Ecstasy Literature Review

## What is ecstasy?

MDMA (3,4-Methylenedioxymethamphetamine), commonly referred to as "Ecstasy," "E," "X," or "XTC" is a psychoactive, sympathomimetic drug derived from amphetamines. Its chemical structure strongly resembles that of amphetamine and mescaline (Karch 2011). It is often taken orally in tablet form, typically containing 60 to 160 milligrams of MDMA (Bialer 2002; Schifano 2004). Users describe euphoric, stimulant, and minor hallucinogenic effects, resulting in mood enhancement. Terms such as "enatogenesis" – contentment with the world – and "empathogenesis" – an emotional rapport with others – are used to describe MDMA's effects (Bialer 2002). Ultimately, the subjective user experience is resultant from the pharmacological content of the ecstasy tablet (Brunt et al. 2011).

Purportedly synthesized as an appetite suppressor in 1914 (Adlaf 1997), recent literature suggests that MDMA was in fact created as a "precursor compound" for medical purposes in 1912 (Karch 2011). Various experiments by Merck, the patenting company, and the United States Army were conducted sporadically until the early 1960s. Results of these studies are either unknown or incomplete as no legitimate biological research was conducted (Karch 2011). From there, university, industry, and psychiatric parties took interest. Chemist Alexander Shulgin and psychologist Leo Zeff, enthused about the therapeutic potential of MDMA, began promoting the drug to other mental health professionals throughout the 1970s. Both college students and U.S. Drug Enforcement Agency personnel took notice. Despite its purported benefits, the potential for neurological damage exhorted Congress (Karch 2011). Under emergency powers, the DEA officially declared MDMA a Schedule I drug in 1985, just as recreational demand erupted (Kahn 2012; Karch 2011). DEA reasoning addressed reports of severe toxicity and high potential for abuse (Dowling 1987). Derivatives of MDMA began appearing in 1986 with the intent of bypassing legal regulations and increasing potency (Christophersen 2000). Europe and its growing "rave" scene soon adopted the drug in the late 1980s, beginning on the Spanish island Ibiza (Karch 2011). Today, it has become one of the world's most popular illicit drugs, particularly among young people (UNODC 2013).

"Molly", short for "molecular", is the supposed pure form of MDMA, free of adulterants. While it is "commonly perceived as a safer form of MDMA," Kahn (2012) suggests that, to the contrary, "Molly" may represent a "particularly dangerous form of MDMA." The recent proliferation of "Molly" poses a mounting public health risk as perceptions of increased purity may hinder harm minimization practices. MDMA's desirable subjective effects surpass those of all other psychoactive substances, driving demand (Brunt et al. 2011).

A group of chemicals known as MDMA-like substance (MLS) include MDMA and its structural analogues. 3,4-methylene-dioxyamphetamine (MDA), 3,4-methylene-

dioxyethylamphetamine (MDEA) and N-methyl-a-(1,3-benzodixol-5-yl)-2-butamine (MBDB) belong to a drug group termed phenthylamines, and more specifically "entactogens" (meaning "touching within") (Duterte et al. 2009; Karch 2011). MDMA-like substances generally produce desirable effects among users, with the exception of MDA alone (Brunt et al. 2011). MDMA analogues such as 5,6-Methylenedioxy-2-aminondane (MDAI)) are "legal highs" that reportedly lack the neurotoxicity of MDMA; however, proper toxicological evaluation is yet to be conducted (Gibbons 2012; Kelleher et al. 2011).

