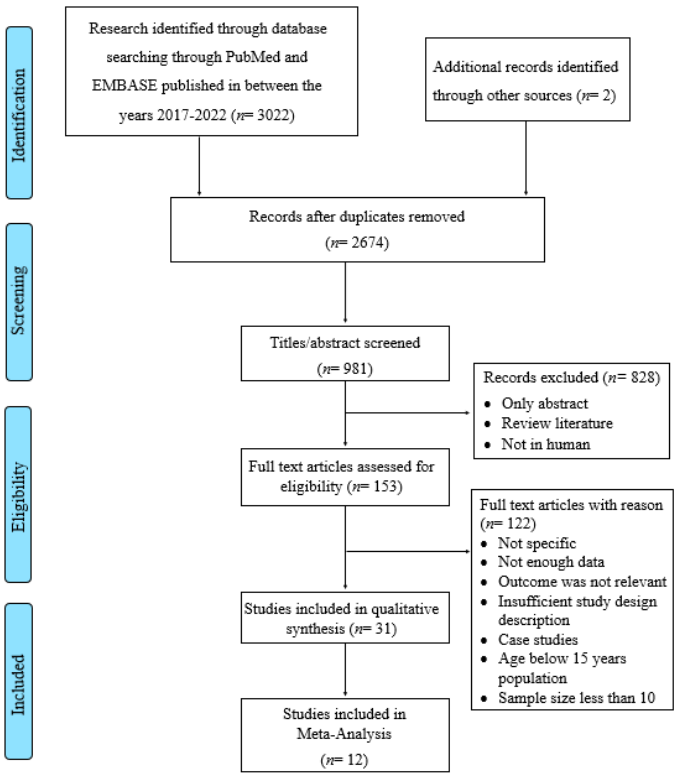

Figure 1: The PRISMA flow diagram of inclusion in this meta-analysis; *n*=number of articles.

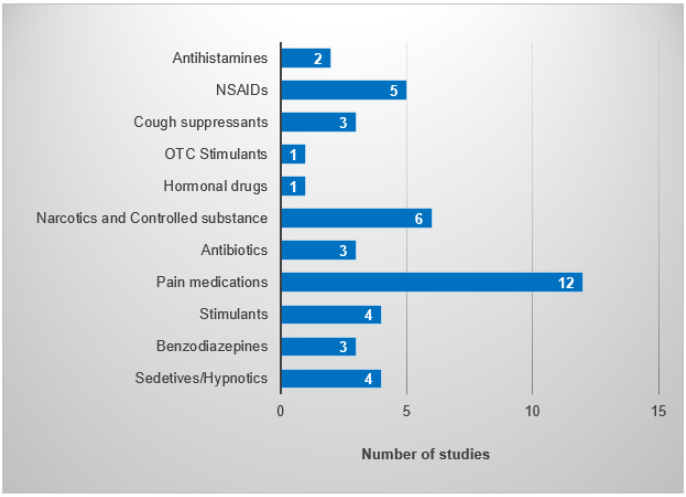

Figure 2: Number of studies mentioned about the misuse of class of drugs.

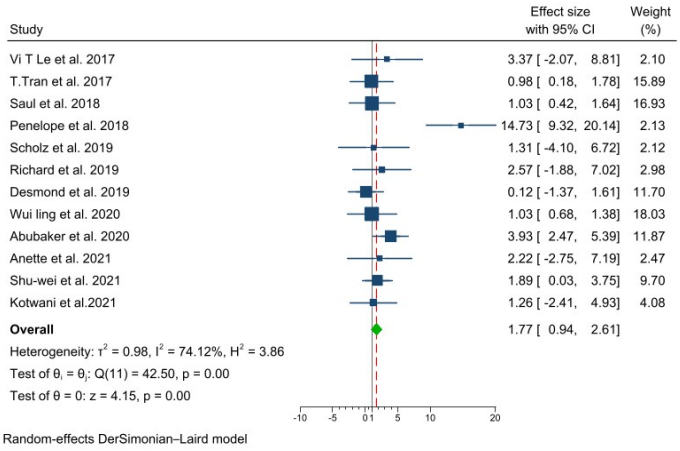

Figure 3: Forest plot of included studies.[34]

