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WORKPLACE DRUG TESTING IN ITALY: NINE YEARS OF EXPERIENCES VIEWED FROM THE OCCUPATIONAL HEALTH PHYSICIAN'S PERSPECTIVE

Doctoral thesis

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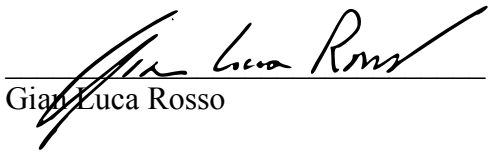


Gian Luca Rosso

Dedication

to my wife
and my kids, Pietro, Maria Luisa and Tommaso

CONTENTS

LIST OF ABBREVIATIONS

WDT.....workplace drug testing

CI.....confidence interval

OHP.....occupational health physician

MDMA.....methamphetamine

SIMLII.....Italian Society of Occupational Medicine and Hygiene

EWDTS.....European Workplace Drug Testing Society

SE.....standard errors

GENERAL INTRODUCTION

In Italy, Workplace Drug Testing (WDT) has been compulsory by law for specific categories of workers since 2008. The law that introduced this testing (Legislative Decree 81/2008) has significantly modified not only the work of the occupational health physician (OHP) but also his/her role. In fact, the OHP who deals with WDT has essentially become a controller. Almost 10 years after the introduction of the Italian WDT law it is possible to make some considerations about the efficacy and weaknesses of this legislation.

Through a literature review, the publications covering the question of WDT in Italy were researched in the following areas: criticalness in the application of the Italian legislation, effectiveness of the tests and of the biological matrix (urine) used for the WDT, results from the execution of the WDT, problems that emerged in the material execution of the WDT.

Since the early months of the date of publication of the law, important criticisms of the regulatory provisions have emerged: alcohol being considered in a very different way from all other psychotropic substances, the non-compulsory nature of screening tests for the self-employed or companies based abroad, different regional applications of the law. More scientific contributions have also questioned the effectiveness of on-site and bench-top screening tests (provided for by Italian law), both in terms of sensitivity and specificity. At the same time, doubts have arisen about the appropriateness of the biological matrix used. Recent systematic reviews have indicated that the positivity of the first-level screening test is around 1.5%, a much lower value than expected, with high false positive rates (among those who tested positive). Moreover, a substantial proportion of workers know well in advance the date of the test or do not have a legal obligation to undergo the screening.

In conclusion, a complete overhaul of the Italian law on workplace drug and alcohol testing is needed. To pursue this target it is important to clearly define, well in advance, what the aim is that we want to reach.

ABSTRACT

In Italy, WDT is compulsory by law for specific categories of workers since 2008, offering the opportunity to compare studies conducted within a single regulatory framework.

Aims: (i) To estimate the overall prevalence of WDT positivity (at screening survey) among Italian workers. (ii) To evaluate the percentage of true and false positives at confirmation analysis.

Methods: Systematic review and meta-analysis of the scientific literature on WDT in Italy from January 2008 to March 2015, according to the MOOSE Guidelines. A random effects model was utilised to calculate pooled prevalence. Potential sources of heterogeneity were explored using sensitivity test and subgroup analysis.

Results: The overall meta-analytical prevalence of positivity at WDT among Italian workers was 1.4% [95% confidence interval (CI) = 1.1–1.7%]. It was significantly lower among workers screened with an on-site test (1%; 95% CI = 0.5–1.5%), compared with a bench-top test (1.7%; 95% CI = 1.3–2.1%). Nine studies provided data on false positives at the screening test, with a combined prevalence estimate - calculated on positive cases - of 30% (95% CI = 16-44%).

Conclusion: In Italy, the number of true positives at first level workplace drug testing is low, while the frequency of false positives is relatively high. A revision of the Italian legislation on the subject seems advisable.

INTRODUCTION

WDT is a widespread worldwide practice [1-5]. However, when considering prevalence rates from WDT programs, to compare apparently similar experiences from heterogeneous backgrounds may lead to erroneous conclusions, due to significant differences in legislation and methodology among different countries and cultures [1]. More appropriate appears the comparison of studies performed within a single regulatory framework, that univocally defines executors, methods, timing, purposes, and categories of workers to be tested.

In Italy, the Legislative Decree n. 81 (09 April 2008) reorganized the legislation on health and safety at work, contemplating the need for WDT, which had been forbidden until then [6-7]. In the same year, the Italian State-Regions Conference published the procedure to be utilized for screening [8]. The purpose is to detect drug-addicted employees, as well as occasional users, with the aim of protecting third parties from the consequences of drug use by workers. WDT is prescribed for specific categories performing 'hazardous jobs', namely transport activities (professional drivers, including train drivers, ship's officers, aircraft pilots, air traffic controllers, fork-lift and excavator operators) and other jobs for which a special qualification or licence is required (e.g., explosives/fireworks sectors, nuclear plant operators). WDT is performed: 1) upon worker's recruitment; 2) on a periodical basis; 3) on a suspicion basis; 4) after an accident at work; 5) at regular intervals before being readmitted to duty (following a previous positive drug test); 6) on the worker's return to hazardous duty after a period of suspension for a previous positive test. The procedure is divided into two steps: a toxicological test on a urine sample that falls under the responsibility of the OHP (first-level survey), and, if there is a confirmed positive result, a second stage, involving both urine and hair analysis, performed at a public drug addiction rehabilitation centre (second-level survey).