Ecstasy pills are often branded – stamped with an insignia in order to differentiate between batches. This practice likely began in European clandestine laboratories (Karch 2011). Despite aesthetic similarities, pills among the same brand name have been found to vary in amounts of active ingredients (Sherlock et al. 1999; Cole et al. 2002). When a particular brand becomes popular, producers take notice, copying the exterior tablet with their own interior ingredients (Schroers 2002). In Bay Area-based interviews of ecstasy sellers, a majority of respondents "viewed Ecstasy brands as identifiers that referenced quality as a marketing strategy" (Duterte et al. 2009). Reliance on brand names was limited as batches have the potential differ in content and could potentially lead back to the supplier. Investigating tableting characteristics, Milliet and colleagues (2009) found that one set of organic impurities determined one set of physical characteristics in 58% of sampled ecstasy tablets while two sets of organic impurities determined one set of physical appearance in 42% of the sample. Therefore, it is difficult to issue warnings to drug users based on tablet appearance as individual pill content may vary. In terms of appearance, Tanner-Smith (2006) suggests that "tablet height and width [are] inversely related to tablet purity."

## Ecstasy Pill Content

Ecstasy pill content deserves in depth analyses because what is sold as Ecstasy often contains more than just MDMA, if MDMA is present at all (Duterte et al. 2009; Heifets et al. 2000; Johnston et al. 2006). The issue is significant enough to warrant use of terms such as Ecstasy and Related Drugs (ERD) that more accurately address drug variance in tablets sold as Ecstasy (Miller et al. 2010). Adulterants vary by intentionality. Those added deliberately are meant to increase bulk, mimic or complement the desired drug, or facilitate transportation. Unintentional adulterants result from poor manufacturing, production, or supply techniques (Cole et al. 2010; Cole et al. 2011). Familiar substances such as caffeine, procaine, paracetamol, and sugars are most common due to their availability (Cole et al. 2011). On the other hand, substances such as dextromethorphan, amphetamines, and an array of others, attempt to stimulate the user at a low production cost (Cole et al. 2010). Adverse public health effects are a major concern. In the 2013 World Drug Report, the United Nations Office on Drugs and Crime stated that a "large proportion of seized drugs marketed on the street as 'ecstasy' continue to contain substances other than MDMA." Thus users may be unaware of the substances – both licit and illicit – they

are ingesting (Kalasinsky, Hugel & Kish 2004). Exact tablet content is not easily discernable without advanced equipment (Hayner 2002).

Laboratory testing services tailored towards MDMA began in 1972 with Analysis Anonymous. Run by PharmChem Laboratories, Inc. in Menlo Park, California, the operation provided purity information to the general public, spanning over 10 years (Renfroe 1986). Today, EcstasyData.org, operated by Erowid Center, and the Drug Information and Monitoring System (DIMS) in the Netherlands perform tablet analyses and report the results online. Purity information is made public, compliant with national drug laws. The data possess inherent limitations, such as self-selection bias in the case of user submission and sampling bias in the case of police seizures. Tablets taken from the latter often yield a more homogeneous sample than those taken from numerous sources, such as individual users (Cole et al. 2002). Thus tablet purity reported by sources with differing sampling techniques, even in the same year and location, often appear at odds. Nevertheless, laboratory analyses reveal purity trends in the larger population of ecstasy tablets. Examination of trends reveals fluctuations in ecstasy purity over time, beginning with recreational proliferation in the 1970s.

From 1973 to 1983, Analysis Anonymous reported general purity in analyzed Ecstasy tablets. Besides MDMA, MDA appeared most frequency, both by itself and in combination with MDMA. Other reported substances were found to be chemical precursors or synthetic by-products (Renfroe 1986). Through surveys and empirical reports, Parrott (2004) found few impurities in ecstasy tablets during the 1980s and early 1990s. By the mid-1990s, an estimated 4-20% of pills contained "non-amphetamine drugs." From the late 1990s to early 2000s, tablets containing MDMA increased to 80-90%, then to 90-100% respectively (Parrott 2004). Analyzing EcstasyData.org data from the United States, Tanner-Smith (2006) found that between 1999 and 2005 39% of tablets contained MDMA only, 46% contained solely other substances, and 15% were mixtures. Baggott (2000) found that between February 1999 and March 2000, 63% of tablets in the US contained MDMA or an MLS, 29% contained no MDMA, and 8% were unidentifiable (n=107). In the Netherlands, DIMS tested tablets between 1993 and 1997 (n=8229), reporting an average of 50.98% contained MDMA only. An average of 13.26% contained substances other than MDMA. Disparities between years 1996 and 1997 should be noted, where 5.9% of the sample contained exclusively other substances in the former and 18.2% in the latter (Spruit 2001). Among tablets analyzed in France between July 1999 and June 2004, 82% contained MDMA (Giraudon & Bellow 2007). From 1999 to 2008, 80% to more than 95% of ecstasy tablets analyzed in the Netherlands contained MDMA-like substances (e.g. MDMA, MDA, MDEA, and MBDB) (Parrott 2004). In 2007, ecstasy tablets in 11 participating European nations contained an average MDMA content between 19 and 75 mg (EMCDDA 2009).

