

Psychoactive drug consumption among truck-drivers: a systematic review of the literature with meta-analysis and meta-regression

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Keywords

Truck-drivers • Psychoactive drug consumption • Systematic review • Meta-analysis and meta-regression • Occupational health and wellbeing • Road safety

Summary

Few studies have assessed the extent of psychoactive drug consumption in the occupational setting. The trucking sector, in particular, is an important cause for concern, since psychoactive substance use has a relevant impact on the drivers' health and safety, increasing the risk of injuries and traffic accidents, potentially affecting the general public health as well. A systematic review of the literature and meta-analysis was performed in order to provide Occupational Health Professionals and policy-makers with an updated epidemiological perspective regarding this important issue. The results showed a prevalence of overall

drug consumption of 27.6% [95%CI 17.8-40.1], particularly high considering illicit CNS-stimulants (amphetamine consumption of 21.3% [95%CI 15.7-28.1], and cocaine consumption of 2.2% [95%CI 1.2-4.1]). It appears that truck-drivers choose stimulant substances as a form of performance enhancing drug, in order to increase productivity. However, chronic and high dose consumption has been shown to decrease driving skills, placing these professional drivers at risk for health and road safety. Further research is required, particularly in Europe, in order to fill the knowledge gap and improve the strength of evidence.

Introduction

Illicit drug and psychoactive substance misuse is an important contributor to the global burden of disease. According to data presented in the World Drug Review 2018 published by the *United Nations Office on Drugs and Crime* (UNODC), 5.6% of the global population aged 15-64 years has used drugs in the previous year. Moreover, medical and non-medical prescription drug abuse, especially opioids, is reaching epidemic proportions in many parts of the world [1].

These figures represent an increasing trend over the years, especially in developed countries. In its European Drug Report 2018, the *European Monitoring Centre for Drugs and Drug Addiction* (EMCDDA) has reported an annual prevalence of drug users equal to 7.4%, and drug-induced mortality surpassing 5 thousands deaths in EU countries [2]. Since working age population makes up most of the overall population, substance use among workers is of primary interest from an occupational perspective. Indeed, it can cause loss of productivity, workplace injuries, absenteeism and increased illness [3].

Few international and national surveys using a systematic approach have studied drug use in the workplace: the *Center for Behavioral Health Statistics and Quality (CBHSQ) report regarding substance use and substance use disorder by industry* published by the *Substance Abuse and Mental Health Services Administration* (SAMHSA) reported an annual prevalence of illicit drug

use of 9.5% among workers in the USA between the years 2008-2012 [3]. In Europe, there is a lack of up-to-date and high quality epidemiological data about prevalence of drug use in the workplace. The trucking sector, in particular, is an important cause for concern: truck-drivers are a vulnerable working population due to a wide variety of hazards [4-6] including physical and ergonomic ones with the risk of developing musculoskeletal disorders [7], hypertension [8], obstructive sleep apnea (OSA) and sleep deprivation [9, 10], exposure to diesel exhaust and risk of developing lung cancer [11]. Stressful conditions due to irregular working schedules, night shifts, being distant from families for long periods [12], the need for constant mental alertness, and high productivity demands [13] increase risky behaviors such as smoking, drinking, using psychoactive substances, and having casual sexual contacts [14]. In particular, psychoactive drugs affect the functioning of the brain by delaying cognitive and executive functions, which may lead to impaired driving [15]. These can have a relevant impact on truck-drivers' health, as well as on work safety, increasing the risk of injuries and traffic accidents [16, 17], often fatal: 21% of all lethal injuries occurred among "transportation and warehousing" workers in Iowa in 2005-2009 had a positive toxicology test for substance use [18]. Indeed, while the effects of ethanol on driving have been thoroughly studied by the literature, as shown in the previously published article by the Authors [19], the impact of other substances on driving is not as clear. The vast variety of substance classes,

each with specific effects on physical and mental health, requires a detailed understanding of the interaction and effect on work specific tasks. Italian law has identified several occupational categories as at risk of harm to their and others' health and safety, to which it prohibits drug use, even occasional [20]. Nevertheless, not much is known regarding on site health surveillance and drug testing in this occupational sector.

A comprehensive analysis of this issue can adequately inform policy-makers in order to address legislative shortcomings and implement preventive measures in the workplace, reducing in turn the contribution of work-related drug health problems arising from working conditions to the general public.

The aim of the present systematic review and meta-analysis is to provide Occupational Health Professionals and policy-makers with updated epidemiological data regarding drug consumption among truck-drivers, in order to reduce the knowledge gap, and in turn to allow the implementation of effective countermeasures taking place in the workplace. The reduction of drug-related health problems induced by working conditions will also beneficially contribute to public health. This study adds to the findings regarding alcohol consumption in this occupational category, presented in our previously published article, and significantly updates and expands, through a rigorous quantitative analysis, the work performed by Giroto and colleagues [4].

Materials and methods

SYSTEMATIC REVIEW

The current systematic review of the literature with meta-analysis and meta-regressions is reported according to the *Preferred Reporting Items for Systematic reviews and Meta-Analyses* (PRISMA) guidelines [21]. The study protocol was registered in the "International database of prospectively registered systematic reviews in health and social care" (PROSPERO database [22]; registration code CRD42016037077) [23]. The results of the study are reported in line with the PRISMA guidelines [24].

Briefly, a comprehensive pool of scholarly databases (namely, PubMed/MEDLINE (NLM), Scopus, SciVerse ScienceDirect, Science Citation Index Expanded (SCIE) and Social Sciences Citation Index from ISI/Web of Science, ProQuest Research Library, ABI/INFORM, CB-CA), via the UNO per TUTTI Primo Central (Ex Libris) platform) was searched from inception using the following string of keywords: (truckers OR truck-drivers OR lorry OR commercial vehicles OR large good vehicles OR large vehicles OR heavy vehicles OR long vehicles OR trucking industry OR haul transport) AND (drugs OR psychostimulants OR psychoactive substances OR amphetamine OR benzodiazepines OR cocaine OR heroin OR opioids OR cannabis OR cannabinoids). Medical Subject Headings (MeSH) terms and wild-card option (truncated words) were used when necessary. Last search was carried out on 3rd December 2018. No lan-

guage restriction or time filter were applied. Gray literature was consulted via Google Scholar. Further details of the search strategy are reported in Table I.

Literature search was performed by 2 researchers independently (NLB and AR). In case of disagreement, consensus was reached through discussion and consultation. Based on the PECO criteria, articles were included if: 1) focused on truck-drivers (P = truck-drivers); 2) investigating drug consumption (E = exposure to abuse substances); 3) stratifying according to parameters such as age, gender, marital status, experience years, mean distance travelled (per trip), work-load, night-shift or educational level, in terms of primary schooling level (C = any comparison); and 4) reporting prevalence rate of drug consumption (O = drug consumption rate). Concerning the study design, articles were selected if devised as prevalence studies. Articles were excluded if not meeting with the above-stated PECO criteria and if designed as letter to editor, editorial, commentary, expert opinion, review article (of any type).

Reviews were, anyways, scanned for reducing the chance of missing potentially relevant articles. Relevant information was extracted from each included article by two researchers independently (NLB and AR). In case of disagreement, a third researcher (GD) acted as final referee. For data extraction, an ad hoc Excel spreadsheet was designed and utilized. Besides tables, relevant information was summarized by means of a narrative review.

METHODOLOGICAL APPRAISAL OF STUDIES QUALITY

Study quality was assessed utilizing the "Joanna Briggs Institute Critical Appraisal tools for use in JBI Systematic Reviews-Checklist for Prevalence Studies". This tool explores different domains of quality: namely, 1) the appropriateness of the sample frame to address the target population; 2) the participants sampling technique; 3) the adequateness of the sample size; 4) the completeness of the description and details concerning the study subjects and the setting; 5) the coverage of the sample; 6) the validity of the methods; and 7) their reliability; 8) the appropriateness of the statistical analyses; and, finally, 9) the adequateness of the response rate. Based on the JBI tool, studies were deemed of high, medium and low quality, respectively.

