

# Trends in the association between prescribed and non-prescribed use of tranquillisers or sedatives among adolescents in 22 European countries

ANASTASIOS FOTIOU & ELEFThERIA KANAVOU & CLIVE RICHARDSON & ANNA KOKKEVI

## ABSTRACT

**AIMS** – Tranquillisers and sedatives are valuable medicines with high misuse potential, increasingly used by adolescents without a doctor's prescription. We examined the changing association between lifetime non-prescribed use of tranquillisers or sedatives and their prescribed use in European adolescents in 2003–2011. **DESIGN** – Cross-sectional data from 199,231 16-year-old students were collected through anonymous questionnaires administered in schools in 22 European countries participating in the European School Survey Project on Alcohol and Other Drugs (ESPAD) in 2003, 2007 and 2011. **RESULTS** – Logistic regression analyses showed a modest increase in lifetime non-prescribed use of tranquillisers or sedatives (adjusted OR [AOR] = 1.08, 95% CI: 1.06–1.11,  $p < 0.001$ ) and a decrease in prescribed use (AOR = 0.89, 95% CI: 0.87–0.91,  $p < 0.001$ ) between 2003 and 2011. Adjusting for gender and survey year, any versus no prescribed use increased the odds tenfold for non-prescribed use (AOR = 10.15, 99% CI: 9.60–10.74,  $p < 0.001$ ). Adjusting also for changes in cannabis use did not affect the strength of the association. Interactions of factors with survey year showed that between 2003 and 2011, there was an increase of 38% in the odds that tranquilliser or sedative misusers had not used these drugs also with a doctor's prescription (AOR = 1.38, 99% CI: 1.28–1.50,  $p < 0.001$ ). **CONCLUSION** – The waning strength of the association between prescribed and non-prescribed use of tranquillisers or sedatives among adolescents may suggest changes both in the patterns of use and the channels of diversion and access to this class of medication in Europe.

**KEYWORDS** – tranquillisers, sedatives, non-prescribed use, prescribed use, cannabis, European adolescents, trends, ESPAD

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## Introduction

Tranquillisers and sedatives include benzodiazepines, barbiturates and non-benzodiazepine anxiolytics and are typically prescribed to treat anxiety, panic disorder or insomnia. They exert their effect by depressing the central nervous system. They have a sedative effect, relieve feelings of stress while also allaying feelings of isolation and emptiness, and decrease inhibitions (Caplan, Epstein, Quinn, Ste-

vens, & Stern, 2007). At low doses and taken as indicated by the doctor, these drugs are expected to be safe. However, their use induces euphoria similar to that of alcohol, with psychoactive effects being greater when taken with alcohol or other drugs: hence the high potential for their misuse by younger groups. Some may use tranquillisers and sedatives to temper the effects of cocaine or other stimulants

(American Medical Association Council on Science and Public Health, 2008).

Data from studies in representative population samples coupled with emergency department surveillance data, especially from the USA, suggest high prevalence rates of non-prescribed use of tranquillisers and sedatives and related morbidity and sedatives in adolescents, following increases during the 2000s (Johnston, O'Malley, Bachman, & Schulenberg, 2013; Substance Abuse and Mental Health Services Administration [SAMHSA], 2013; Young, Glover, & Havens, 2012). The non-prescribed use of tranquillisers or sedatives is established at relatively high prevalence among European adolescents as well (Hibell et al., 2012), while tranquillisers or sedatives are present in many of the polydrug use patterns reported in school surveys, with an increasing trend (e.g., Kokkevi, 2012).

The high prevalence of non-prescribed use of tranquillisers or sedatives – and more generally of prescription psychotropic drugs – has led to renewed public health interest in this behaviour, its size, related risks and necessary responses (Council of the European Union, 2012, December 29; International Narcotics Control Board [INCB], 2011; Rehm, 2013). Ultimately, this trend has been linked to the rapidly changing environment of drug production and marketing that includes online pharmacies, new medical products and psychoactive substances, and novel patterns of production (Griffiths, Evans-Brown, & Sedefov, 2013).

Non-prescribed use of tranquillisers and sedatives by adolescents has typically been presented as an emerging pattern within broader illicit drug use behaviour

(Zacny & Lichtor, 2008). This may be partly because non-prescribed use has been measured in the context of school surveys which have a drug-related focus (e.g., Hibell et al., 2012; Johnston, O'Malley, Miech, Bachman, & Schulenberg, 2014). Furthermore, prescription drug misuse has consistently been found to be associated with illicit drug use, which is typically explained as part of the broader context of drug use and problem behaviour among adolescents (Boyd, Young, Grey, & McCabe, 2009; Fleary, Heffer, & McKyer, 2011; Kokkevi, 2012; McCabe, 2005; McCabe, Boyd, & Young, 2007; Rigg & Ford, 2014; Young et al., 2012).

Against this background, the role that prescribed use plays in non-prescribed drug use has been largely overlooked. Examining the association between prescribed and non-prescribed use of tranquillisers or sedatives is important for at least two reasons.