In 2009, the Netherlands reported a sharp decline in ecstasy tablets containing MDMA by over 50%. Other EU countries experienced similar declines, most likely due to disrupted supply chains and crackdowns on MDMA precursors, such as

piperonylmethlketone (PMK) (EMCDDA 2009; Brunt et al. 2012; UNODC 2013). The data suggests that MDMA-like substances supplemented the scarcity of MDMA. DIMS reported significantly low MDMA levels in 2008 in 2009, yet 70% of ecstasy pills contained solely MDMA-like substances (UNODC 2013). Severe declines occurred in the first six months of 2009, with only 40% of analyzed tablets containing MLS (Brunt et al. 2010). In 2010 and 2011, the proportion rebounded to 82% and 85% MLS, respectively (UNODC 2013).

Despite the complexity of the global ecstasy market, tablet analyses have revealed various consistencies. For example, certain adulterant substances and tablet location appear to be correlated. Tablets from Luxembourg, Spain, and Turkey commonly contain new amphetamines uncontrolled by international drug law. Nine other European countries (west, north, and eastern inclusive) identified mCPP in at least 20% of analyzed pills. New Zealand reports 4-methylethcathinone (4-MEC) as the most common substance in ecstasy tablets (UNODC 2013). East and South-East Asia report widespread ketamine adulteration. Variation is likely tied to regional drug availability and, consequently, production costs. The high demand for ecstasy incentivizes producers to package readily available substances in tablet form. Global drug operations, however, complicate the assessment of manufacturing's role in tablet purity. In Hong Kong, "cross contamination" among smuggled drugs rather than the manufacturing process is credited with high levels of detected ketamine adulteration (Cheng et al. 2006). As is the case in East Asia, the larger regional drug market manifests itself in ecstasy pill content.

Whether intentional due to manufacturing or collateral due to illicit supply chains, the United Nations Office of Drugs and Crime in 2013 established that for several years, ketamine has been sold or substituted for ecstasy in East Asia (UNODC 2013). Analyzing 89 tablet seizures between 2002 and early 2004, Cheng et al. (2006) detected the substance in 80% of the sample. While ketamine abuse remains prevalent in the region, ecstasy pill content may continue to reflect this. The nature of adulteration in East Asia speaks to ecstasy markets' susceptibility to larger, preexisting drug operations. The connection likely varies in extremity relative to location. Despite regional differences, global ecstasy analyses reveal a plethora of substances, both new and old.

A variety of synthetic drugs have substituted MDMA in tablets sold as ecstasy. In an attempt to replicate MDMA's psychoactive properties while sidestepping global drug laws, some "designer drugs" are produced in tablet form and sold as ecstasy. Substances such as methylone and meta-chlorophenylpiperazine (mCPP) are common, providing "serotonergic substitutes for ecstasy" (Bossong et al. 2005; Brunt et al. 2011). While little is known about resultant health effects, user response varies by substance. Mephedrone (4-methylmethcathinone), for example, provides enjoyable subjective effects in users. Upon rising prevalence in 2009 (Gibbons 2012), 11.5% of ecstasy tablets in the Netherlands contained mephedrone exclusively (Brunt et al. 2011). The drug continued to be sold as ecstasy for a period of two years. Subsequent federal action in Australia caused sharp declines in

mephedrone use among ecstasy and amphetamine users (16% in 2010 to 5% in 2012). Classification as a controlled substance by the UK and other nations caused mephedrone's presence in tablets sold as ecstasy to decline from 1% in 2010 to 0.3% in 2011 (UNODC 2013). The story of mephedrone is indicative of the larger struggle between drug manufacturers attempting to bypass legislation and government regulation. Ultimately, as nations take action on the legality of both designer drugs and precursors to MDMA synthesis, synthetic adulterants are likely to vary by year and country.