The following are important aspects of the first-level survey: (a) workers are notified of WDT 24 hours before sampling; (b) the following substances are tested: cannabinoids, cocaine, opiates, methadone, buprenorphine, amphetamine, methamphetamine, 3,4-methylenedioxy-methamphetamine (MDMA); (c) the screening test can be performed with rapid on-site devices (based on an immunoenzymatic reaction), or with a benchtop immuno-enzymatic instrumentation; (d) if there is a positive result, the worker is precautionally suspended from duty, and a mandatory confirmation test through chromatographic techniques coupled with mass spectrometric systems is performed [9-11]. Confirmed "first level positives" remain "temporarily not fit for the job", and undergo the second level survey to establish whether the drug use is occasional, intermittent or continuative.

Numerous reports on the prevalence of positive WDT in Italy have been published, mainly presenting results of the first level survey carried out by the OHP. The reported prevalence rates markedly differ among the different studies. This could be related to the year-of-data collection (the percentage of positive workers seems to have gradually decreased since the emanation of the law) [12-15] and/or to the screening method utilized (bench-top tests seem more accurate than on-site tests) [16-17]. Additionally, the heterogeneity might be due, at least partly, to intrinsic flaws of the first level procedure (for example the Italian law does not provide sanctions in cases of violation of the 24-hour notification term or if diluted samples are provided), allowing the involved subjects (workers, employers, and OHPs) to influence the outcome of the test [11,18].

In this study, we conducted a systematic review and meta-analysis to estimate the overall prevalence of WDT positivity (at the first level survey) among Italian workers, and to provide a clear and comprehensive presentation of available data through subgroup analyses (investigating the possibility that the prevalence rates vary between subgroups). An additional goal was to verify the weighted average percentage of false positives at first level survey, distinguishing on the basis of the method used.

To our knowledge, this is the first comprehensive analysis of data deriving from a national legislation on WDT. To examine the experience of a single state reduces the risk of bias generated from pooling data collected in various countries with different WDT laws (due, for example, to the purpose and type of control, biological matrix, procedure and method used, investigators, and duties included in the programs).

METHODS

Literature search strategy

The investigation was conducted according to the MOOSE Guidelines for Meta-Analyses and Systematic Reviews of Observational Studies [19]. To identify the articles published on WDT in Italy from January 2008 to March 2015, we carried out an electronic literature search through Scopus, Pubmed MEDLINE and Google scholar, using different combinations of the following keywords: "workplace", "work", "surveillance", "drug", "substance", "Italy", "Italian". Oral communications and posters presented at the annual National Congress of the Italian Society of Occupational Medicine and Industrial Hygiene (SIMLII) were also searched with relevant English and Italian keywords.

Search sensitivity was checked by considering duplicated papers. We manually searched the reference lists of eligible articles and relevant reviews, and traced their citations using the ISI Web of Knowledge portal. If the full text of articles was not accessible, e-mails were sent to authors. In the absence of a response within one month, informative abstracts were used for data extraction. Articles with no informative abstracts were omitted.

Study selection

Published studies in English, Italian, Spanish and French were eligible if they met the following criteria: 1) appropriate design: cross-sectional, case-control, and case-series or cohort; 2) clear information on the number of confirmed positive workers (at first level WDT survey) and sample size. Exclusion criteria were: a) studies solely presenting data on second-level WDT surveillance; b) papers merely reporting the prevalence rate, without any possibility to calculate the sample size; c) studies on police or armed forces (these are particular categories of workers that usually undergo a strict selection in the hiring phase, thus the comparison with other categories of workers could generate a bias); d) updates of previous experiences without clear information on new cases. The names of the authors or journals had no influence on the decision to include or exclude the articles.

Eligibility assessment

Two investigators independently identified the articles, screened their titles and abstracts, and assessed the full texts for eligibility. A critical evaluation was performed using the MOOSE check list form. Disagreement was solved by a third assessor.