First, prescribed use of tranquillisers or sedatives increases the risk of non-prescribed use. At least two studies have shown prescribed use to be a strong independent correlate of non-prescribed use of tranquillisers or sedatives in adolescents (Kokkevi, Fotiou, Arapaki, & Richardson, 2008; Opaleye et al., 2013). One study assessed the characteristics of non-prescribed use of tranquillisers or sedatives in a large sample of 16-year-old students from 31 European countries. After controlling for other correlates, prescribed use of the drug multiplied the odds of its non-prescribed use by almost 11 times in males and 7 times in females (Kokkevi et al., 2008). Another study looking at the correlates of non-prescribed use of tranquillisers or sedatives in a large repre-

sentative sample of high school students in Brazil found that having received a prescription of tranquillisers or sedatives in the past independently increased the risk of non-prescribed use by almost 7 times (Opaleye et al., 2013). Strong associations have been also noted in studies examining the risk profiles of non-prescribed users of tranquillisers and sedatives (McCabe, West, Teter, & Boyd, 2014, in a college sample) and other classes of psychotropic medicines such as prescription stimulants (Herman-Stahl, Krebs, Kroutil, & Heller, 2006; McCabe, Teter, & Boyd, 2006) and opioid analgesics (Fotiou, Kanavou, Richardson, Ploumpidis, & Kokkevi, in press; McCabe, West, Teter, & Boyd, 2012).

Second, in terms of policy and drug use-related harm, a stronger association between prescribed and non-prescribed use of tranquillisers or sedatives may be preferable to a weak association. Our assumption is that non-prescribed use which is associated with the prescribed use of the drug is likely to be related more to self-medicating motives of use (that is, medical misuse as opposed to sensation-seeking) and to safer diversion channels (that is, own prescriptions as opposed to other sources of diversion) – both of which correspond to milder risk profiles of non-prescribed users. Research has shown, for example, that for a substantial proportion of misusers, non-prescribed use of tranquillisers or sedatives is driven simply by an effort to self-manage psychological distress, most notably anxiety and difficulties with sleeping (Boyd, McCabe, Cranford, & Young, 2006; Boyd et al., 2009; McCabe, Boyd, & Teter, 2009). Other studies suggest that a substantial minority of misusers have access to tranquillisers through their

own past prescriptions (Johnston et al., 2014; McCabe, West, & Boyd, 2013). What is important in these studies is that adolescents whose non-prescribed use was driven by self-medicating motives or whose source of diversion was their own prescription exhibit milder health risk profiles than those who misuse the drug for recreational purposes or report diversion sources other than their own prescriptions (Boyd et al., 2006; Boyd et al., 2009; McCabe et al., 2009; McCabe et al., 2013). Thus, a 2005 study of high school students in a US city found that compared to students who reported self-medicating motives for non-prescribed opioid use, those who endorsed multiple motivations (including explicitly recreational ones) were significantly more likely to engage in marijuana and alcohol use and also had higher scores in the Drug Abuse Screening Test (Boyd et al., 2006). Another study examining substance use behaviours among high school seniors in relation to diversion source concluded that non-prescription opioid users who have misused their own prescription had lower risk of using other drugs or of using inappropriate routes of administration in comparison to those who reported other means of gaining access to these medicines (McCabe et al., 2013).

The prescribed use of tranquillisers or sedatives may increase vulnerability to their misuse. At the same time, non-prescribed use that clusters with prescribed use may pose fewer health risks for misusers compared to non-prescribed use without previous prescription use. Despite mounting concern over the possibility that non-prescribed use of tranquillisers and sedatives may be becoming a prevalent trend among adolescents in Europe, little

is known about how non-prescribed use has evolved in association with prescribed use in recent years. Nor do we know how this association may have been moderated by changes in the prevalence of illicit drug use among adolescents. The present study addresses this crucial gap. Drawing on data from a large sample of 16-year-old students from 22 European countries, it looks into the associations between prescribed and non-prescribed use of tranquillisers or sedatives and use of the most popular illicit drug – cannabis – over the course of eight years from 2003 to 2011.

## Method

### *The study*

We employed individual-level data from 22 European countries that had participated in all three of the most recent cycles (2003, 2007 and 2011) of the European School Survey Project on Alcohol and Other Drugs (ESPAD). The ESPAD study is a European collaborative research project conducted every four years since 1995 with the aim of providing nationally representative data on the distribution and correlates of tobacco, alcohol and other drug use among 16-year-old students (Hibell et al., 2012).

Sampling, questionnaire, data collection and data management in participating countries follow standard procedures in line with the international ESPAD study protocol. The target population consists of 16-year-olds who are present in the classroom on the day of the survey (March or April of the survey year). ESPAD countries employ sampling procedures that produce nationally representative random samples of 16-year-olds with minimum net samples of 2,400 students per country. Sam-

ples consist of randomly selected classes (sampling unit) from all grades that contain at least 10% of students aged 16. Sampling frames include regular, vocational, general or academic schools but exclude special schools or classes for students with learning disorders or severe physical handicaps.

In 2011, most countries used stratified random or stratified simple random sampling (Table 1). All countries adhered to their national ethical and legal research standards. Data were collected through anonymous self-completion questionnaires group-administered in the classroom. School and student participation was voluntary; the average rates of school participation in the 22 countries were 95%, 93% and 86% for 2003, 2007 and 2011, respectively.

Data were obtained from the ESPAD official database consisting of the standardised country data sets submitted to the project's databank manager. Responses to all items were subjected to consistency checks during standardised cleaning procedures. Full accounts of the methodology of the study in each survey year and country can be found in the respective reports of the ESPAD project (Hibell et al. 2004; Hibell et al. 2009; Hibell et al., 2012).

### *Population*

Table 1 presents data on key characteristics of the studies in each country and survey year. A further eighteen European countries or regions that had participated in the ESPAD study in 2011 were not included in the present analysis because they had not participated in all three study cycles (eleven countries), data were unavailable in the 2003 and/or 2007 study cycle (five

**Table 1.** Sample size, student representativeness and non-response for the item on non-prescribed use of tranquillisers or sedatives by country and year – ESPAD 2003, 2007, 2011. Countries are listed alphabetically.