META-ANALYSIS

For each outcome (amphetamine, benzodiazepines, cannabis, cocaine, heroin, opioid, OTC stimulants, overall drug consumption and poliabuse rates), effect size (ES) was computed pooling together the various prevalence rates, using the logit transformation approach.

Heterogeneity among studies was quantitatively assessed computing the I^2 statistics. An amount greater than 50% was considered statistically significant [25, 26]. Based on the amount of heterogeneity, a fixed- or a random-effect model was chosen.

Publication bias was studied both by visually inspecting the funnel plot in terms of asymmetry and by computing the Egger's regression test [27] and the Duval and Tweedie's trim-and-fill analysis [28]. Sensitivity analyses and cumu-

Tab. I. Pooled drug consumption rates and respective ranges stratified according to the type of study (studies based on questionnaires, urine or saliva samples).

Drug	Drug consumption		
	Questionnaire	Urine sample	Saliva sample
Amphetamine	21.3% [95%CI 15.7-28.1]	3.8% [95%CI 1.7-8.2]	1.3% [95%CI 0.7-2.4]
Benzodiazepines	1.0% [95%CI 0.1-6.1]	0.4% [95%CI 0.2-0.6]	NA
Cannabis	5.9% [95%CI 3.5-9.8]	2.1% [95%CI 1.0-4.3]	0.5% [95%CI 0.3-1.0]
Cocaine	2.2% [95%CI 1.2-4.1]	1.1% [95%CI 0.7-2.0]	1.1% [95%CI 0.4-3.1]
Opioid	4.3% [95%CI 0.6-26.4]	2.0% [95%CI 0.6-6.6]	NA
OTC stimulants	4.1% [95%CI 2.7-6.2]	9.0% [95%CI 4.3-18.0]	NA
Overall drug consumption	27.6% [95%CI 17.8-40.1]	6.1% [95%CI 2.9-12.4]	4.1% [95%CI 1.2-13.1]
Poliabuse	2.7% [95%CI 0.2-25.6]	0.6% [95%CI 0.1-4.8]	0.3% [95%CI 0.1-0.7]

NA: not available; OTC: over-the-counter.

relative meta-analyses were further performed, in order to verify the reliability and the consistency of the findings.

All analyses were carried out with the commercial software *Comprehensive Meta-Analysis* (CMA version 3.0, for Windows).

For further details, the reader is referred to our previous publication [19].

Results

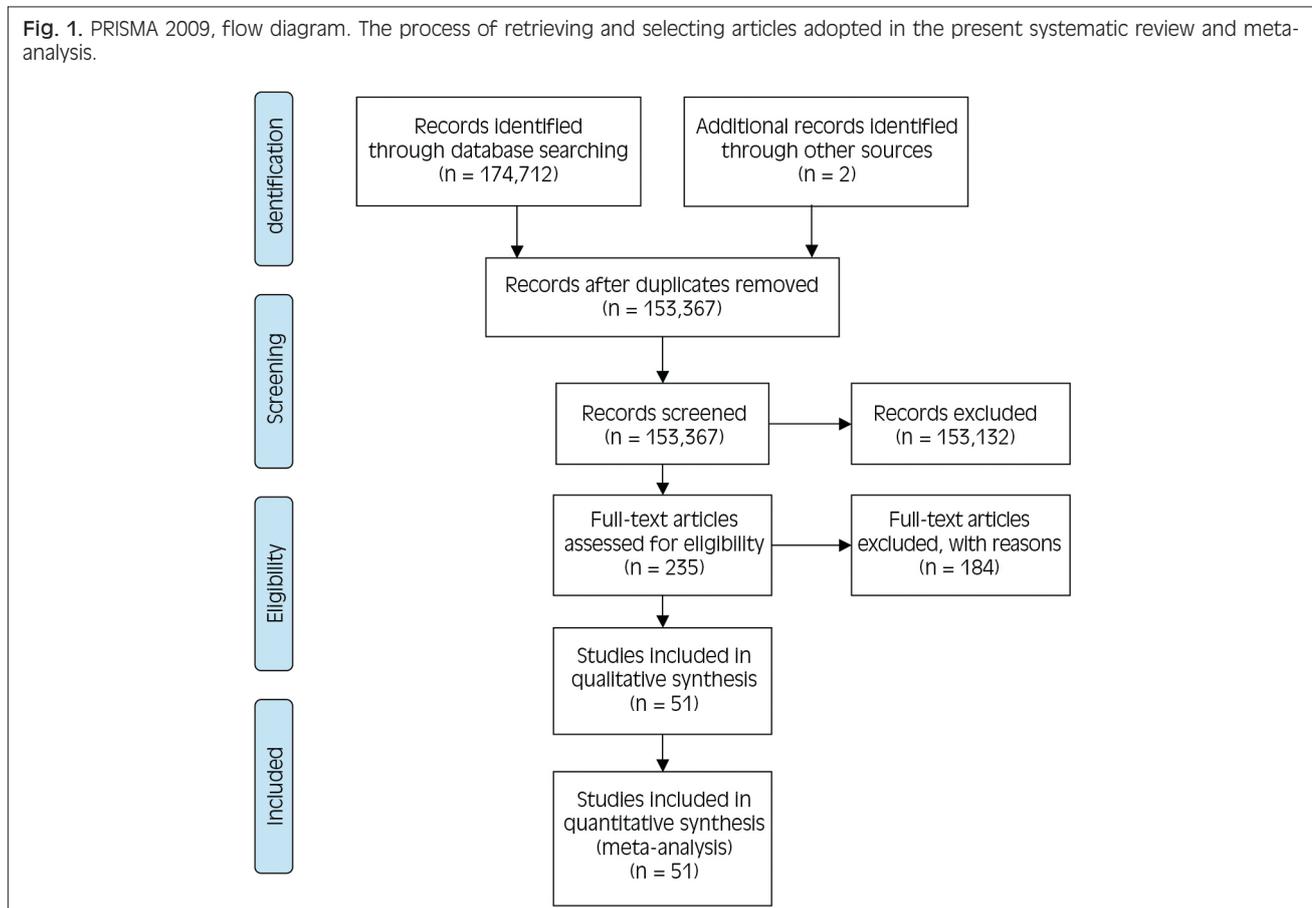
SYSTEMATIC REVIEW

The initial search resulted in a pool of 174,712 articles. After deleting duplicates, a set of 152,367 unique items

was obtained. Screening titles and/or abstracts led to the exclusion of 153,132 items. A pool of articles was retrieved and accessed in full-text. Finally, 51 studies were included (Fig. 1).

Investigations were carried out between 1983 and 2018. Sample sizes ranged from 30 to 11,242 subjects, with a total of 43,673 participants. 31 studies investigated drug consumption among truck-drivers utilizing questionnaires, whilst 14 and 6 studies utilized urine and saliva samples, respectively. 35 studies were performed in the Americas (1 in Canada, 6 in the USA, and 28 in Brazil), 5 in Asia (3 in Thailand, 1 in Pakistan, and 1 in Iran), 5 in Europe (3 in Italy, 1 in France and 1 in Norway), 4 in Australia and 2 in Africa (1 in Morocco and 1 in Nigeria).

Fig. 1. PRISMA 2009, flow diagram. The process of retrieving and selecting articles adopted in the present systematic review and meta-analysis.



Age went from 33.5 to 43.85 years, with male percentage varying in the range 90.6-100.0%. Concerning the marital status, percentage of married subjects ranged from 62.0% to 94.9%. Percentage of truck-drivers with at least primary education varied between 35.2% and 100.0%, with schooling years going from 4.6 to 8.7 years. Work-load ranged from 7.8 to 14.8 hours, with mean distance travelled varying between 270 km and 1,159.7 km. Percentage of truck-drivers working for companies was highly variable, in the range 0-76%. Experience years went from 10 to 18.5 hours. Finally, percentage of truck-drivers doing night-shifts ranged from 10.7% to 33.0%.

Concerning the outcomes, amphetamine consumption ranged from 0.0% to 82.5%, whereas cannabis and cocaine use went from 0.0% to 29.9%, and from 0.1% to 8.9%, respectively. Heroin consumption varied between 0.1% and 0.9%. Opioid use ranged from 0.2% to 33.0%, while benzodiazepines consumption went from 0.0% to 2.1%. OTC stimulant use ranged from 4% to 13%, while poliabuse prevalence was more variable (0.0-8.9%). Finally, overall drug use was in the range 1.3-80.4%.