Data analysis

The following data were extracted and entered into Microsoft Office Excel 2011: the first author's name and year of publication, year of study, sample size, WDT positive frequency,

and the number of false positives. WDT prevalence was calculated in two different subgroups, identified on the basis of the first level screening test declared by authors: bench top versus on-site. Standard errors (SE) were calculated using the following formula: $SE = \sqrt{(P*(1-P)/N)}$ (P = prevalence, N = sample size). Prevalence data were summarised by screening method and year-of-data collection. A meta-analysis was conducted for variables identically defined across studies. The study-specific estimates were pooled using a random effects meta-analysis model to obtain an overall summary estimate of the prevalence across studies. Heterogeneity was assessed using the χ^2 test and quantified by calculating the I^2. Values of 25%, 50% and 75% for I^2 represent, respectively, low, moderate and high heterogeneity. To study possible publication bias, we evaluated funnel plots. A deficiency in the base of the funnel with asymmetry indicates the presence of possible publication bias from small studies. Publication bias was assessed by Egger's regression asymmetry test. All analyses were implemented on Stata software (version 11.0 STATA Corporation, College Station, TX, USA).

Ethics

The present study was approved by the local ethics committee and was registered on PROSPERO, registration number: CRD42015020327.

RESULTS

Selected studies

The literature search identified 202 publications on PubMed, 21 presentations at the SIMLII national congress, and 15 publicly available papers on Google Scholar. After the removal of duplicate papers, 230 unique articles were identified: 187 were excluded after reading the title or abstract, 43 were assessed for eligibility, 26 of which were excluded after complete reading. One publication [33] was added after a manual search through reference lists, review articles, and publicly available data. Seven authors were contacted by e-mail in order to clarify year-of-data collection and/or method used [13, 20, 25-28, 33]. All of them answered and completed the missing data.

On the whole, 18 studies [12-15, 18, 22-34] were included in the final review and meta-analysis to estimate the overall prevalence of positivity at WDT (Table 1). They were all cross-sectional, for a total of 212,654 participants. Nine studies were included in the meta-analysis to estimate the percentage of false positives emerging at the first level survey [13, 20, 21, 25-27, 30, 32-33], including two papers [20, 21] removed from the primary analysis since their results are present in other articles [14, 22] (Table 1).

Two studies [14, 15] reported data available to the Department for Anti-drug Policies (results of first level testing in 2009 and 2010, respectively), supplied by the Italian State Railways Group, ANMA (National Association of Company Doctors), SIMLII and LAMM s.r.l. (Medical Testing Laboratory, Mestre). Since the provenance of data was heterogeneous, it was not possible to know the prevalence rate according to the screening method used. For example, ANMA reported (in a different publication [21]) that its data were from 18 different OHPs, and that in two thirds of cases an on-site test had been utilised. Thus, the two reports to the Anti-drug Policies Department were excluded from the sub-groups analysis (testing the hypothesis that prevalence does not differ when using an on-site or a bench-top screening test).

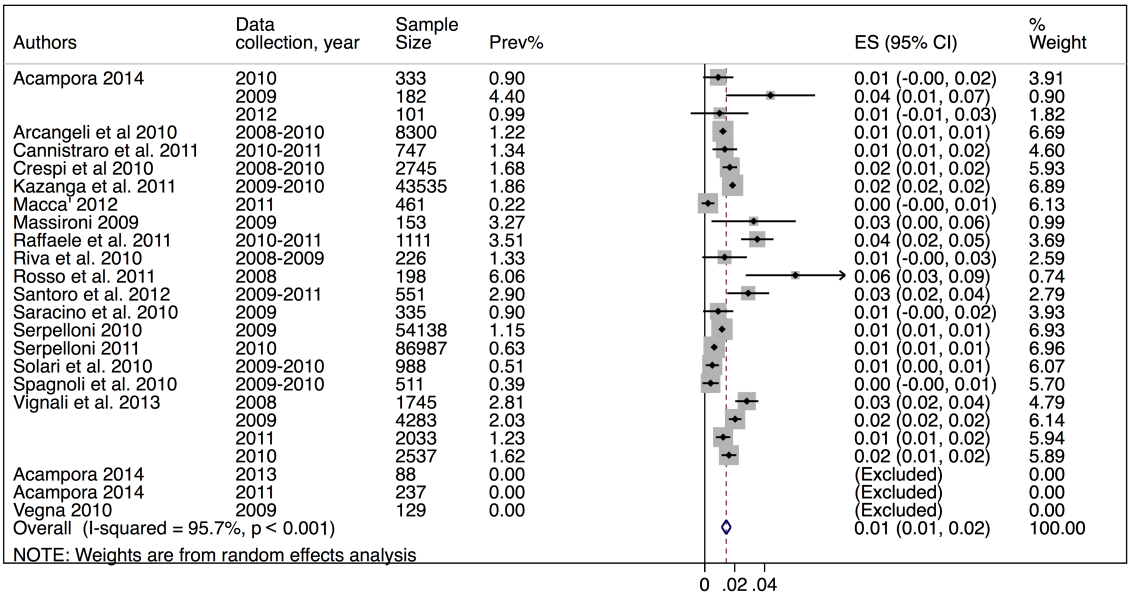
Two studies [12, 13] reported detailed prevalence rates according to the year of sampling and were subdivided accordingly to examine the possible effect of the data collection year on the percentage of WDT positivity.