Countries	Sample size (n)						Student representativeness (%) <sup>a</sup>						Students' school presence rates (%) <sup>b</sup>						Non-response (%) in the item for non-prescribed use of tranquillisers or sedatives														
	Total (n)			Girls (%)			2003			2007			2011			2003			2007			2011			2003			2007			2011		
	2003	2007	2011	2003	2007	2011	2003	2007	2011	2003	2007	2011	2003	2007	2011	2003	2007	2011	2003	2007	2011	2003	2007	2011	2003	2007	2011	2003	2007	2011			
1. Bulgaria	2740	2353	2217	52.9	48.9	48.9	100	88	90	85	86	82	1	1	1																		
2. Croatia	2884	3008	3002	49.9	48.3	50.7	97	97	96	88	89	89	0	0	0																		
3. Cyprus	2152	6340	4243	53.6	51.4	51.8	74	na	67	88	na	83	0	0	2																		
4. Czech Republic	3195	3901	3913	53.9	52.5	51.3	68	99	95	95	89	89	0	0	0																		
5. Estonia	2463	2372	2460	49.4	50.0	50.9	80	85	98	86	79	82 <sup>c</sup>	2	1	0																		
6. Faroe Islands	640	552	557	49.7	52.7	48.3	92	88	94	86	82	87	2	1	0																		
7. Finland	3543	4988	3744	50.9	53.9	51.5	93	94	93	91	91	90	1	3	0																		
8. France	2199	2916	2572	50.6	48.9	53.6	93	99	95	91	90	87	1	0	0																		
9. Germany <sup>d</sup>	5110	5011	2796	52.5	52.1	54.0	84	85	87	89	88	89	0	0	0																		
10. Greece	1906	3060	5908	53.5	53.2	50.5	93	99	98	83	91	90	0	0	1																		
11. Hungary	2677	2817	3063	47.8	51.9	47.5	91	95	95	82	89	86	0	1	0																		
12. Iceland	3348	3510	3333	47.9	48.8	48.5	99	98	96	81	81	81	0	0	1																		
13. Latvia	2841	2275	2622	51.7	50.8	49.1	89	92	95	84	83	85	0	0	1																		
14. Lithuania	5036	2411	2476	50.0	51.4	50.0	97	98	80	88	86	89	0	0	0																		
15. Malta	3500	3668	3377	55.5	53.1	50.0	75	80	89	83	84	78	1	0	0																		
16. Netherlands	2095	2091	2044	49.4	52.5	49.3	92	94	92	93	93	93	1	0	0																		
17. Norway	3833	3482	2938	49.3	48.9	49.0	100	100	100	87	89	88	4	4	3																		
18. Romania	4371	2289	2770	58.3	55.9	53.8	79	83	99	84	84	79	1	0	0																		
19. Slovak Republic	2276	2468	2009	53.6	50.6	50.0	67	98	95	87	89	82	1	1	1																		
20. Slovenia	2785	3085	3186	49.5	48.7	51.0	84	88	90	88	86	89	1	0	0																		
21. Sweden	3232	3179	2569	50.7	51.2	49.0	95	94	93	87	84	85	2	1	1																		
22. Ukraine	4173	2447	2210	54.0	54.6	53.6	97	95	94	83	82	83	1	0	1																		
Total	66999	68223	64009	51.8	51.4	50.7	88	93	92	87	86	86	1	1	1																		

Notes: <sup>a</sup>Proportion of 16-year-olds covered by the sampling frame (Hibell et al., 2004; Hibell et al., 2009, 2012); <sup>b</sup>Rates refer to all students present in participating classes, not only to the 16-year-olds included in the present analysis (2003 rates refer to participating students); <sup>c</sup>Calculated differently from other countries; <sup>d</sup>Participated with 6, 7 and 5 Bundesländer in 2003, 2007 and 2011, respectively; na: non-available data. In 2011, countries 7, 8, 11, 13, 14 and 17–21 used stratified random sample types, countries 1, 2, 4, 9, 10, 16 and 22 used stratified simple random sample types, countries 3, 6, 12 and 15 included all 16-year-old students and one country, 5, used a systematic random sample type (Hibell et al., 2012).

countries) or low school participation rate raised doubts over representativeness and rendered trend comparisons problematic (two countries). The average number of students with data in the present study was about 66,000 per survey year. The 22 countries included in the present analysis represent 65%, 65% and 58% of ESPAD's total samples in the 2003, 2007 and 2011 survey cycles, respectively. Overall, about 86% of the students who were enrolled in the selected classes were present in the class during the survey administration. No more than 1% of them refused to participate.

#### *Measures*

Tranquillisers and sedatives are measured in the ESPAD survey as a single category. Questions on prescribed and non-prescribed use of tranquillisers or sedatives and on cannabis use are core items that have remained unchanged since the first ESPAD survey in 1995. The following introductory text within the questionnaire preceded the question on prescribed use: "Tranquillisers and sedatives, like [countries insert here nationally relevant examples], are sometimes prescribed by doctors to help people to calm down, get to sleep or to relax. Pharmacies are not supposed to sell them without a prescription." Prescribed use of tranquillisers or sedatives was subsequently measured with the following item: "Have you ever taken tranquillisers or sedatives because a doctor told you to take them?" Response options were "No, never", "Yes, but for less than 3 weeks", and "Yes, for 3 weeks or more". Further down in the questionnaire, the question on lifetime non-prescribed use of tranquillisers or sedatives was placed

first in a battery of items asking for lifetime use of various substances. Students were asked: "On how many occasions in your lifetime (if any) have you used... [t]ranquillisers or sedatives (without a doctor's prescription)?" Response options were: "0", "1–2", "3–5", "6–9", "10–19", "20–39", and "40 or more". In the absence of data on use of tranquillisers or sedatives during the last 12 months or last 30 days, we took lifetime non-prescribed use as the key dependent variable. In the vast majority of countries with available data for the present study the rate of missing responses in the item on non-prescribed use of tranquillisers or sedatives did not exceed 1% (Table 1).