AMPHETAMINE CONSUMPTION

Based on questionnaires, the overall amphetamine consumption rate was 21.3% ([95%CI 15.7-28.1], $z = -6.94$, $p < 0.0001$, $k = 22$) (Supplementary Fig. 1A). Due to the high statistically significant heterogeneity ($I^2 = 97.15\%$), a random-effect model was applied ($I^2 = 64.91\%$). No evidence of publication bias could be found. At the meta-regression analyses, significant moderators were found to be country ($Q = 39.20$, $p < 0.0001$, with the highest ES in Brazil, and the lowest ES in Nigeria) (Supplementary Fig. 2), age (coefficient = -0.24 , $SE = 0.06$ [95%CI -0.36 to -0.12], $z = -3.82$, $p = 0.0001$) (Supplementary Fig. 3), marriage (coefficient = -0.02 , $SE = 0.01$ [95%CI -0.04 to 0.00], $z = -1.99$, $p = 0.0470$), experience years (coefficient = -0.34 , $SE = 0.10$ [95%CI -0.54 to -0.14], $z = -3.37$, $p = 0.0008$) (Supplementary Fig. 4), working for companies (coefficient = -0.04 , $SE = 0.01$ [95%CI -0.06 to -0.01], $z = -2.72$, $p = 0.0065$) and primary schooling level (coefficient = -0.02 , $SE = 0.01$ [95%CI -0.03 to -0.01], $z = -2.69$, $p = 0.0071$). Male ($p = 0.1040$), mean distance ($p = 0.7928$) and work-load ($p = 0.3804$) were not statistically significant. For the other moderators, meta-regression analyses could not be run due to insufficient number of studies.

Based on studies utilizing urine samples, the overall amphetamine consumption rate was 3.8% ([95%CI 1.7-8.2], $z = -7.70$, $p < 0.0001$, $k = 13$) (Supplementary Fig. 5A). Due to the high statistically significant heterogeneity ($I^2 = 97.36\%$), a random-effect model was carried out ($I^2 = 42.38\%$). No evidence of publication bias could be detected. At the meta-regression analyses, only country ($Q = 23.64$, $p < 0.0001$, with the highest ES in Thailand and the lowest ES in France) resulted a statistically significant moderator. Age ($p = 0.1673$), male ($p = 0.0511$) were not statistically significant moderators. For the other moderators, meta-regression analyses could not be run due to insufficient number of studies.

Based on studies utilizing saliva samples, the overall amphetamine consumption rate was 1.3% ([95%CI 0.7-2.4], $z = -13.63$, $p < 0.0001$, $k = 5$) (Supplementary Fig. 6A). Due to the high statistically significant heterogeneity ($I^2 = 83.68\%$) a random-effect model was applied ($I^2 = 47.67\%$). No evidence of publication bias could be found. For all the moderators, meta-regression analyses could not be run due to insufficient number of studies.

CANNABIS CONSUMPTION

Based on questionnaires, the overall cannabis consumption rate was 5.9% ([95%CI 3.5-9.8], $z = -9.88$, $p < 0.0001$, $k = 10$) (Supplementary Fig. 1B). Due to the high statistically significant heterogeneity, ($I^2 = 96.81\%$), a random-effect model was carried out ($I^2 = 62.28\%$). No evidence of publication bias could be found. At the meta-regression analyses, a significant moderator was found to be only country ($Q = 15.85$, $p = 0.0146$, with the highest ES in Pakistan, and the lowest ES in Iran). Age ($p = 0.1044$), male ($p = 0.5799$), marriage ($p = 0.5939$), mean distance ($p = 0.4235$), experience years ($p = 0.7688$), working for companies ($p = 0.2192$), and primary schooling level ($p = 0.3200$) were not statistically significant. For the other moderators, meta-regression analyses could not be run due to insufficient number of studies.

Based on studies utilizing urine samples, the overall cannabis consumption rate was 2.1% ([95%CI 1.0-4.3], $z = -9.97$, $p < 0.0001$, $k = 11$) (Supplementary Fig. 5B). Due to the high statistically significant heterogeneity ($I^2 = 97.62\%$), a random-effect model was chosen ($I^2 = 4.52$). At the meta-regression analyses, only age (coefficient = -0.50 , $SE = 0.09$ [95%CI -0.68 to -0.33], $z = -5.56$, $p < 0.0001$) resulted a statistically significant moderator. Country ($Q = 3.97$, $p = 0.5537$), male ($p = 0.2427$) were not statistically significant moderators. For the other moderators, meta-regression analyses could not be run due to insufficient number of studies.

Based on studies utilizing saliva samples, the overall cannabis consumption rate resulted 0.5% ([95% 0.3-1.0%], $z = -15.69$, $p < 0.0001$, $k = 4$) (Supplementary Fig. 6B). Due to the high statistically significant heterogeneity ($I^2 = 68.12\%$), a random-effect model was applied ($I^2 = 0.00\%$). The visual inspection of the funnel plot showed evidence of publication bias. At the Duval and Tweedie's trim-and-fill analysis, 2 studies were censored, resulting in a "real" ES of 0.3% ([95%CI 0.1-0.7], $Q = 33.21$) (Supplementary Fig. 7). For all the moderators, meta-regression analyses could not be run due to insufficient number of studies.

COCAINE CONSUMPTION

Based on questionnaires, the overall cocaine consumption rate was 2.2% ([95%CI 1.2-4.1], $z = -11.75$, $p < 0.0001$, $k = 9$) (Supplementary Fig. 1C). Due to the high statistically significant heterogeneity ($I^2 = 91.66\%$), a random-effect model was applied ($I^2 = 50.78\%$). No evidence of publication bias could be found. Country ($Q = 6.06$, $p = 0.1951$), age ($p = 0.2460$), male ($p = 0.2433$), marriage ($p = 0.0541$), mean distance

($p = 0.8952$), experience years ($p = 0.2604$), working for companies ($p = 0.3851$), primary schooling level ($p = 0.5713$) were not statistically significant moderators. For the other moderators, meta-regression analyses could not be run due to insufficient number of studies.

Based on studies utilizing urine samples, the overall cocaine consumption rate was 1.1% ([95%CI 0.7-2.0], $z = -15.59$, $p < 0.0001$, $k = 10$) (Supplementary Fig. 5C). Due to the high statistically significant heterogeneity ($I^2 = 88.74\%$), a random-effect model was carried out ($I^2 = 19.33\%$). No evidence of bias was found. At the meta-regression analyses, no statistically significant moderators could be found. Country ($Q = 6.47$, $p = 0.1668$), age ($p = 0.5273$), male ($p = 0.3568$) were not statistically significant moderators. For the other moderators, meta-regression analyses could not be run due to insufficient number of studies.

Based on studies utilizing saliva samples, the overall cocaine consumption rate resulted 1.1% ([95%CI 0.4-3.1], $z = -8.29$, $p < 0.0001$, $k = 3$) (Supplementary Fig. 6C). Due to the high statistically significant heterogeneity ($I^2 = 88.18\%$), a random-effect model was chosen ($I^2 = 0.00\%$). No evidence of bias publication could be found.

OPIOID CONSUMPTION

Based on questionnaires, the overall opioid consumption rate was 4.3% ([95%CI 0.6-26.4], $z = -2.92$, $p = 0.003$, $k = 4$) (Supplementary Fig. 1D). Due to the high statistically significant heterogeneity ($I^2 = 98.12\%$), a random-effect model was performed ($I^2 = 0.00\%$). No evidence of publication bias could be found. At the meta-regression analyses, only age (coefficient = -0.49 , SE = 0.13 [95%CI -0.75 to -0.23], $z = -3.70$, $p = 0.0002$) resulted a statistically significant moderator. For the other moderators, meta-regression analyses could not be run due to insufficient number of studies.

Based on studies utilizing urine samples, the overall opioid consumption rate was 2.0% ([95%CI 0.6-6.6], $z = -6.13$, $p < 0.0001$, $k = 4$) (Supplementary Fig. 5D). Due to the high statistically significant heterogeneity ($I^2 = 95.97\%$), a random-effect model was chosen ($I^2 = 0.00\%$). No evidence of publication bias was found. It was not possible to compute meta-regressions due to insufficient number of studies/missing information.