By 2013, Piperazines such as 1-benzylpiperazine (BZP) and 1-(3-chlorophenyl)piperazine (mCPP), notable for their "central nervous system stimulant properties," had emerged in markets in Argentina, Brazil, Chile, Costa Rica, and Mexico, although on a limited basis (UNODC 2013). Combinations such as BZP and 3-trifluoromethylphenylpiperazine (TFMPP) attempt to mimic MDMA's effects (Christie et al. 2011). Appearing in the Netherlands in 2004, mCPP prevalence rose through 2007 (Brunt et al. 2010). mCPP was reported as a present substance in 5% of tested ecstasy tablets in 2010 and 4% in 2011 (UNODC 2013). As opposed to mephedrone, mCPP's subjective effects are described as predominantly negative (Brunt et al. 2010; Brunt et al. 2011). While proportionally limited in terms of the global ecstasy supply, mephedrone and piperazines exemplify the risk synthetic adulterants pose, independent from user experience. There is little research addressing chemistry, pharmacology, or toxicology of designer drugs and related "legal highs", making short and long-term health effects uncertain (Gibbons 2012). The acute harms of ecstasy, in relation to purity especially, are a topic of public health concern.

**Related Acute Harms, Including Hospitalization**

Addressing drug adulteration on the whole, Cole and company (2010) report that adverse health effects or death result most commonly from poisoning, inferior manufacturing practices, inadequate storing or packaging, or lethal substances sold as the desired drug. Ecstasy is especially susceptible to the latter. At least two case reports attribute tablets adulterated with paramethoxymethamphetamine (PMMA) and/or paramethoxyamphetamine (PMA) to user mortality (Cole et al. 2010; Hayner 2002). In the UK, 31 ecstasy-related deaths were reported in 1994, 78 in 2002, and 48 in 2003. In total 394 deaths were reported, 165 of which ecstasy was the sole drug mentioned (Schifano et al. 2005). Furthermore, deaths due to MDMA appear to be increasing (Kaye, Darke & Duflou 2009).

While the "incidence of serious acute adverse events related to ecstasy is low," the potential and unpredictability of physical and psychological harm, as well as mortality, cannot be overlooked (Gowing et al. 2002). Common physical side effects include jaw clenching, bruxism, blurred vision, palpitations, headache, nausea, and increased body temperature (Kaye, Darke & Duflou 2009). Psychological side effects include anxiety, depression, and paranoia (Kaye, Darke & Duflou 2009). Reported

toxic effects of MDMA include: asystole, arrhythmias, delirium, tachycardia, tachypnea, profuse sweating, hyperthermia, hypertension, metabolic acidosis, acute renal failure, cardiovascular collapse, disseminated intravascular coagulation, hepatic failure, hyponatremia, cerebral infarct or hemorrhage, coma, and death (Bialer 2002; Schifano 2004). Users are warned of cognitive side effects, disrupted sleep patterns, heightened impulsivity, and depression (Hayner 2002). Public perception of harms may hinder necessary preventative measures.

Recreationally, MDMA is often perceived as safer than other stimulants such as methamphetamine and cocaine (Kahn 2012). Morbidity reports support this notion, as mortality and hospitalization due to MDMA rank lower than cocaine, methamphetamine, and opioids, particularly relative to user prevalence (McKenna 2002; Kaye, Darke & Duflou 2009; Morefield et al. 2011). Despite this relativity, Kahn (2012:260) suggests that even the pure form of the drug may lead to "potentially life threatening intracranial hemorrhage even in the absence of pre-existing vascular malformations." Additional substances in tablets sold as Ecstasy may combine with MDMA to increase toxicity and augment negative health effects (Baggott et al. 2000; Kalasinsky, Hugel & Kish 2004; Kaye, Darke & Duflou 2009). Given Ecstasy users' high rate of polydrug use (Indig et al. 2010; Johnson et al. 2006; Kaye, Darke & Duflou 2009; Morefield et al. 2011; Schifano 2004) in addition to widespread adulteration, it is difficult to attribute exact causality of adverse health effects (Karch 2011; Kelleher et al. 2011).