Lifetime cannabis use was measured with the following item: "On how many occasions (if any) have you used marijuana or hashish (cannabis) in your lifetime?" The response options were the same as for non-prescribed use of tranquillisers/sedatives. Although non-prescribed use of tranquillisers or sedatives may be associated in various ways with the different types of licit and illicit drugs (McLarnon, Darredeau, Chan, & Barrett, 2013), the use of cannabis was chosen as the best indicator for illicit drug use given that the vast majority of adolescents who report use of illicit drugs have taken cannabis (Hibell et al., 2012).

Other measures used in the present analysis concerned perceptions of "easy" or "difficult" access to tranquillisers or sedatives (response options: "impossible", "very difficult", "fairly difficult", "fairly easy", "very easy", "don't know"), and whether these drugs had been used without prescription by friends (response options: "none", "a few", "some", "most",

“all”) or older siblings (response options: “yes”, “no”, “don’t know”, “don’t have any”).

### *Statistical analysis*

Percentage prevalences of items in the entire survey are calculated in the pooled sample across countries and are also presented, in accordance with the method adopted by ESPAD (Bjarnason, 2012), as the unweighted average of the separate prevalences across the 22 countries.

Trends in prescribed and non-prescribed use of tranquillisers or sedatives for each country and for the total of participating countries were examined using logistic regression of individual-level data. Each variable was taken separately as dependent variable, while the survey year (coded 1, 2 and 3) and gender were applied as independent variables. Cases with missing values for any of the variables were excluded.

The main analysis examined the relationship between prescribed and non-prescribed use across the three survey cycles using multivariate logistic regression of individual-level data. Four models were fitted. Model 1 included only gender, survey year and prescribed use of tranquillisers or sedatives as independent factors. In Model 2, lifetime cannabis use was added to the independent variables. Models 3 and 4 included interactions with gender and survey year, respectively. Interactions were added in order to examine the possibility that the associations of non-prescribed use of tranquillisers/sedatives with their prescribed use and cannabis use differed between genders (Model 3) and among survey years (Model 4). To aid presentation of interactions which had been found to

be significant, the usual dummy variables for the factor and the interaction were replaced by others. Two dummy variables were created for the gender effect, one among users of non-prescribed tranquillisers or sedatives and one among non-users. Four dummy variables were similarly created for the survey cycle effect.

The design weights of each country, where applicable, and the effect of the clustered sampling design were all incorporated into the analyses with country as stratum. It was not feasible to include the cluster effect at the school level in the absence of school identifiers in the 2003 survey and in the Faroe Islands and Norway for all surveys. All analyses were performed using the Complex Samples procedure of IBM SPSS (v. 22.0, Armonk, NY: IBM Corp.).

## **Results**

Table 2 presents data on lifetime prescribed and non-prescribed use of tranquillisers or sedatives among 16-year-old students in the 22 European countries with data available for all three survey years. Any lifetime prescribed use of tranquillisers or sedatives was reported by 7.9% of 16-year-old students in the total sample in 2011, with 6.4% reported non-prescribed use. The majority of those who reported non-prescribed use said that they had done this 1–2 times; only 2.8% of all respondents reported non-prescribed use 3–5 times or more often. It was therefore decided to restrict analysis to any non-prescribed use in the lifetime.

More girls than boys reported tranquilliser or sedative use, whether prescribed (8.6% and 7.3%, respectively) or non-prescribed (7.8% and 5.2%, respectively; not



shown in table). Among countries, prescribed use ranged from 3.1% (Faroe Islands and Germany) to 15.3% (Lithuania). Six out of the 22 countries had a prevalence of prescribed use of 10% or higher in 2011: Lithuania, France, the Czech Republic, the Slovak Republic, Norway and Iceland. Only the first three of these also had high prevalence of non-prescribed use of tranquillisers or sedatives. Non-prescribed use ranged from about 2% (Faroe Islands, Germany and Ukraine) to 13.1% (Lithuania). The countries with the highest non-prescribed use rates – but not among the highest in prescribed use – were Cyprus (11.4%), Greece (9.4%) and Hungary (9.3%). No geographical patterning was evident.

Trends in prescribed use of tranquillisers or sedatives among 16-year-old students in the 22 European countries have been decreasing overall between 2003 and 2011 (adjusted OR [AOR] = 0.89, 95% CI: 0.87–0.91,  $p < 0.001$ ) (Table 2). The trend was driven mainly by decreases observed in France, Germany, Iceland (Western Europe), Malta (Southern Europe), Croatia, Slovenia, the Czech Republic, Romania (Central Europe), and Estonia, Latvia (Eastern Europe). Significant increases were observed only in Bulgaria and Lithuania.

Although moderate, the overall time trend in non-prescribed use of tranquillisers or sedatives has been an increasing one between 2003 and 2011 (AOR = 1.08, 95% CI: 1.06–1.11,  $p < 0.001$ ). The increase was driven mainly by changes observed in Malta, Greece and Cyprus (Southern Europe); Bulgaria, Latvia and Ukraine (Eastern Europe); Croatia (at 10% of significance) (Central Europe); and Swe-

den and Norway (at 10% of significance) (Northern Europe). A significant decrease was observed only in Romania.

Based on the 2011 survey data, lifetime use of cannabis was 17.7% overall, ranging from 4.9% (Faroe Islands and Norway) to 42.3% (Czech Republic). Despite variation in trends among countries, an overall decrease was observed in lifetime cannabis use in the 22 countries between 2003 and 2011 (AOR = 0.98, 95% CI: 0.96–0.99,  $p < 0.01$ ).