BENZODIAZEPINES CONSUMPTION

Based on questionnaires, the overall benzodiazepines consumption rate was 1.0% ([95%CI 0.1-6.1], $z = -4.81$, $p < 0.0001$, $k = 2$). Due to the high statistically significant heterogeneity ($I^2 = 70.57\%$), a random-effect model was carried out ($I^2 = 0.00\%$). Since there were only 2 studies, it was not possible to conduct a publication bias analysis and meta-regressions.

Based on studies utilizing urine samples, the overall benzodiazepines consumption rate was 0.4% [95%CI 0.2-0.6], $z = -21.71$, $p < 0.0001$, $k = 4$). Due to the absence of heterogeneity ($I^2 = 0.00\%$), a fixed-effect model was applied. There was no evidence of publication bias. For all the moderators, meta-regression analyses could not be run due to insufficient number of studies.

OVER-THE-COUNTER STIMULANT CONSUMPTION

Based on questionnaires, the overall OTC stimulant consumption rate was 4.1% ([95%CI 2.7-6.2], $z = -14.09$, $p < 0.0001$, $k = 3$). Due to the high statistically significant heterogeneity ($I^2 = 76.18\%$), a random-effect model was conducted ($I^2 = 28.35\%$). The visual inspection of the funnel plot gave evidence of publication bias. At the Duval and Tweedie's trim-and-fill analysis, one study was censored, with a "real" ES of 3.5% ([95%CI 2.3-5.3], $Q = 15.46$) (Supplementary Fig. 8). For all moderators, meta-regression analyses could not be run due to insufficient number of studies.

Based on studies utilizing urine samples, the overall OTC stimulant consumption rate was 9.0% ([95%CI 4.3-18.0], $k = 2$). Due to the high statistically significant heterogeneity ($I^2 = 92.41\%$), a random-effect model was chosen ($I^2 = 0.00\%$). Since there were only 2 studies, it was not possible to conduct a publication bias analysis and meta-regressions.

POLIABUSE RATE

Based on questionnaires, the overall poliabuse rate was 2.7% ([95%CI 0.2-25.6], $z = -2.80$, $p = 0.005$, $k = 2$). Due to the high statistically significant heterogeneity ($I^2 = 96.14\%$), a random-effect model was applied ($I^2 = 0.00\%$). Since there were only 2 studies, it was not possible to conduct a publication bias analysis and meta-regressions.

Based on studies utilizing urine samples, the overall poliabuse rate was 0.6% ([95%CI 0.1-4.8], $z = -4.77$, $k = 5$). Due to the high statistically significant heterogeneity ($I^2 = 90.76\%$), a random-effect model was carried out ($I^2 = 0.00\%$). No evidence of publication bias could be found. At the meta-regression analyses, only country ($Q = 17.45$, $p = 0.0002$, with the highest ES in the USA and the lowest ES in Italy) resulted a statistically significant moderator. For the other moderators, meta-regression analyses could not be run due to insufficient number of studies.

Based on studies utilizing saliva samples, the overall poliabuse rate was 0.3% ([95%CI 0.1-0.7], $z = -12.98$, $p < 0.0001$, $k = 3$). Due to the statistically significant heterogeneity ($I^2 = 61.68\%$), a random-effect model was performed ($I^2 = 0.00\%$). No evidence of publication bias could be found. For all moderators, meta-regression analyses could not be conducted due to insufficient number of studies.

OVERALL DRUG CONSUMPTION

Based on questionnaires, the pooled overall drug consumption rate was 27.6% ([95%CI 17.8-40.1], $z = -3.36$, $p = 0.001$, $k = 14$) (Supplementary Fig. 1E). Due to the high statistically significant heterogeneity ($I^2 = 99.04\%$), a random-effect model was applied ($I^2 = 21.28\%$). There was no evidence of publication bias. At the meta-regression analyses, only age (coefficient = -0.22 , SE = 0.07 [95%CI -0.36 to -0.08], $z = -3.13$, $p = 0.0018$) resulted a statistically significant moderator. On the contrary, country ($Q = 1.47$, $p = 0.8326$), male ($p = 0.9460$), marriage ($p = 0.3583$), mean distance ($p = 0.9759$), experience years ($p = 0.1128$), work-load ($p = 0.9902$), working

for companies ($p = 0.8486$), and primary schooling level ($p = 0.3112$) were not statistically significant moderators. For the other moderators, meta-regression analyses could not be run due to insufficient number of studies. Based on studies utilizing urine samples, the pooled overall drug consumption rate was 6.1% ([95%CI 2.9-12.4], $p < 0.0001$, $k = 8$) (Supplementary Fig. 5E). Due to the high statistically significant heterogeneity ($I^2 = 98.44\%$), a random-effect model was conducted ($I^2 = 0.00\%$). The visual inspection of the funnel plot showed evidence of publication bias. At the Duval and Tweedie's trim-and-fill analysis, 1 study was censored, resulting in a "real" ES of 5.1% ([95% 2.4-10.1], $Q = 543.42$) (Supplementary Fig. 9). At the meta-regression analyses, only age (coefficient = -0.36 , $SE = 0.09$ [95%CI -0.53 to -0.19], $z = -4.13$, $p < 0.0001$) resulted a statistically significant moderator. Country ($Q = 1.65$, $p = 8003$), and male ($p = 0.8430$) were not statistically significant moderators. For the other moderators, meta-regression analyses could not be run due to insufficient number of studies.

Based on studies utilizing saliva samples, the pooled overall drug consumption rate was 4.1% ([95%CI 1.2-13.1], $z = -4.90$, $p < 0.0001$, $k = 5$) (Supplementary Fig. 6D). Due to the high statistically significant heterogeneity ($I^2 = 98.89\%$), a random-effect model was conducted ($I^2 = 0.00\%$). For all the moderators, meta-regression analyses could not be run due to insufficient number of studies.

Pooled drug consumption rates stratified according to the type of study are summarized in Table I.

STUDY QUALITY

Findings of the critical appraisal of included studies are shown in Table II.

Discussion

To the best of our knowledge, this is the first systematic review with meta-analysis and meta-regressions on drug

consumption rate among truck-drivers. Considering the meta-analysis performed on data extracted from questionnaires, the findings show an increased prevalence of drug use among truck-drivers, especially central nervous system (CNS) stimulants, compared to the general population. In particular, the overall annual prevalence of amphetamine use among truck-drivers of 21.3%, compared to the estimated global prevalence of consumption in the general population of 0.7% [1], shows an almost 30-fold higher rate.

Similarly, but to a lesser degree, the results regarding cocaine use showed a higher prevalence (2.2%) compared to the general population (0.37%) [1]. In previous studies, stimulant consumption among truck-drivers has been associated with night shifts, length of travel and younger age [17, 75, 76]. Other authors have suggested that also external factors play a role, such as productivity-based payments [73]. In the present analysis, being younger and having less professional experience showed the most significant correlations with stimulant use.

Drivers often take stimulants as a form of Performance Enhancing Drugs (PEDs), in order to sustain ever increasing work-loads and busy work schedules. Several studies performed in controlled clinical settings have suggested that low dose amphetamines could improve psychomotor skills, such as driving ability, even in fatigued subjects [77]. However, chronic and high dose users, taken in real life settings, showed poorer compliance with traffic rules and working hours regulations [78], with an increased risk of traffic accidents [79], mainly as a consequence of after effects such as hypersomnolence and fatigue [80, 81]. Some authors have suggested that blood concentration above 0.27-0.53 mg/l is associated with psychomotor impairment [79]. Similar considerations have been made regarding cocaine use and its effects on psychomotor skills [82-85]. Amphetamine use has been estimated to increase the risk of fatal accidents by 5-times, causing in 2013 around half of all road traffic deaths caused by illicit drug consumption worldwide, resulting in around 20 thousand deaths [15].

The *European Agency for Safety and Health at Work* (EU-OSHA) has acknowledged the spread and normalization

Tab. II. Critical appraisal of studies included in the present systematic review and meta-analysis.