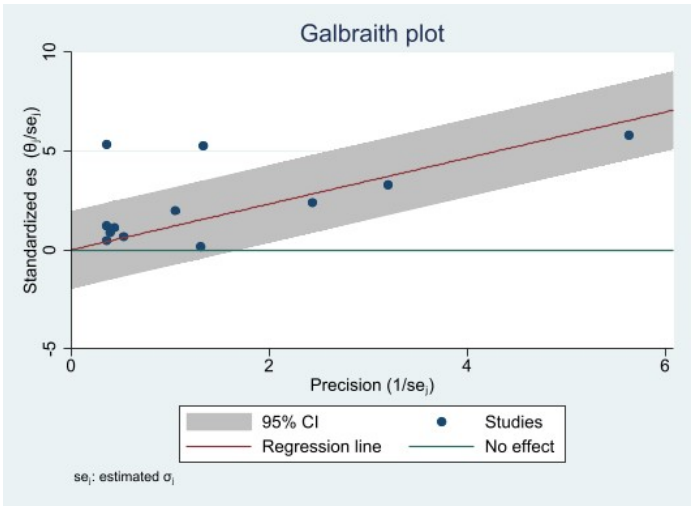

Figure 4: Galbraith plot which represents the heterogeneity of the studies.[34]

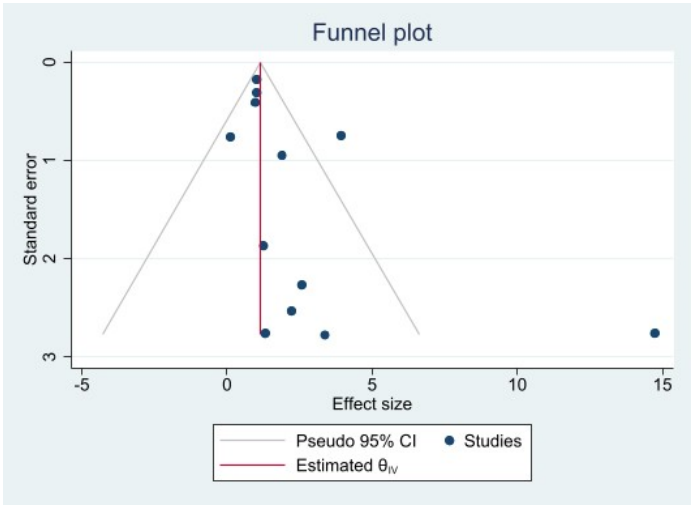

Figure 5: Funnel plot which represents the Publication bias.[34]

of 41.07% that can be acceptable and shows association between misuse of prescription/OTC drugs and the role of pharmacist in prevention and management of drug abuse with the overall effect size of 1.96 (at 95% CI 1.21, 2.71) (Figure 6).

Galbraith plot is the magnificent of forest plot which consists of studies close to y-axis have low precision. The regression line represents the effect size. In the absence of significant heterogeneity. The researchers can assume around 95% of the studies to remain within the 95% CI section (shaded area). The funnel plot is asymmetric with smaller, less precise studies. This might suggest the existence of publication bias.

The objective of this study is to statistically summarise the drugs misuse and role of pharmacist in prevent and managing drug abuse. A meta-analysis is conducted according to the PRISMA 2009 guidelines and statistical analysis is conducted through the STATA Version 17.0. The result is reported through the PRISMA flow diagram, forest plot, galbraith plot, funnel plot and presented the characteristics of the included studies. This study concluded that the drug misuse is the global burden and pharmacist can endeavour to offer the management and prevention of drug abuse.