Table 3 presents the results of the multivariate logistic regression analyses for examining the relationship between prescribed and non-prescribed use of tranquillisers or sedatives. After adjusting for gender and survey year, any lifetime prescribed use of tranquillisers or sedatives increased tenfold the odds for their non-prescribed use compared to never having a prescription (AOR = 10.15, 99% CI: 9.60–10.74,  $p < 0.001$ ) (Model 1). The lifetime use of cannabis also increased the odds for non-prescribed use of tranquillisers or sedatives by almost 4 times (AOR = 3.79, 99% CI: 3.58–4.01,  $p < 0.001$ ) (Model 2). The inclusion of cannabis in the model did not affect substantially the strength of the association between prescribed and non-prescribed use of tranquillisers or sedatives. Entering interactions with gender (Model 3) showed a higher effect of female gender in students with no prescribed use of tranquillisers or sedatives than in those with prescribed use. Model 4 included interactions of factors with survey cycle: between 2003 and 2011 there was a much bigger increase in the probability of reporting non-prescribed use among students with no prescribed use of tranquillisers or sedatives (AOR = 1.38,



**Table 2.** Prevalence of lifetime prescribed and non-prescribed use of tranquillisers or sedatives and lifetime use of cannabis among 16-year-old students in 22 European countries, by country and survey year, with trend expressed as odds ratio for substance use by survey cycle (1,2,3).

	Prescribed use of tranquillisers or sedatives (lifetime)						Non-prescribed use of tranquillisers or sedatives (lifetime)						Cannabis use (lifetime)														
	2003		2007		2011		95% CI		p	2003		2007		2011		95% CI		OR <sup>a</sup>	2003		2007		2011		95% CI		p
		%		%		%	Lower	Upper			%		%	Lower	Upper		%		Lower	Upper		%		%	Lower	Upper	
Bulgaria	4.1	4.6	5.8	1.21	1.06	1.38	<b>0.006</b>			2.0	2.9	3.2	1.26	1.07	1.50	<b>0.007</b>			20.9	22.4	23.5	1.07	1.00	1.15	<b>0.044</b>		
Croatia	15.0	9.4	9.6	0.76	0.70	0.83	<b>&lt;0.001</b>			6.4	4.7	5.3	0.89	0.80	1.00	0.058			22.2	18.3	17.5	0.86	0.81	0.92	<b>&lt;0.001</b>		
Cyprus	8.1	6.1	8.3	1.07	0.96	1.18	0.238			5.9	7.0	11.4	1.52	1.38	1.68	<b>&lt;0.001</b>			3.4	5.2	6.9	1.42	1.26	1.59	<b>&lt;0.001</b>		
Czech Rep.	19.6	9.6	11.0	0.70	0.65	0.75	<b>&lt;0.001</b>			11.0	9.1	10.1	0.96	0.89	1.04	0.362			43.6	45.1	42.3	0.97	0.92	1.01	0.154		
Estonia	10.5	5.9	7.4	0.81	0.72	0.90	<b>&lt;0.001</b>			9.1	7.0	8.1	0.93	0.84	1.03	0.174			23.0	26.1	24.2	1.04	0.97	1.11	0.257		
Faroe Islands	4.1	3.7	3.1	0.86	0.63	1.18	0.362			3.3	3.3	2.0	0.79	0.56	1.12	0.187			9.0	6.2	4.9	0.71	0.56	0.90	<b>0.005</b>		
Finland	5.1	5.1	4.2	0.90	0.81	1.01	0.064			6.5	6.6	7.2	1.06	0.96	1.16	0.257			10.8	7.7	10.7	1.01	0.92	1.10	0.887		
France	17.4	14.5	12.1	0.81	0.74	0.89	<b>&lt;0.001</b>			12.6	15.1	11.3	0.94	0.86	1.03	0.220			38.2	31.5	38.8	1.02	0.95	1.09	0.585		
Germany	5.3	3.3	3.3	0.74	0.63	0.86	<b>&lt;0.001</b>			1.8	2.8	2.2	1.14	0.95	1.36	0.151			28.7	20.2	19.1	0.74	0.69	0.80	<b>&lt;0.001</b>		
Greece	4.3	2.9	4.6	1.13	0.98	1.32	0.102			3.8	4.2	9.4	1.82	1.59	2.08	<b>&lt;0.001</b>			5.7	6.3	8.3	1.24	1.10	1.39	<b>&lt;0.001</b>		
Hungary	6.9	8.6	7.9	1.07	0.97	1.18	0.186			10.2	8.9	9.3	0.95	0.86	1.04	0.282			16.7	13.2	19.4	1.10	1.02	1.19	<b>0.016</b>		
Iceland	11.9	7.9	10.3	0.92	0.84	1.00	<b>0.040</b>			8.6	7.4	7.7	0.96	0.86	1.07	0.408			12.8	8.7	10.4	0.88	0.81	0.96	<b>0.003</b>		
Latvia	13.3	9.5	9.6	0.83	0.76	0.91	<b>&lt;0.001</b>			3.2	4.4	4.2	1.16	1.01	1.33	<b>0.040</b>			16.0	18.2	24.0	1.29	1.20	1.38	<b>&lt;0.001</b>		
Lithuania	10.6	12.2	15.3	1.23	1.15	1.32	<b>&lt;0.001</b>			13.6	15.6	13.1	1.00	0.93	1.07	0.888			13.5	18.2	19.6	1.27	1.19	1.35	<b>&lt;0.001</b>		
Malta	8.4	7.0	7.0	0.90	0.82	0.99	<b>0.026</b>			2.7	4.7	3.5	1.14	1.01	1.28	<b>0.028</b>			10.2	12.9	9.8	0.97	0.90	1.04	0.364		
Netherlands	8.6	8.3	8.8	1.01	0.91	1.13	0.813			7.3	7.2	8.6	1.11	0.98	1.25	0.093			28.5	28.5	27.4	0.97	0.90	1.04	0.353		
Norway	10.3	10.8	11.2	1.05	0.96	1.14	0.298			2.7	3.5	3.5	1.14	1.00	1.31	0.056			8.9	5.7	4.9	0.71	0.64	0.79	<b>&lt;0.001</b>		
Romania	11.3	5.2	4.3	0.57	0.50	0.64	<b>&lt;0.001</b>			5.5	4.1	3.0	0.74	0.65	0.85	<b>&lt;0.001</b>			2.6	3.5	7.2	1.72	1.51	1.96	<b>&lt;0.001</b>		
Slovak Rep.	13.6	12.9	12.5	0.95	0.87	1.04	0.305			3.7	5.2	4.0	1.05	0.91	1.20	0.522			26.6	32.1	26.8	1.00	0.94	1.07	0.919		
Slovenia	6.9	4.6	5.1	0.84	0.75	0.95	<b>0.005</b>			5.2	5.2	4.6	0.94	0.83	1.05	0.269			28.4	22.0	23.4	0.88	0.83	0.93	<b>&lt;0.001</b>		
Sweden	8.3	6.4	7.6	0.94	0.85	1.04	0.259			5.9	7.2	7.9	1.17	1.06	1.29	<b>0.002</b>			7.5	7.0	8.5	1.06	0.96	1.17	0.245		
Ukraine	5.8	5.6	5.4	0.96	0.86	1.07	0.469			1.5	4.1	2.2	1.27	1.10	1.46	<b>0.001</b>			18.6	13.6	10.8	0.71	0.65	0.76	<b>&lt;0.001</b>		
Total sample	9.6	7.3	7.9	0.89	0.87	0.91	<b>&lt;0.001</b>			6.0	6.4	6.9	1.08	1.06	<b>1.11</b>	<b>&lt;0.001</b>			17.9	16.5	17.3	0.98	0.96	0.99	<b>0.002</b>		
Average of countries	9.5	7.5	7.9							6.0	6.4	6.4							18.0	16.9	17.7						