Study	Domain I	Domain II	Domain III	Domain IV	Domain V	Domain VI	Domain VII	Domain VIII	Domain IX
Bombana et al. 2017 [29]	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Cerqueira et al. 2011 [30]	Yes	No	No	Yes	Yes	Yes	Yes	Yes	Yes
Couper et al. 2002 [31]	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
De Oliveira et al. 2015 [32]	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes
De Oliveira et al. 2016 [33]	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Drummer et al. 2007 [34]	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Girotto et al. 2015 [17]	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Gjerde et al. 2012 [35]	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Gjerde et al. 2014 [36]	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes

continues

Tab. II. *follows.*

Study	Domain I	Domain II	Domain III	Domain IV	Domain V	Domain VI	Domain VII	Domain VIII	Domain IX
Guinn et al. 1983 [37]	No	No	No	No	Yes	No	No	Yes	Yes
Ingsathit et al. 2009 [38]	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Knauth et al. 2011 [39]	Yes	No	Yes	No	Yes	No	No	Yes	Yes
Korelitz et al. 1993 [16]	Yes	No	Yes	No	Yes	Yes	Yes	Yes	Yes
Labat et al. 2008 [40]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Laraqui et al. 2011 [41]	Yes	No	Yes	Yes	Yes	No	No	Yes	Yes
Lemire et al. 2002 [42]	No	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes
Leopoldo et al. 2015 [43]	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Leyton et al. 2012 [44]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Lund et al. 1988 [45]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Maarefvand et al. 2016 [46]	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Mabbott and Hartley 1999 [47]	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	No
Mansur Ade et al. 2015 [48]	No	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes
Masson, Monteiro 2010 [49]	Yes	No	No	Yes	Yes	No	No	Yes	Yes
Mieczkowski 2010 [50]	No	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes
Mir et al. 2012 [51]	Yes	Yes	Yes	No	Yes	No	No	Yes	Yes
Mongkolsrichaikul et al. 1988 [52]	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes
Moreira, Gadani 2009 [53]	No	No	No	No	Yes	No	No	Yes	Yes
Nascimento et al. 2007 [54]	Yes	No	No	No	Yes	No	No	Yes	Yes
Okpataku 2016 [55]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Peixe et al. 2014 [56]	Yes	No	No	Yes	Yes	Yes	Yes	Yes	No
Penteado et al. 2008 [57]	Yes	No	Yes	Yes	Yes	No	No	Yes	Yes
Pereira et al. 2014 [58]	Yes	No	No	Yes	Yes	No	No	Yes	Yes
Pidetcha et al. 1995 [59]	No	No	No	No	Yes	Yes	Yes	Yes	Yes
Pinheiro et al. 2015 [60]	Yes	No	No	Yes	Yes	No	No	Yes	Yes
Pinho 2005 [61]	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Remor et al. 2015 [62]	Yes	No	Yes	Yes	Yes	No	No	Yes	Yes
Riva et al. 2010 [63]	Yes	No	Yes	Yes	Yes	No	No	Yes	Yes
Riva et al. 2018 [64]	Yes	No	Yes	Yes	Yes	No	No	Yes	Yes
Sangaleti et al. 2014 [65]	Yes	No	Yes	Yes	Yes	No	No	Yes	Yes
Silva et al. 2003 [66]	No	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes

continues

Tab. II. *Follows.*

Study	Domain I	Domain II	Domain III	Domain IV	Domain V	Domain VI	Domain VII	Domain VIII	Domain IX
Sinagawa et al. 2014 [67]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Souza et al. 2005 [68]	Yes	No	Yes	Yes	Yes	No	No	Yes	Yes
Starmer et al. 1997 [69]	No	No	Yes	No	Yes	Yes	Yes	Yes	Yes
Takitane et al. 2012 [70]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Teles et al. 2008 [71]	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Valway et al. 2009 [72]	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Williamson 2007 [73]	Yes	No	Yes	Yes	Yes	No	No	Yes	Yes
Yonamine et al. 2012 [74]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes

of stimulant use among certain groups of workers, particularly transportation workers, shift workers, and workers in high pressure, competitive or bullying work cultures [86]. It highlighted the need to evaluate the potential effect of non-medical drug used as cognitive enhancers in the workplace, and to consider the work environment and the interaction between workers and their working conditions as important factors in the use of PEDs.

Opiates, opioids, and CNS depressants, such as cannabinoids and benzodiazepines, showed a lower prevalence in the study population, and a smaller difference compared to the prevalence in the general population. In particular regarding cannabinoid use, the relatively high prevalence shown (5.9%), with the highest rates extracted from North American and European studies, follows the overall increasing rate of recreational and medical use of this type of drug in the general population: while an estimated 3.9% of the global population has used cannabinoids in the previous year, in North America the prevalence was higher at 13% [1], reaching over 14% in the European Union with an increasing trend of high-risk use, meaning consuming cannabinoids 20 or more days in the past month [2]. Many CNS depressant have been found to reduce lane control by increasing the standard deviation of lateral position (SDLP) [87-93]. Cannabis has been shown to impair cognitive, particularly affecting working memory and divided attention, and psychomotor performances, increasing the chance of road accidents [94]: according to systematic review and meta-analysis performed by Asbridge and collaborators, acute cannabis consumption among drivers doubles the risk of crashes compared to non-user [95].

Authors have suggested that tetrahydrocannabinol (THC) impairs mainly lateral control of the vehicle, while not affecting longitudinal control [96, 97]. Moreover, interaction between cannabis and alcohol has been shown to have an additive effect on driving performance [91, 94, 98, 99] causing an increased risk of road accidents [100]. Indeed, cannabinoids are estimated to cause one fifth of all road traffic deaths caused by illicit drug consumption [15]. The importance of cannabis use in the workplace may grow further as countries reform medicinal and recreational cannabinoid

laws enabling an increase in the rate of consumption [101]. Concerning the results of opiate/opioid use among truck-drivers, the present analysis shows a prevalence of 4.3%, significantly higher compared to the rate of persons who use opiates and persons who use prescription opioids for non-medical purposes among the general population equal to 0.7% worldwide [1], and 0.4% in Europe [2].

However, similarly to cannabis, data show that there is a growing trend in the use of prescription drugs such as opioids and sedatives, for medical and non-medical reasons, reaching epidemic proportions in some Western countries. In particular, past-year users of opioids in North America have reached a prevalence of 4.2% [1], similar to the results found in the present study. Moreover, opioids cause most of the negative health impact of drug use, accounting for three quarters of deaths from drug use disorders in 2015 [1]. Although the role of opiates and opioid use in impairing driving ability is still unclear [102-106], there is suggestive evidence that opioids can cause an increased risk of vehicle collisions [1, 107].

Although the consumption of benzodiazepine was not found to be as common among truck-drivers, it must not be underestimated, as there is ample evidence of their impairing effect on driving skills, particularly regarding long-term benzodiazepines [108-110]. Moreover, non-medical use of benzodiazepines is the most common type of misuse of prescription drugs in the world [1].

Concerning drug testing for recent use, the results obtained through saliva sampling showed generally lower rates than those found on urine. This might be explained by the fact that urine drug testing can detect consumption occurred days or weeks before the sampling, resulting in low specificity for recent substance use. Research has suggested that saliva sampling has a stronger correlation with blood concentrations compared to urine, being also easier and faster to analyze and less intrusive to drivers [111-113]. However, there is a lack of conclusive evidence, with other authors considering urine testing as a more accurate method for identification of substance use and disorders in the workplace [114]. Based on the prevalence of overall drug use obtained through biological sampling, around 1 every 20 workers was driving under the influence of drugs. It is

worth noting that the country of origin of the driver was an often found association with drug use. Indeed, considering the data obtained from the included studies, there appears to be a pattern of consumption of specific substances in different areas, such as prevalent stimulant use in South America, cannabis use in North America and Europe, and opioid use in parts of Asia, likely because of availability, as well as historic and cultural reasons.