WDT positivity prevalence

The point prevalence of positivity at WDT (at the first level survey) among Italian workers within the 18 selected study populations ranged between 0 and 6.1%, with an overall meta-

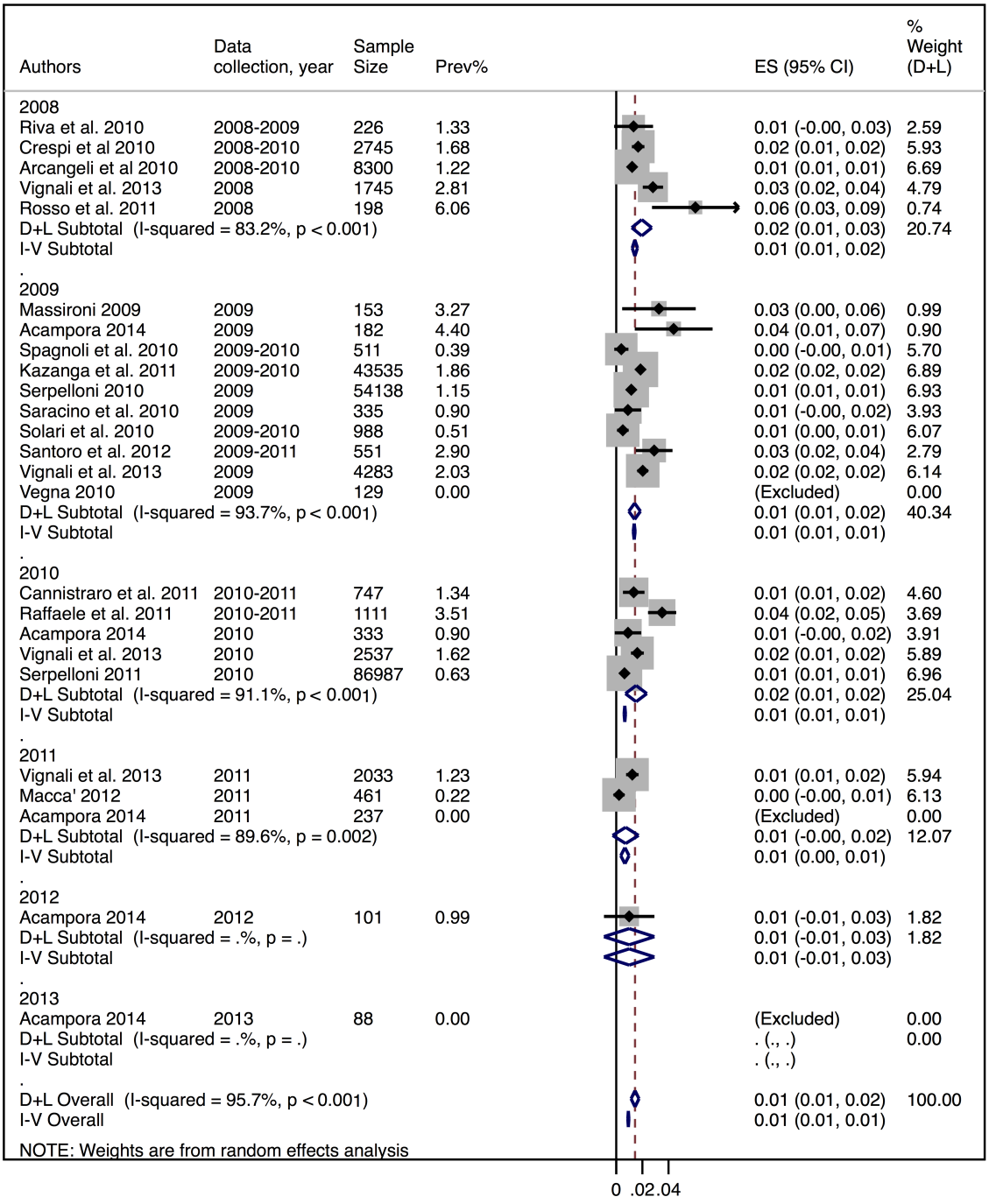
analytical prevalence of 1.4% (95% CI = 1.1–1.7%), and evidence of high-level heterogeneity between estimates (I^2=95.7%, P<0.001) (Figure 1).

FIGURE 1. Forest plot of studies on prevalence of WDT positivity among Italian workers.



A slightly decreasing trend was revealed when separating according to year-of-data collection, with an overall meta-analytical prevalence of 2% (95% CI = 1.2–2.7%) in 2008, 1.4% (95% CI = 1–1.9%) in 2009, 1.5% (95% CI = 0.7–2.3%) in 2010, 0.7% (95% CI = -0.3–1.7%) in 2011, and 1% (95% CI = -0.9–2.9%) in 2012 (Figure 2).