Similar symptoms among substances sold as Ecstasy, as is the case with MDMA and dextromethorphan (DXM), complicate diagnosis (Mendelson 2001). As MDMA detection in urine is not guaranteed, a negative urine screen cannot rule out MDMA toxicity. Medical personnel must be aware of other substances while continuing to suspect MDMA (Boyer et al. 2001). Hospitalizations due to Ecstasy are not uncommon, as evident by the current body of literature.

Due to medical record constraints, small amounts of literature compare Ecstasy toxicology to mortality. Of 82 MDMA-related deaths in Australia, Kaye, Darke & Duflou (2009) found that 91% were due to drug toxicity. 25% were attributed to MDMA alone while 66% cited MDMA in combination with other drugs. 87% of cases involved other drugs.Over a 7-month period in Israel, Halpern and colleagues (2010) discovered 52 ecstasy-related emergency department admissions at 5 geographically representative locations. 15 admittances (29%) required hospitalization, six (11%) of which were taken into intensive care. Symptoms ranged from restlessness and agitation to brain edema and coma. Subjects consumed between 0.5 and 15 tablets. Cases were significantly higher in August, suggesting seasonality among users. Relative to nationwide ecstasy use, the rate of morbidity was, at minimum, 0.23. Banta-Green el al. (2005:1304) reported that between 1995 and 2002 Seattle-area emergency department mentions of MDMA "increased from 10 to 86 mentions, with a peak in 2000 of 128 mentions." In 2002, 70% of these cases involved other drugs, so the causal role of MDMA in acute hospitalizations is unclear. Morbidity is certainly present, however limited due to

toxicological questions (i.e. unknown ingested drugs) (Halpern et al. 2011; Kaye, Darke & Duflou 2009).

In Sydney, Australia, ecstasy was reported in 642 (12%) of emergency department admissions between 2004 and 2006 (n=263 937). Among six individual substance categories (amphetamines, heroin, cannabis, cocaine, alcohol, and Ecstasy), Ecstasy-related admissions displayed various anomalies. Nearly half of the sample (46%) was female. The percentage of male ED admittances was significantly greater in all other categories. Furthermore, Ecstasy-related admits presented the youngest average age (25.7 years). 78% were under the age of 30. ED admittances for Ecstasy were most likely to be after hours (48%) and during the weekend (58%), a trend found in other studies (Halpern 2010). Ecstasy patients reported the highest rate of polydrug use (68%) suggesting a wider range of medical possibilities. By diagnostic code, Ecstasy was the least commonly detected drug in ED visits (2%). Ultimately, 61% of patients received an "anxiety-related diagnosis" (Indig et al. 2009). The neurotoxicity of MDMA has put into question its effect on mental health.

There is confounding evidence on the relationship between MDMA and neurochemical changes, particularly serotonin function. While animal experiments reveal long-term change, human evidence remains unclear and at times conflicting. In any case, there is compelling evidence that MDMA use causes some form of serotonergic disruption (McCann, Ridenour & Shaham 1994; de Win et al. 2008). Upon reviewing 36 psychiatric case reports, Bango et al. (1998:263) concluded that the main contributor to psychiatric symptoms was not ecstasy use, but rather "individual vulnerability" and "lasting of consumption." Indig et al. (2009) reported that one in eight ecstasy-related ED patients (n=642) had a mental health-related diagnostic. Halpern et al. (2011) found 73% of subjects (n=52) to have "some behavioral or psychiatric disturbances." Causality proves difficult to establish. As tablets vary in milligram content, the neurotoxicity of a single dose is indiscernible (Cole et al. 2002). Proper analyses require both quantity of tablets consumed and their pharmacological content (Morefield et al. 2011). New evidence suggests a degree of cardio-toxicity (Karch 2011; Kaye, Darke & Duflou 2009). MDMA use, especially in tandem with other substances, likely increases chances of an acute cardiovascular event (Kaye, Darke & Duflou 2009). Certain adulterants increase the likelihood of such adverse effect.