**Note.** <sup>a</sup>Odds ratios for substance use in relation to survey cycle (scored 1,2,3), adjusted for gender

99% CI: 1.28–1.50,  $p < 0.001$ ) than among students with prescribed use. This differentiation was not seen between 2003 and 2003 (Table 3). Interactions of recent cannabis use with gender and survey year and between gender and survey were not statistically significant.

Additional analyses (not shown in tables) demonstrated that the levels of perceived “easy or very easy” access to tranquillisers or sedatives in 2011 were similar to those observed in 2003 (22.4% and 22.8%, respectively), although with significant variation in between. Increases were observed, nonetheless, in the reported non-prescribed use by “friends” and “older siblings”. More specifically, 16.3% of the 16-year-old students mentioned that at least one of their friends took tranquillisers or sedatives non-medically in 2011 compared to 11.9% in 2003 (AOR = 1.20, 95% CI: 1.18–1.22,  $p < 0.001$ ). Modest increases were also observed in reported non-prescribed use by older siblings between 2003 (1.7%) and 2011 (2.4%) (AOR = 1.18, 95% CI: 1.14–1.22,  $p < 0.001$ ). Apart from a small difference in perception of easy access (25.6% among girls compared to 21.2% among boys in 2011), these results were similar for both genders and with similar trends for both genders.

## Discussion

Although a strong association is expected between prescribed and non-prescribed use of tranquillisers or sedatives, changes in this association across time have been unexplored. This is the first study to provide information on the trends in the association between prescribed and non-prescribed use of tranquillisers or sedatives among 16-year-old students in 22 European

countries between 2003 and 2011. Our data demonstrate three major results: first, while the lifetime prevalence of prescribed use has been declining, non-prescribed use of tranquillisers or sedatives has been increasing; second, the association between prescribed and non-prescribed use, although still present, has become weaker in the course of the eight-year period, while this association does not seem to be affected by trends in cannabis use; third, observed trends in the association between prescribed and non-prescribed use apply to boys and girls equally.

Lifetime non-prescribed use of tranquillisers or sedatives among 16-year-old students in our European sample was 6.4% in 2011, similar to that observed in comparable samples in the USA (6.3% for tranquillisers among 10<sup>th</sup> graders and 6.9% for sedatives among 12<sup>th</sup> graders) (Johnston et al., 2014). Similarly to the position of prescription drugs in the USA, in 2011 tranquillisers or sedatives in Europe were the most popular type of substance after cannabis and inhalants. It is noteworthy, nonetheless, that during the same period the respective rates of lifetime cannabis use among 16-year-olds differ substantially between these two parts of the world: 17% in Europe and 35% in the USA (Hibell et al., 2012; Johnston et al., 2014). This suggests that the proportional weight of non-prescribed use of tranquillisers or sedatives against other drugs is higher in Europe than in the USA. Increased policy attention should be paid to combating the problem.

Our study demonstrated moderately increasing trends in non-prescribed use of tranquillisers or sedatives among 16-year-old students in our sample of European

**Table 3.** Results of logistic regression analysis with non-prescribed use of tranquillisers or sedatives as dependent variable.