FIGURE 2. Forest plot of studies on prevalence of WDT positivity among Italian workers, grouped by year-of-data collection.

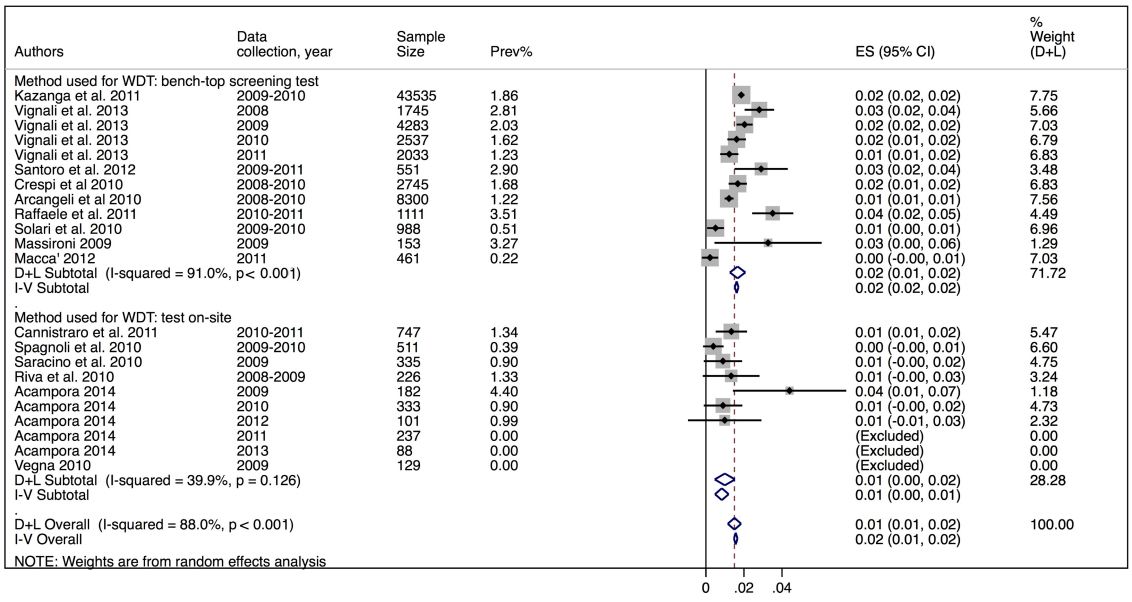


The funnel plot appeared asymmetric, with some smaller studies tending to have larger prevalence rates. Thus, we used the metabias command to perform a test of small-study effects employing the Egger test. The test provided evidence for the presence of small-study effects (p = 0.046). In order to reduce bias, we removed one study [30] reporting the highest prevalence rate (6.1%) from sub-group analysis due to our awareness (Rosso is the main author of both the excluded study and the present meta-analysis) that such a result was affected by two factors: the relatively small sample size (n = 198) and the time of data collection (July - December 2008), immediately after the enactment of the law, when several

workers were taken by surprise by the new WDT program (in 2009, in the same context, the prevalence rate dropped down significantly: unpublished personal observation). Removing the study by Rosso et al., the Egger test provided weak evidence for the presence of small-study effects (p = 0.064), and heterogeneity significantly decreased in the sub-group of on-site screening test.

Analysis stratified by method used showed a higher prevalence of positivity at WDT among workers screened with a bench-top test (1.7%; n = 1225/68442; 95% CI = 1.3–2.1%) compared with those screened with an on-site test (1%; n = 30/2889; 95% CI = 0.5–1.5%) (Figure 3). The difference was statistically significant (Pearson χ^2 test p = 0.0026).

FIGURE 3. Forest plot of studies on prevalence of WDT positivity among Italian workers, grouped by method used.