Piperazines BZP and mCPP have been linked to hospitalization in numerous reports (Gee, et al. 2005; Wilkins, et al. 2007; Brent et al. 2010). Brent and colleagues (2010) report that despite mCPP's "lack of neurotoxic potential," induced nausea and hallucinations required two hospitalizations from a sample of 79. Gee et al. (2005) describes the toxicity of BZP to be unpredictable and serious in certain individuals. Although a majority of users experience mild adverse effects, the potential for more severe consequences after the initial dose appears high (Brent et al. 2010). Acute harms, however, are not limited to the substances themselves.

There is evidence that environmental factors strongly influence adverse effects of club drugs as opposed to solely toxicity (Bellis 2002). Temperature appears to be a major causality of hospitalization, with heatstroke being the most reported cause of death (Bellis 2002; London Drugs Policy Forum 1996). Continuous dancing and crowded settings combine to heighten the severity of MDMA's induced hyperthermia (Kaye, Darke & Duflou 2009). Unaware of these acute risks in the 1980s, European users experienced the first MDMA-related deaths during recreational use, likely due to temperature (Karch 2011). Hyperthermia, however, remains possible in "quiet settings," as a majority of MDMA-related mortalities in one study occurred in private homes (Kaye, Darke & Duflou 2009). Today, preventative measures focus on reducing overheating and dehydration, curbing but not eliminating serious injury (Hayner 2002). Harm minimization practices have grown in tandem with the rise of dance culture. User education is essential, as Morefield et al. (2011) found no correlation between amount of MDMA in a tablet and the quantity participants decided to consume.

In Melbourne, Australia, Ecstasy-related emergency department admissions (*n*=1347) declined from 26% in 2008 to 14% in 2009. Although length of stay was short and symptoms mild, ecstasy-related admittances place a "significant burden" on EDs (Horyniak 2013). Harm reduction practices are necessary to lessen this burden.

**Drug Testing and Harm Minimization Practices**

A healthy settings approach acknowledges the impact environmental factors have on individual health. A number of harm minimization practices are recognized in areas associated with drug and alcohol use, such as raves and nightclubs. Proper hydration, avoiding potentially fatal mixtures, such as alcohol and ecstasy, and periodic cool down periods are often advised (London Drugs Policy Forum 1996; Bellis 2002). Ultimately, levels of implementation vary by location. In 2009, the European Monitoring Centre for Drugs and Drug Addiction reported "limited availability of simple measure to prevent or reduce health risks and drug use in European nightlife settings." A majority of of nightclubs in 18 countries lacked "outreach prvention work" (EMCDDA 2009). Often times, users take harm minimization practices upon themselves.

Policymakers fear that establishing drug checking at venues encourages drug use, even among non-users. Schroers (2002) found that this is not the case. Information obtained from drug checking may be valuable for alerting users of dangerous substances detected at the venue. In an Australian survey, Johnston et al. (2006) found that 84% of total respondents (n=810) had, at some point, tried to determine the contents of their ecstasy tablet prior to ingestion. 53% reported doing so all or most of the time. Akram (1999) found that over 80% of survey respondants (n=125) practice some form of harm-reduction. Females are significancly more likely to exert caution than men through means of smaller initial and subsequent dosages. Among

users utilizing testing kits, however, males have been found to report higher frequency of use (Johnston et al. 2006). Thus harm-reducing information should "not assume that one message or one approach [for both genders] is sufficient" (Akram 1999). Young people often obtain information on Ecstasy via the Internet (Duterte 2009; Miller et al. 2010). Therefore, harm reduction messages should be geared towards this medium. Forum postings, particularly about new psychoactive substances, are a limited yet valuable source of information (Kelleher et al. 2011). Options for purity testing are limited but generally available to the public.