Parameter	Model 1: Survey year, gender and prescribed use of tranquilisers or sedatives (n = 194,920)				Model 2: plus cannabis use (n = 194,252)				Model 3: plus interactions with gender <sup>a</sup> (n = 194,252)				Model 4: plus interactions with survey year <sup>a</sup> (n = 194,252)			
	Sig.	AOR <sup>b</sup>	99% CI		Sig.	AOR	99% CI		Sig.	AOR	99% CI		Sig.	AOR	99% CI	
			Lower	Upper			Lower	Upper			Lower	Upper			Lower	Upper
Survey cycle																
2011 vs. 2003	<b>&lt;.001</b>	<b>1.28</b>	1.20	1.36	<b>&lt;.001</b>	<b>1.29</b>	1.21	1.38	<b>&lt;.001</b>	<b>1.29</b>	1.21	1.38				
2007 vs. 2003	<b>&lt;.001</b>	<b>1.20</b>	1.13	1.28	<b>&lt;.001</b>	<b>1.21</b>	1.14	1.29	<b>&lt;.001</b>	<b>1.21</b>	1.14	1.29				
Female gender	<b>&lt;.001</b>	<b>1.54</b>	1.46	1.62	<b>&lt;.001</b>	<b>1.74</b>	1.65	1.84	<sup>c</sup>				<sup>c</sup>			
Prescribed use of tranquilisers or sedatives	<b>&lt;.001</b>	<b>10.15</b>	9.60	10.74	<b>&lt;.001</b>	<b>9.04</b>	8.53	9.58	<b>&lt;.001</b>	<b>9.72</b>	8.88	10.64	<b>&lt;.001</b>	<b>10.52</b>	9.33	11.86
Cannabis use (lifetime)					<b>&lt;.001</b>	<b>3.79</b>	3.58	4.01	<b>&lt;.001</b>	<b>3.79</b>	3.58	4.00	<b>&lt;.001</b>	<b>3.79</b>	3.58	4.00
<i>Interactions with gender</i>																
Prescribed use of tranquilisers or sedatives * Gender																
Female vs. Male gender in students with prescribed use					<b>&lt;.001</b>	<b>1.60</b>	1.45	1.76	<b>&lt;.001</b>	<b>1.60</b>	1.45	1.76	<b>&lt;.001</b>	<b>1.60</b>	1.45	1.76
Female vs. Male gender in students with no prescribed use					<b>&lt;.001</b>	<b>1.81</b>	1.69	1.93	<b>&lt;.001</b>	<b>1.81</b>	1.69	1.93	<b>&lt;.001</b>	<b>1.81</b>	1.70	1.93
<i>Interactions with survey year</i>																
Prescribed use of tranquilisers or sedatives * Survey year																
2011 vs. 2003 in students with prescribed use									.040	1.10	.98	1.24				
2007 vs. 2003 in students with prescribed use					<b>&lt;.001</b>	<b>1.21</b>			<b>&lt;.001</b>	<b>1.21</b>	1.08	1.36	<b>&lt;.001</b>	<b>1.21</b>	1.08	1.36
2011 vs. 2003 in students with no prescribed use					<b>&lt;.001</b>	<b>1.38</b>			<b>&lt;.001</b>	<b>1.38</b>	1.28	1.50	<b>&lt;.001</b>	<b>1.38</b>	1.28	1.50
2007 vs. 2003 in students with no prescribed use					<b>&lt;.001</b>	<b>1.22</b>			<b>&lt;.001</b>	<b>1.22</b>	1.13	1.32	<b>&lt;.001</b>	<b>1.22</b>	1.13	1.32

**Note.** Dependent variable is Non-prescribed use of tranquillisers or sedatives. Reference category is no use. <sup>a</sup>Only significant interactions are presented (Survey cycle\*Gender, Cannabis use\*Gender and Cannabis use\*Survey cycle were found to be non-significant). <sup>b</sup>AOR: Adjusted Odds Ratio; <sup>c</sup>Main effect is not coded separately in the presence of a significant interaction with prescribed use of tranquillisers or sedatives; see text for explanation.

countries, in contrast to the declining ones observed in prescribed use. Observed country differences in prevalence and in changes in the association between non-prescribed and prescribed use of tranquillisers or sedatives in our sample of European countries are hard to explain – not least without taking into account country-specific contextual data. Observed differences across countries and across years may be driven, for example, by changes in policy contexts, psychiatric morbidity, prescribing practices, pharmaceutical marketing and in the degrees of normalisation of prescribed and non-prescribed use of medicines, as well as by changes in national youth drug cultures (e.g., “pill-popping culture”). Observed trends may also reflect factors pertinent to adolescents (such as adoption of novel drug use patterns and changing risk perceptions) or their proximal environments (e.g., availability and diversion of tranquillisers and sedatives in the household or among peers).

Of note, our study showed that the strength of the association between non-prescribed and prescribed use has waned over time: between 2003 and 2011 there was an increase of 38% in the odds of non-prescribed use not being matched with a corresponding prescribed use of the drug. Our data essentially suggest that, with time, having been prescribed a tranquilliser or sedative has become progressively weaker as a risk factor for also reporting its non-prescribed use.

Against this backdrop, it would be tempting to suggest that the declining role of past prescriptions in non-prescribed use among adolescents is an indication of a shift towards patterns of use which are

increasingly dominated by recreational motives (as opposed to self-medicating). Although plausible, such an assumption would nonetheless discount evidence suggesting that self-treating is as common as sensation-seeking as a motive for non-prescribed use (Boyd et al., 2006; Boyd et al., 2009), that a large proportion of those engaging in tranquilliser or sedative misuse also suffer from adverse mental conditions such as depression (Conway, Compton, Stinson, & Grant, 2006), and that non-prescribed use most likely starts on the basis of some psychological-somatic complaint or mental condition and only later may lead to recreational misuse (Cicero, Lynskey, Todorov, Inciardi, & Surratt, 2008). Moreover, the presence of a psychological condition (such as suffering from anxiety, insomnia or depressive mood) may not lead to a visit to a doctor nor to issuing a prescription (Simoni-Wastila, Yang, & Lawler, 2008; Sung, Richter, Vaughan, Johnson, & Thom, 2005). The long delays in seeking treatment for these disorders that have been reported elsewhere (Olsson, Kessler, Berglund, & Lin, 1998; Wang et al., 2005), coupled with increasing access to the tranquillisers or sedatives that are readily available in the adolescents' environment without a doctor's prescription, may explain why a gradually smaller proportion of adolescents who report non-prescribed use also report prescribed use of these drugs.