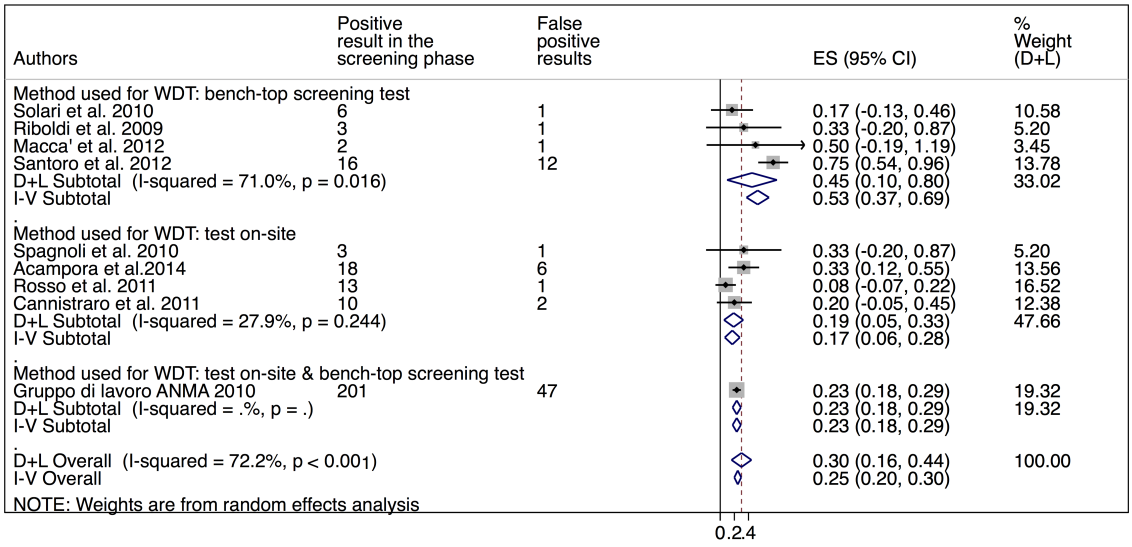
In 3 studies, the following factors were associated with WDT positivity: younger age [18, 22], gender (F/M gender ratio was significantly lower in positives) [18], time-of-day of sample collection (higher rates occurred from 6-9 am and 2-5 pm) [18], declared use of any drug during the week preceding sampling [18], type of duty (more frequent cocaine-positives among professional road drivers than among fork-lift users; more frequent cannabis-positives among fork-lift users than among professional road drivers) [12], the presence of another positive sample in the same firm [22], and >5% diluted urine samples (urine creatinine ≤20 mg/dL) in the same firm [22].

Cannabinoids were the most frequently detected drugs, followed by cocaine. In the studies with the largest sample size [13, 14, 18, 21-23, 25], positivity to cannabinoids varied in a range between 50 and 65% of all positive tests (Table 1).

WDT false positivity prevalence

Nine studies provided data on false positives at the screening test [13, 20, 21, 25-27, 30, 32-33], with a combined prevalence estimate of 30% (95% CI = 16-44%) and a moderate heterogeneity (I^2=72.2%, P<0.001) (Figure 4).

FIGURE 4. Forest plot of studies reporting false positive prevalence emerging from Italian WDT screening.



Analysis stratified by method used showed a higher percentage of false positives among workers screened with a bench-top test (45%; 95% CI = 10-80%; I^2=71%, P=0.016) compared with those screened with an on-site test (19%; 95% CI = 5-33%; I^2=27.9%, P=0.244) (Figure 4).

DISCUSSION

The most striking result of our investigation is the low percentage of confirmed positive Italian workers at first level WDT: the calculated overall meta-analytical prevalence of 1.4% is much lower than the positivity rate that might be predicted (4–10%) on the basis of epidemiological data [35]. The percentage found in the present study is inconspicuous also when compared with similar experiences conducted abroad [1, 36], where WDT programs based on unannounced sampling found positivity rates between 2 and 30% [4, 37].

To explain such discrepancies, it has been hypothesized that workers performing hazardous duties (e.g., professional drivers) tend to refrain from drugs-of-abuse more than other categories with lower responsibility [18]. Though plausible, this explanation is not sufficient to justify the low meta-analytical prevalence reported here, that probably ensues from pitfalls in the Italian law, already pointed out by several Authors [11, 12, 16, 18]. Critical issues are: 1) WDT is usually performed without surprise effect (in a recent study, 50% of the subjects declared that they knew well in advance the day of the test [11]). Moreover, Italian companies are often small, and a worker resulting positive may have an immediate economical negative effect (thus, it may be in the employer's interests to invalidate the WDT surprise effect) [11, 18]. 2) No specific actions are contemplated if: a) the OHP does not respect the 24-hour notification term (due to negligence or accidental mistake); or b) diluted samples are provided and, though a second urine collection should be performed in case of low creatinine level (< 20 mg/dL), this procedure is seldom followed. 3) Drivers who are owners of the company they work for are not required to undergo WDT nor to nominate an OHP [11, 38]. 4) There is no control system for effectiveness of the WDT program, in terms of reduction of accidents and/or morbidity. 5) While on-site and bench-top instrumentations are adequate in terms of analytical sensitivity [16, 17, 35-41], urine analysis lacks to detect occasional drugs consumers, except for cannabinoids, due to the relatively low window of detection. Alkaloids such as opiates and cocaine, as well as amphetamine derivatives, are usually eliminated through urine within one to two days.

In the present study, the meta-analytical prevalence varied when considering the screening test used for the first level survey: bench-top appear more sensitive than on-site screening tests, with an increase of the prevalence rate of 70% (unfortunately we have no information about cut-offs of the various on-site and bench-top tests used). On the other hand, the on-site test seems to generate fewer false positives, in contrast with the majority of the studies on the subject [39, 40]. Indeed, bench-top instruments are more sophisticated and usually provide a

semi-quantitative result through a calibration curve, while on-site tests are based on the evaluation of a simple coloured line, and may be misleading, especially when the analytes concentrations are close to the cut-offs. A possible explanation for our finding (better specificity of on-site testing) might be that the OHP who utilises an on-site test, sometimes immediately re-tests a worker who had tested positive, especially when the latter categorically denies any drug use.