Overall, the findings of the present study, adding to the results of the previously published systematic review and meta-analysis concerning at-risk drinking, show that substance use is widespread among truck-drivers globally, putting workers and the general public at an increased risk of harm. The *EU Action Plan on Drugs 2017-2020* states that, in order to reduce and prevent drug use, effective evidence-based prevention measures must take into consideration situational factors, including workplace conditions [115]. There is indeed an urgent necessity for updated epidemiological data and research studying effective Occupational Health Promotion programs, particularly in Europe, required in order to make and enforce effective policies, putting in place countermeasures such as regular worksite drug testing, which has been shown to deter drug use among workers [116], as well as assessing working conditions that facilitate drug consumption, such as excessive workloads demanded by companies.

STRENGTHS AND LIMITATIONS

The strengths of our study consist in its methodological rigor, reproducibility and transparency. We deposited a priori study protocol, which further corroborates our meta-analysis. However, despite its novelty and its methodological robustness, our study is not without limitations, which should be properly acknowledged.

The high statistically significant heterogeneity may affect the generalization of the findings and calls up for caution in their interpretation. For some outcomes, few studies were available. In some cases, such paucity limited the possibility of conducting a full extensive series of analyses, including publication bias analysis and meta-regressions.

Conclusions

The present systematic review of the literature with meta-analysis and meta-regressions showed a relevant drug consumption rate among truck-drivers. As such, this study has practical implications for Occupational Physicians dealing with the health and wellbeing of truck-drivers. In particular, it appears that truck-drivers choose mainly stimulant substances as a form of performance enhancing drug, in order to increase productivity. However, chronic and high dose consumption has been shown to decrease driving skills, placing these professional drivers, as well as the general public, at risk.

Current literature is lacking in updated and reliable epidemiological data, especially in Europe. Therefore, further research in the field is urgently needed in order to provide Occupational Health Professionals with up-to-date data, necessary for the implementation of preventive programs and effective workplace measures. More-

over, this can be useful for decision and policy-makers in order to fill the gaps and shortcomings in the regulations.

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Conflict of interest statement

None declared.

Authors' contributions

GD, NLB and PD conceived the study, AM and AR performed a search of the literature, extracted and collected data, AM and AR critically appraised the literature, GD and NLB analyzed data, GD, NLB, AM, AR and PD drafted and revised the manuscript. All authors have read and approved the latest version of the manuscript.

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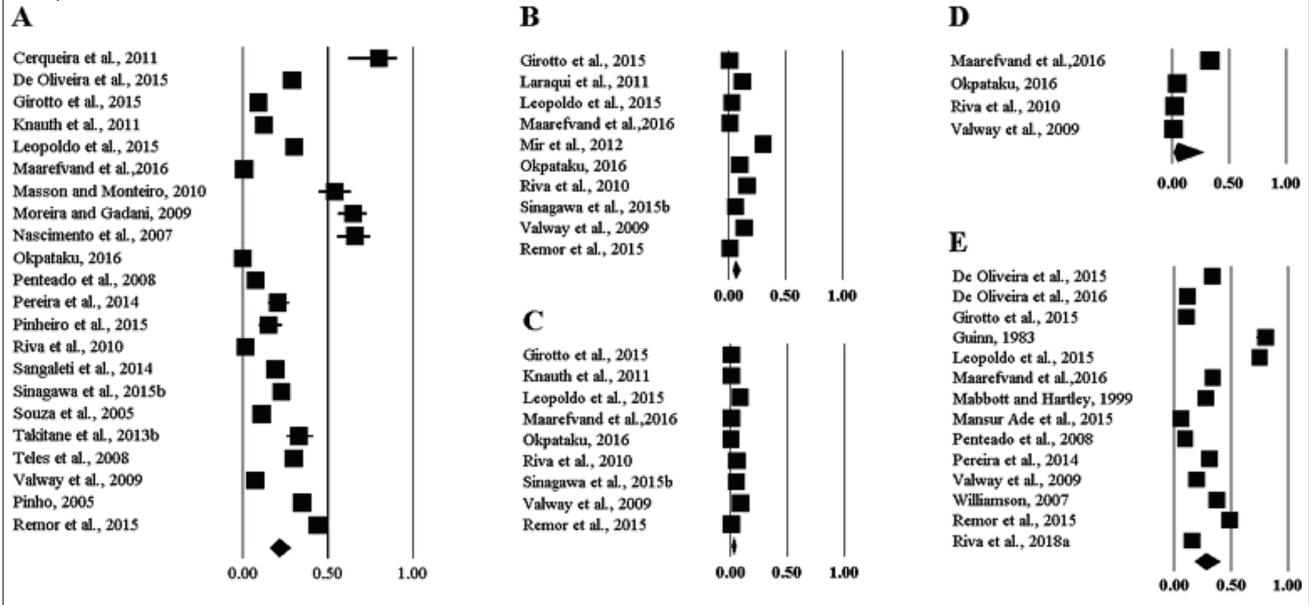
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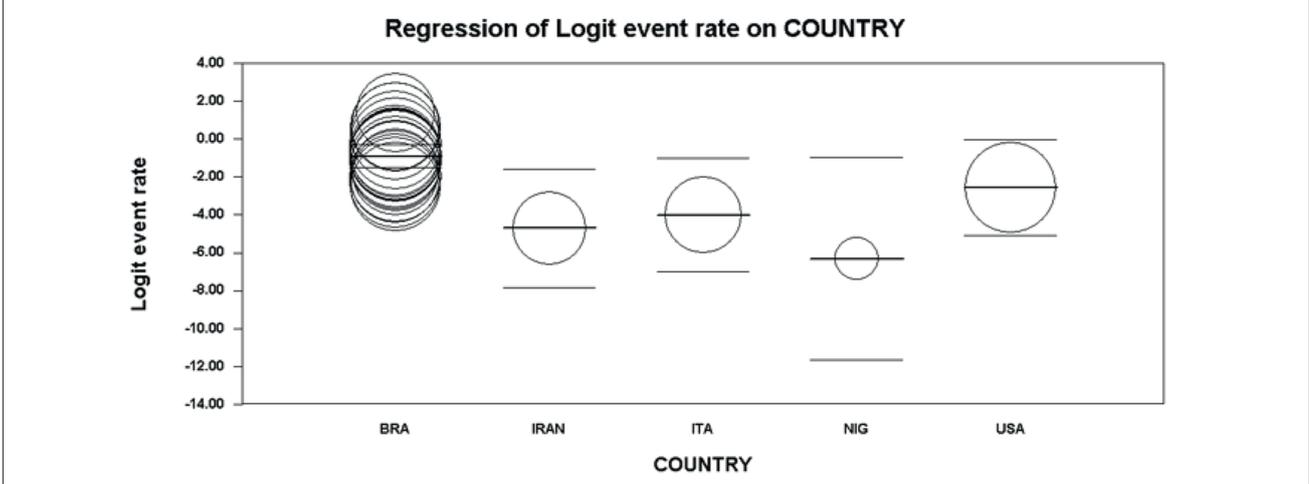
■ Correspondence: Nicola Luigi Bragazzi, Dipartimento di Scienze della Salute (DISSAL), Università degli Studi di Genova, I.go R. Benzi 10 (Padiglione 3), 16132 Genova, Italy - E-mail: dottornicolaui brigazzi@gmail.com

Supplementary material

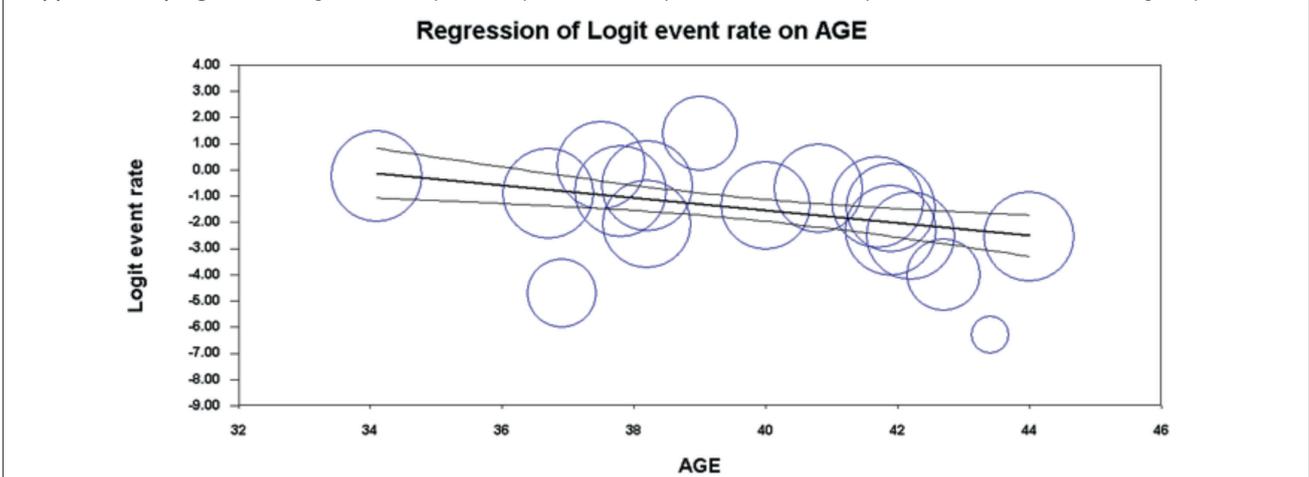
Supplementary Fig. 1. Forest plots of amphetamine (A), cannabis (B), cocaine (C), opioids (D) and overall drug (E) use prevalence based on questionnaires.