DISCUSSION

Main findings

Out of 12 included studies, total sample size of 25,499 for assessment of prescription/OTC drug misuse and role of pharmacist in prevention and management of drug abuse. There is an relation between these two outcome variables.[2] There is a substantial association between Non-medical use of OTC drugs and Non-medical use of prescription drugs.[27] Risk of hospitalization or death is higher in those individuals who simultaneously misuse prescription benzodiazepines with opioids and alcohol co-use.[27] The pharmacist vigilance in the doctor's prescription and providing proper counselling to the patients limits the drug misuse.[31,33] There is an decrease in the number of Emergency visits, rapid response team activity and code blue events related to prescription and OTC drugs abuse.[25,30]

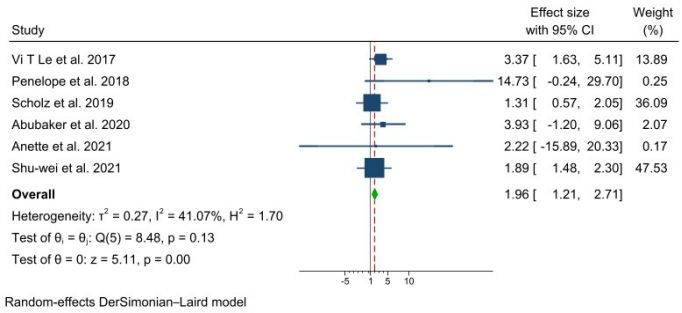

Figure 6: Forest plot showing association between drugs misuse and role of pharmacist in prevention and management of drug abuse after exploring the heterogeneity.[34]

Implications

Dextromethorphan, cough suppressant found in about 140 OTC cold medications, when it is misused it shows the effect of euphoria, dissociative and stimulant effects that results psychosis, dependence, and tolerance.[27] The Benzodiazepines which commonly prescribed for insomnia and anxiety disorders. Patients may continue these types of drugs after resolving the condition due to improper awareness about the misuse of prescription drugs. Benzodiazepines, the most common misuse of prescription drugs.[22] There are 6.7% population who misuse the prescription drugs in their lifetime and 4.8% population who have past year misuse of prescription drug misuse.[24] The 8.5% population who misused prescription drugs had a prevalence of lower levels of self-rated health, psychological distress, and suicidality.[22] The involvement of pharmacist in the opioid stewardship decreases the opioid prescription for unintended uses from 57.24% to 8.79%[30] and increase in the higher NSAID naloxone co-prescribing by 3.4%. to 37.2%.[32] The main reasons for misuse of drugs includes lack of awareness, insufficient knowledge in pharmacists about the dispensing of medicines,[23] patient's perceptions and believes, prescriber's practice and conditions.[28,35] The 39.7% of pharmacists dispense the antibiotics and other prescription drugs without proper prescription to the consumers.[23]

Strengths, limitations, and future directions

This study has a number of strengths. First, this study inclusion criteria include only scientific studies with statistical analysis and the researchers excluded the studies that shows inappropriate outcome and irrelevant study outcome. Second, the researchers explored the heterogeneity through the exclusion of number of studies and proved that there is an association between the misuse of prescription/OTC drugs and role of pharmacist in prevention and management of abuse. Third, the researchers exclude the studies which shows generalised results. However, this study has some limitations. First, most of included studies were conducted in U.S.A. The researchers did not select those studies intentionally but the researchers primarily focused on the studies which are significant to this study inclusion and which are having appropriate outcome. Second, the studies included were not conducted on same class of drug misuse. Future studies can interpret the meta-analysis by selecting the same class of drugs misuse and their effects. Furthermore, this study can be considered as base for the assessment of relation between the importance of pharmacy profession in the preventing and Managing drug abuse.

CONCLUSION

With this study, the researchers confirmed that there is huge number of prescription/OTC drugs misuse occurs with the substance abuse. The misuse of drugs is associated with additional illicit drugs co-use and ethanol co-use. Individuals who misused drugs had a greater prevalence of psychological distress and suicidality as well as lower levels of self-rated health. Confirms the Pharmacists' involvement in the prevention of drug abuse is crucial. The malpractice was associate with the lack of awareness about the medicinal discrepancies. Determines the potential benefits of clinical pharmacy services includes medication use, prescribing pattern and their potential effects on patient outcomes in the management of drug abuse. The researchers concluded that the drug misuse is the global burden and pharmacist can endeavour to offer the management and prevention of drug abuse.

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CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

ABBREVIATIONS

OTC: Over-the-Counter; **U.S.A.:** United States of America; **CI:** Confidence Interval.

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