Regardless of the method used, the overall high number (30%) of false positives emerging in this study is impressive. Probably, this is not due to the specificity of the screening tests and instruments. In fact, though some investigators observed different specificities of the kits, in particular among those for on-site testing [17], the percentage of false positives seldom exceeds 3% [39]. We believe that the found high percentage of positives at first level survey not confirmed at second-level analysis is due to: 1) calculation of specificity on positive cases, and not on the entire population; 2) urine samples positive for opiates from subjects under therapy with medications containing codeine, morphine or similar substances.

Anyhow, the above results should lead Italian legislators to carefully re-consider whether suspension from duty after an initially positive result is appropriate (confirmatory testing usually requires several days). We think that the OHP should have the freedom to evaluate if the worker is a significant job safety risk.

We found a slight, though significant, reduction in the prevalence of positive WDT with time, when separating for year-of-data collection. This does not necessarily mean that there were fewer drug consumers among the workers tested. In other words, it would be hurried to consider these data as a signal of safety improvement (due to a deterrent effect of the law), especially considering that no single study, of the 43 assessed for eligibility in the meta-analysis, has explored the real impact of the Italian WDT legislation on safety. This is in agreement with the conclusions of a recent systematic review, showing that urine tests have low sensitivity in detecting risky employees, and no appreciable impact on job accident rates [2].

The finding that cannabinoids and cocaine are the most frequently detected drugs in Italian workers is consistent with a recent systematic review on psychoactive substance use by truck drivers worldwide, in which marijuana, cocaine and amphetamines were the most common substances identified in different biological samples (the high prevalence of cannabis positivity is partly due to the long persistence of its metabolites in urine) [1]. This is a source of concern, since long-term cannabis use may induce cognitive deficits, which impair work performance and increase the risk of accidents. However, several studies have failed to find

an elevated accident risk among those testing positive for cannabis at urinalysis [2], raising doubts (once again) about the preventive usefulness of the WDT legislation.

Only 3 of the 18 Italian studies included in this review investigated variables possibly associated with WDT positivity, finding associations with young age, male gender, declared drug use, road driving, and the presence of positive or diluted samples in the same company [12, 18, 22]. Studies performed elsewhere have led to the identification of several factors associated with psychoactive substance consumption by truck drivers: higher income, longer trips, alcohol consumption, driving in the night shift, travelling interstate routes, long or short sleep, fewer hours of rest, limited driver experience, connection with small and medium sized companies, income below levels determined by labour agreements, productivity-based earnings and prior involvement in accidents [1]. The role of these risk factors has not been thoroughly investigated in Italy, where, additionally, published results of second level surveys, and their consequences in terms of prevention and rehabilitation, are still lacking seven years after the WDT law came into force.

The detected high-level heterogeneity among studies leads to some considerations. Heterogeneity in meta-analysis refers to the variation in study outcomes between studies. In our case, the outcome considered was always the same, and heterogeneity remained high even after analysing data stratified by method used. Interestingly, heterogeneity was low in the on-site screening test subgroup, and high in the bench-top subgroup. The use of an on-site screening test assumes that a single operator, the OHP, collects and analyses urine samples. On the contrary, when a bench-top screening test is used, collection and analyses are usually made in different places and times. This difference could explain, at least partly, the heterogeneity detected in our study.

CONCLUSIONS

The available Italian data on WDT, though limited, provide important information that should be adequately considered in the future. First of all, the number of true positives at first level survey is very low, clearly under-representing the dimension of the problem, while the frequency of false positives is extremely high. Secondly, there is a substantial difference between the results of on-site versus bench-top screening tests. Thirdly, cannabis prevails as the main drug detected (though this may be partly due to the long persistence of its metabolites in urine after consumption).

We believe that key points for a successful WDT policy are as follows: (i) the scheduling of the test should be kept unknown to the worker; (ii) the organizer and the executor should be adequately trained, and preferably independent of the company where the employee works; (iii) the analytical methodology and the biological matrix should be adequately chosen; (iv) a monitoring system should be established to verify the preventive effectiveness of the implemented program.

NEW FINDINGS OF THE THESIS

- The calculated overall meta-analytical prevalence of 1.4% is much lower than the positivity rate that might be predicted (4–10%) on the basis of epidemiological data. The number of true positives at first level survey is very low, clearly under-representing the dimension of the problem
- The percentage found in the present study is inconspicuous also when compared with similar experiences conducted abroad (where WDT programs based on unannounced sampling found positivity rates between 2 and 30%)
- There is a substantial difference between the results of on-site versus bench-top screening tests
- Cannabis prevails as the main drug detected

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TABLE 1. Characteristics of selected Italian studies reporting the positive rate in the screening test performed by the occupational health physician.