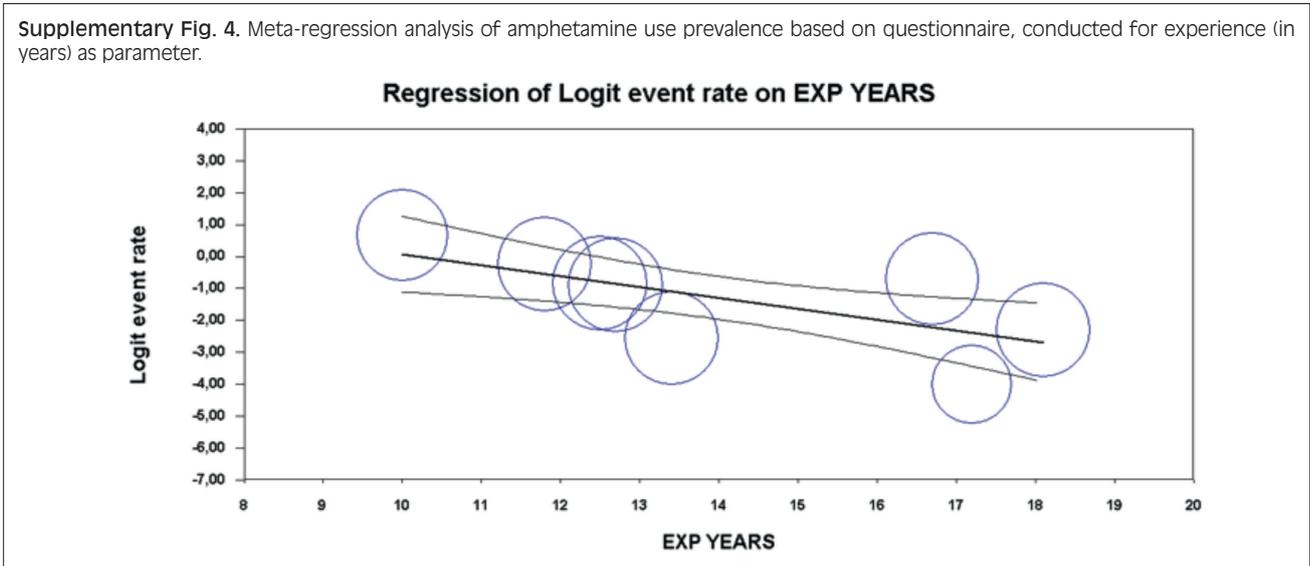
Supplementary Fig. 2. Meta-regression analysis of amphetamine use prevalence based on questionnaire, conducted for country as parameter.



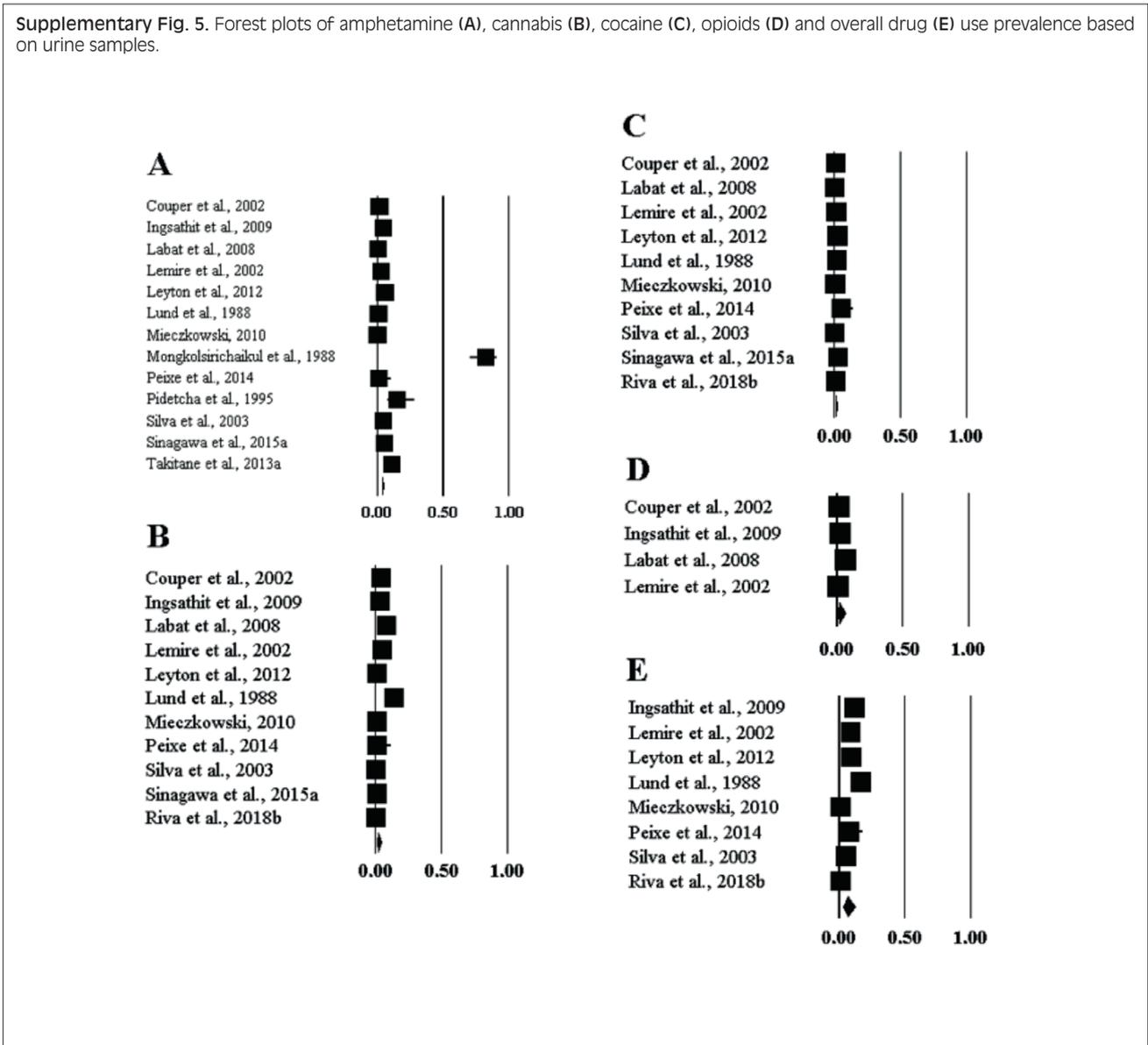
Supplementary Fig. 3. Meta-regression analysis of amphetamine use prevalence based on questionnaire, conducted for age as parameter.