Schroers (2002) identifies two methods of drug checking: On-site testing, often used at raves and large events where ecstasy use is prevalent, and Clinical testing, analysis taking place in a specialized laboratory. The former often involves social workers and volunteers. Due to the need to openly acknowledge the occurrence of drug use, legality varies by country. The latter often involves qualified pharmacists (Schroers 2002). Nicholas (2006) further stratifies drug checking into three categories: laboratory based drug testing, pill identification, and reagent-based pill testing. Pill identification involves judgment based on appearance, such as size and branding, then comparing the results to previous analyses. Even pills among the same brand name, however, have been found to vary in amounts of active ingredients (Sherlock et al. 1999; Duterte 2009). Reagent-based testing refers to the use of on-site testing kits. Users scrape bits of the tablet onto a white ceramic plate, mix in the reagent, and compare any color changes to the included color chart. As the process is dependent on color change, interpretation is inherently subjective. Numerous drugs are identified with similar colors. Furthermore, required materials are not commonly available at dance events, resulting in limitations for both user-level methods of drug checking (Hayner 2002). Only 22% of respondents in an Australian survey reported personal use of a testing kit, with younger and heavier users being more likely. 56% of these respondents acknowledge reagent testing's limitations (Johnston et al. 2006). Laboratory testing is the most objective in nature but does not necessarily influence user rates.

Between January 2004 and September 2010, 22,280 drug users submitted ecstasy tablets to DIMS. 13,445 cited "health concerns" as reason for analyses (Brunt et al. 2011:136). Despite said concerns, Brunt et al. (2011) found that "in the event of reduced ecstasy quality, ecstasy users in The Nerthlands have increasingly used drug testing as a potential harm reduction tool, rather than changing their patterns of drug use." Thus fluctuations in ecstasy quality provide incentives for users to practice harm reduction but ultimately do little to stimy use. In fact, significant declines in tablets containing MLS had no effect on users' decision to change or reduce use.

**Trends in Ecstasy Use**

The United Nations Office on Drugs and Crime estimated global ecstasy prevalence in 2011 to be 19.4 million or 0.4 percent of the population – a decline from 2009's

estimates. Overall, ecstasy use has been "declining globally," yet seemingly increasing in Europe. Use in Western and Central Europe appears to be stabilizing (Karch 2011). Rates of ecstasy use are higher than the global average in Europe (0.7%), North America (0.9%), and Oceania (2.9%), respectively (UNODC 2013). Trends in use and prevalence vary by nation and age.

Rates of ecstasy use are generally higher among young people in urban nightlife settings such as clubs and raves. In 2013, 75% of last year European users were between ages 15 and 34 (UNODC 2013). These differences, however, may be a result of other recreational activities (Adalf 1997). Ecstasy use in these settings is not representative of the entire population.

Estimates published in 2009 suggest that nearly 10 million European adults have tried ecstasy (an average of 3.1%), with 2.5 million using within the last year (ranging between 0.1% and 3.5%, dependent on country). Males report "far higher" use "on all measures" than females. Among young people aged 15 to 34 years, lifetime usage ranges nationally from 0.6% to 14.6% while last year usage ranges between 0.2% and 7.7% (EMCDDA 2009).

The UK population experienced 3% last year usage in 1994, 6.8% in 2001, and 5.4% in 2002-2003 (Schifano et al. 2005). In 2003, undergraduates from a large American midwestern university reported 10% lifetime ecstasy use, 7% within the past year, and 3% within the past month. Ecstasy was the second most used illicit substance after marijuana (Boyd et al. 2003). From 2005 to 2008, ecstasy use among Canadians aged 15 and older increased from 1.1% to 1.4%. Lifetime ecstasy use was found to be 4.1% (Bouchard et al. 2010).

In Australia in 2013, the Ecstasy and Related Drugs Reporting System found that ecstasy is the number one drug of choice among survey participants, designated by 33% of the sample (n=686) (EDRS 2013).