Authors, publication year [reference number]	Period-of-data collection	Sample size (n)	True positives (first-level survey) (%)	False positives (n)	Screening test used	Drugs of abuse detected (% of positive tests, when available)
Kazanga et al., 2011 [18]	March 2009 – February 2010	43535	810 (1.9)	-	bench-top	cannabinoids (65.7) cocaine (20.4) methadone (4) opiates (6.4) buprenorphine (3.3)
Serpelloni, 2010 [14]	2009	54138	624 (1.2)	-	bench-top & on site	cannabinoids (64) cocaine (13) opiates (9) methadone (6) codeine (4) ecstasy/MDMA (1) amphetamines (1)
Serpelloni, 2010 [15]	2010	86987	551 (0.63)	-	bench-top & on site	cannabinoids cocaine
Crespi et al., 2010 [22]	September 2008 – April 2010	2745	46 (1.6)	-	bench-top	cannabinoids (50) cocaine (24)
Arcangeli et al., 2010 [23]	November 2008 – July 2010	8300	101 (1.2)	-	bench-top	cannabinoids (60) opiates (18.1) cocaine (12.7) methadone (9) ecstasy (3.6)
Raffaele et al., 2011 [24]	2010 – 2011	1111	39 (3.51)	-	bench-top	cannabinoids cocaine
Solari et al., 2010 [25]	September 2009 – June 2010	988	5 (0.5)	1	bench-top	cocaine (60) cannabinoids (40)
Cannistraro et al., 2011 [26]	2010 - 2011	747	10 (1.3)	2	on site	cannabinoids cocaine methadone
Spagnoli et al., 2010 [27]	2009 – 2010	511	2 (0.4)	1	on site	cannabinoids cocaine
Saracino et al., 2010 [28]	2009	335	3 (0.9)	-	on site	methadone cannabinoids
Riva et al., 2010 [29]	March 2008 – March 2009	226	3 (1.33)	-	on site	cannabinoids cocaine methadone
Rosso et al., 2011 [30]	July 2008 – December	198	12 (6.1)	1	on site	cannabinoids methadone

	2008					cocaine
Massironi, 2009 [31]	2009	148	5 (3.4)	-	bench-top	cannabinoids (40) cocaine (40) buprenorphine (20)
Santoro et al., 2012 [32]	September 2009 – February 2011	551	4 (0.7)	12	bench-top	cocaine (75) cannabinoids (50)
Vignali et al., 2013 [12]	2008	1745	49 (2.8)	-	bench-top	cannabinoids cocaine methadone opiates buprenorphine amphetamines
	2009	4283	87 (2.0)			
	2010	2537	41 (1.6)			
	2011	2033	25 (1.2)			
Acampora et al., 2014 [13]	2009	182	8 (4.4)	6	on-site	cannabinoids (50) cocaine (41.7) cannabinoids & cocaine (8.3)
	2010	333	3 (0.9)			
	2011	237	0 (0)			
	2012	101	1 (1)			
	2013	88	0 (0)			
Maccà et al., 2012 [33]	2011	461	1 (0.22)	1	bench-top	cannabinoids
Vegna & Vegna, 2010 [34]	January 2009 – December 2009	129	0	-	on site	
Riboldi, 2009* [20]	September 2008 – November 2008	481	2 (0.42)	1	bench-top	cocaine
Gruppo di lavoro ANMA, 2010* [21]	-	16498	154 (0.93)	47	bench-top & on site	cannabinoids (68.4) cocaine (17.7) opiates (8.3) methadone (2.5) amphetamines (1.9) ecstasy/MDMA (1.3)
* studies considered only for false-positive analysis excluded from prevalence analysis because their data are already included in other studies.						

Appendix – Search strategy

PubMed search strategy

#1 workplace[All Fields] AND drug[All Fields] AND Ital*[All Fields].

#2 workplace[All Fields] AND substanc*[All Fields] AND Ital*[All Fields] NOT #1.

surveillance AND work AND ital* AND drug NOT#1 NOT#2

Filters: Publication date from 2008/01/01 to 2015/03/31.

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LIST OF PUBLICATIONS RELATED TO THIS THESIS

1. Rosso GL, Montomoli C, Morini L, Candura SM. Seven years of workplace drug testing in Italy: a systematic review and meta-analysis. Drug Test Anal. 2017 Mar 17. doi: 10.1002/dta.2189. [Epub ahead of print] Review. PubMed PMID: 28304140.
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DATA OF THE PRESENT THESIS WAS PRESENTED TO THE FOLLOWING CONGRESSES

1. SIMLII Congress 2016 (in Rome)
2. EWDTS Congress 2017 (in Turin)