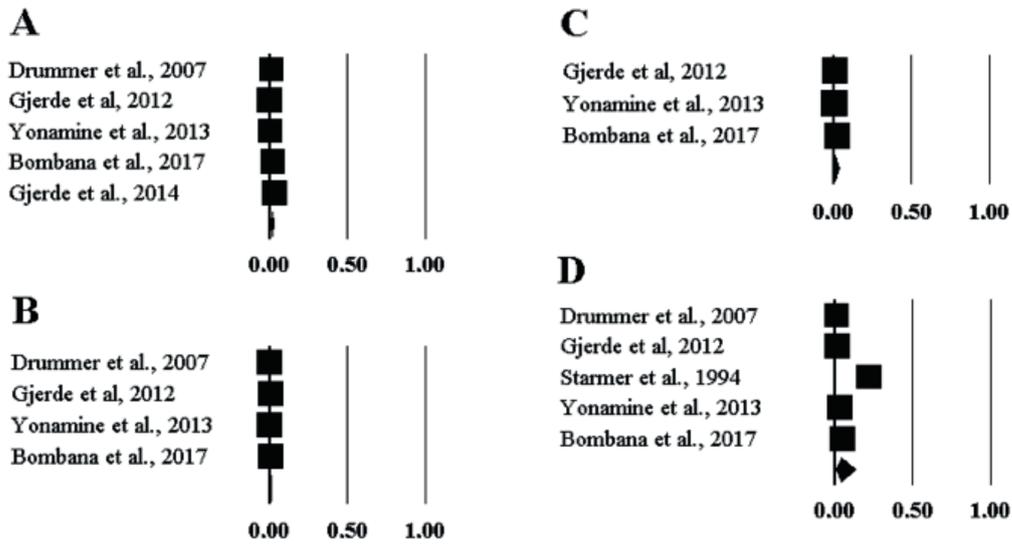
Supplementary Fig. 4. Meta-regression analysis of amphetamine use prevalence based on questionnaire, conducted for experience (in years) as parameter.



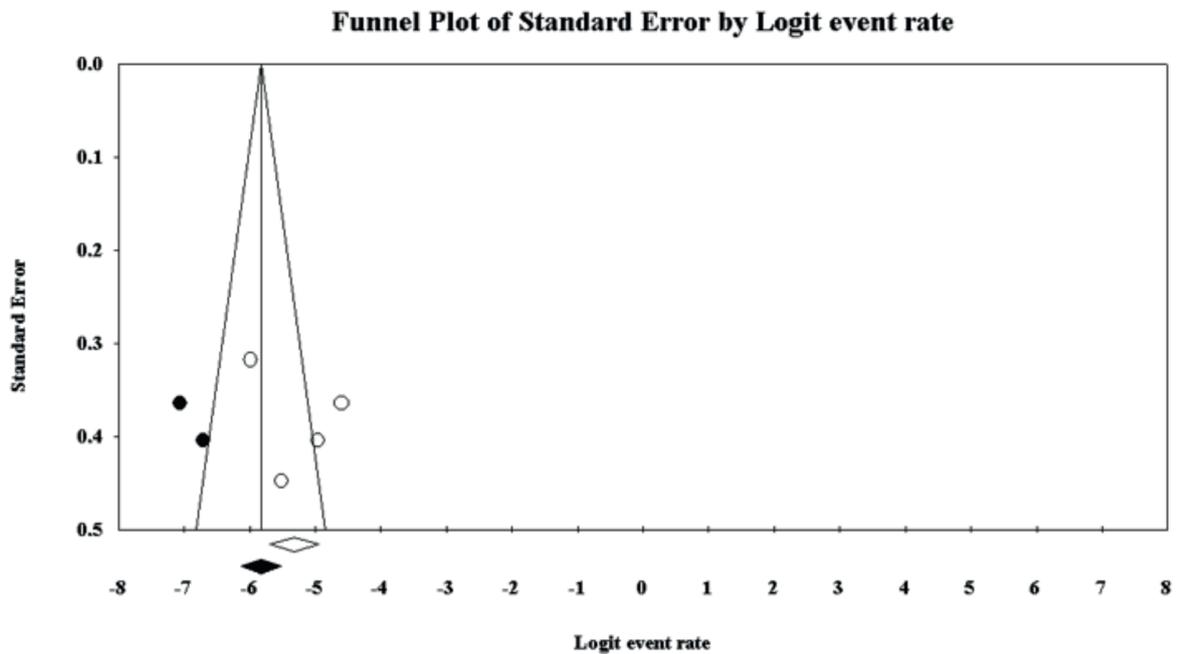
Supplementary Fig. 5. Forest plots of amphetamine (A), cannabis (B), cocaine (C), opioids (D) and overall drug (E) use prevalence based on urine samples.



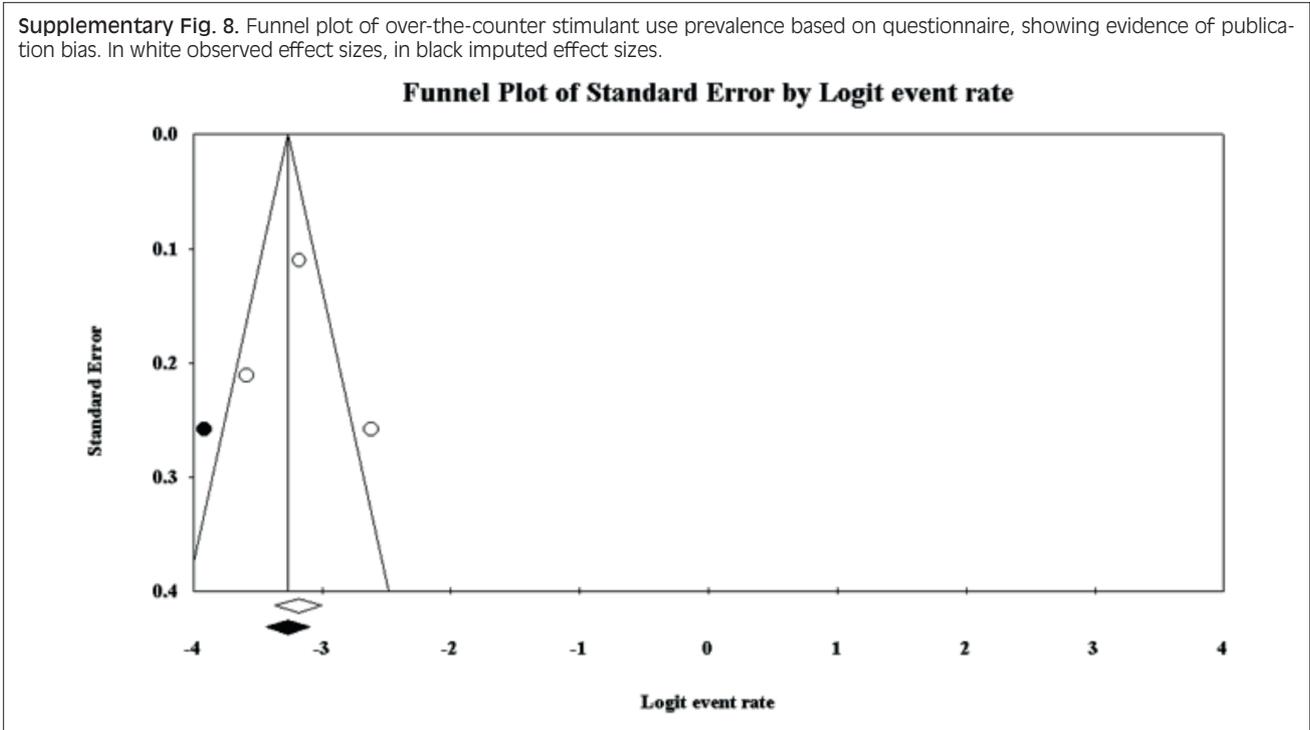
Supplementary Fig. 6. Forest plots of amphetamine (A), cannabis (B), cocaine (C) and overall drug (D) use prevalence based on saliva samples.



Supplementary Fig. 7. Funnel plot of cannabis use prevalence based on saliva samples. showing evidence of publication bias. In white observed effect sizes, in black imputed effect sizes.



Supplementary Fig. 8. Funnel plot of over-the-counter stimulant use prevalence based on questionnaire, showing evidence of publication bias. In white observed effect sizes, in black imputed effect sizes.



Supplementary Fig. 9. Funnel plot of overall drug use prevalence based on urine samples, showing evidence of publication bias. In white observed effect sizes, in black imputed effect sizes.