Another argument in favour of the possible self-medicating paradigm is that – unlike traditional drugs – girls outnumber boys in tranquilliser or sedative use, whether prescribed or non-prescribed. That girls use and misuse tranquillisers or sedatives in higher proportions than boys

is consistent with evidence from several other studies that show that girls report higher levels of health complaints, are more likely to feel emotionally disturbed and are more likely to be prescribed psychotherapeutic medications (Gobina et al., 2011; Ravens-Sieberer et al., 2009; Torshheim et al., 2006). More frequent exposure to these drugs may subsequently lead to a higher rate of non-prescribed use in females (Becker, Fiellin, & Desai, 2007). Importantly, however, not only are girls more likely to be prescription drug users than boys but also, as a study has shown, they are more likely to be driven by self-treating motives when misusing them, whereas no gender difference is observed among sensation seekers (e.g., Boyd et al., 2009).

The waning role of past prescriptions in non-prescribed use among adolescents may also be seen as an indication of changing patterns in prescription drug diversion that rely increasingly on multiple channels of access rather than one's own prescription. Indeed, as the data from the USA Monitoring the Future survey show, there has been a decrease between 2007/08 and 2009/12 in the proportion of past-year non-prescribed users of tranquillisers who reported misusing their past prescriptions (from 18% to 14%), but increases in the proportion of those reporting as the sources of the drug their "friends" (from 60% to 76%) or "relatives" (from 44% to 48%) (Johnston, O'Malley, Bachman, & Schulenberg, 2012). Although not reporting on access to these medicines, our data on peer use at least suggest that also in Europe non-prescribed use of tranquillisers or sedatives becomes increasingly a more prevalent feature in peer environments.

It is important to recognise several limi-

tations in the data presented here. First, because of the cross-sectional design of the ESPAD study we do not know whether prescribed use precedes or follows non-prescribed use. Lack of data on clinical indicators such as anxiety, insomnia and stress prevents us from associating non-prescribed use with self-reported symptomatology. Crucially, in the absence of data on motives, the proportion of adolescents whose non-prescribed use of tranquillisers or sedatives is driven by self-treating motives – as opposed to recreational motives – is unknown. The inclusion in the ESPAD study of measures of the motives for non-prescribed use and of the presence of psychological and somatic symptoms or diagnoses would enhance our understanding of this behaviour. Third, the rates presented here may underestimate prescribed and non-prescribed use of tranquillisers or sedatives because of non-participation in the survey but also – for those participating – due to social desirability biases. Especially with regard to absenteeism, it may be that a large proportion of absences on the day of data collection (percentage shown in Table 1) were due to legitimate psychological reasons, perhaps also associated with the use of tranquillisers or sedatives. Future work in this area could focus on prescription drug use among students who are absent from school. Finally, tranquillisers and sedatives are similar in that they act as central nervous system depressants and are invariably used to assist sleep and relieve anxiety. However, their measurement as a single category prevents us from examining possible variations in their relative reported levels of use across countries and survey years and possible differences in the association between pre-

scribed and non-prescribed use between the two classes of drugs. Future research in Europe should measure tranquillisers and sedatives separately.

Our findings suggest that the non-prescribed use of tranquillisers or sedatives constitutes an important public health issue that may deserve policy attention comparable to that paid to preventing use of the traditional illicit drugs. Monitoring and responding to emerging trends in non-prescribed use of psychotropic medicines is important because early onset of misuse is a significant predictor for the development of prescription drug abuse and dependence (McCabe, West, Morales, Cranford, & Boyd, 2007), while non-prescribed use also increases the risk for the onset of psychopathology later in life (Schepis & Hakes, 2011). Furthermore, prescription drug users tend to overestimate the extent of non-prescribed use (McCabe, 2008) and therefore preventive interventions could focus on changing public perceptions that use and misuse of psychotropic drugs are both normal and widespread. Interventions aimed at altering youth perceptions of no or only limited risk from non-prescribed use and at controlling access to prescription drugs are vital also because adolescents spend increasingly more time online and at the same time online shopping is becoming a rapidly increasing source of licit and illicitly manufactured medicines (INCB, 2011).

In conclusion, as our study suggests, the significant yet waning strength of the association between prescribed and non-prescribed use of tranquillisers or sedatives among adolescents may suggest changes both in the patterns of use and the channels of diversion and access to these drugs in Europe. This finding, coupled with the increasing trend in non-prescribed use of tranquillisers or sedatives in several countries constitutes an important challenge for existing surveillance systems, research, prevention and public health policy.

**Declaration of interest** None.

**Anastasios Fotiou, MA**

University Mental Health Research Institute  
Athens, Greece  
E-mail: afotiou@med.uoa.gr

**Eleftheria Kanavou, MSc**

University Mental Health Research Institute  
Athens, Greece  
E-mail: eleftheria.kanavou@gmail.com

**Clive Richardson, PhD**

Panteion University of Social and Political  
Sciences  
Athens, Greece  
E-mail: crichard@panteion.gr

**Anna Kokkevi, PhD**

University Mental Health Research Institute  
Athens, Greece  
E-mail: akokkevi@med.uoa.gr

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