In Brazil, ecstasy consumption rates are rising, mirroring trends found in other countries. While use is currently "restricted to privileged youngsters," the "rapidly declining price of ecstasy" and "easy procedure of consumption" indicate a progressive increase in popularity (Pereira de Almeida et al. 2014).

In the United States, ecstasy increased in availability after its change in legality. Between the mid-1980s and 2000, perceived riskiness associated with use declined; a trend that would reverse at the turn of the millennium (UNODC 2013). In 2013, youth in the United States reported higher perceptions of risk associated with ecstasy use and a significant decline in availability (30%) compared to youth in 2000 (MTF 2013). Annual prevalence rates in 2012 declined by over 50% compared to 2001's peak (MTF 2012). On the whole, ecstasy use in the United States declined after 2000 due to dismantled supply chains. Simultaneously, ecstasy's perceived riskiness increased (UNODC 2013).

The decline in global ecstasy consumption occurred after, not during, the decline in global ecstasy purity. It appears that users "enduring the shortage of MLS" reduced use after trends were published (Brunt et al. 2012). Goudie et al. (2006) reported "significant" correlation between ecstasy quality and number of units purchased. Relative to income, demand for poor and average quality ecstasy was inelastic. The negative exposure ecstasy received after its 2009 slump in purity, in addition to receiving a "disproportionate amount of press attention" in the realm of drug fatalities, has had a measurable impact on user trends (Forsyth 2001).

**Misc.**

After comparing Scottish toxicological reports to popular newspapers' stories on drug deaths, Forsyth (2001) found that ecstasy "received a disproportionate amount of press attention" when compared to other drug fatalities.

Rates of ecstasy use generally increase among young people vacationing (Elliott et al. 1998).

Literature throughout the late 1980s and 1990s report similar sample demographics: majority male with mean age ranging from 24 to 26 years (Forsyth 2001).

From 1995 to 2005, Tanner-Smith (2006) discovered that the "purity of tablets decreased over time, which was largely a result of an increasing number of tablets comprised of MDMA along with other substances."

Ecstasy's popularity among young people in conjunction with newly synthesized, potentially lethal adulterants prevalent within tablets sold as "ecstasy" (Bossong 2010; EMCDDA 2009) draw a number of public health concerns.

In an Australian survey, 42% of participants (n=686) "reported purity to be medium" while 20% "reported purity to be low." 13% stated that "purity was increasing" while 31% reported that "purity had fluctuated" (EDRS 2013).

Meanwhile, in 2001, all tablets (n=136) submitted to the Forensic Science Service from northwest England contained MDMA. (Cole et al. 2002).

In the United States, Tanner Smith (2006) concluded that "ecstasy tablets from California and Florida had decreased likelihoods of containing non-MDMA substances."

O'Connell and Heffron (1999) found that seized ecstasy tablets analyzed in Ireland ranged from 0 to 180 mg of MDMA. "Caffeine, amphetamine, MDEA, ephedrine/pseudoephedrine and N-MePEA" were also present. A gas chromatographic procedure with mass spectrometric detection was utilized.

Ecstasy use is notably high in nightclubs and dance events known as “raves.”

Due in part to the “complex interactions of supply, demand, and control of illicit drugs”, tablet purity, and thus the availability and reputation of “molly”, has experienced tangible levels of adulteration (Cole et al. 2011).

NPS/Designer Drugs

A Brazilian online survey found that, among users who had used ecstasy at least five times, 43% “fulfilled the criteria for dependence.” The correlation between dependence and age was “significant and inverse,” indicating that younger users are “more vulnerable to harm associated with ecstasy consumption” (Pereira de Almeida et al. 2014).

The national Drug Information and Monitoring System (DIMS) in the Netherlands provides laboratory analyses of ecstasy tablets and other drugs in order to “offer valuable insights into the dynamic recreational drug market, particularly for policymakers.” Information is also exhanged between personnel and drug users themselves, as data are “collected directly on the user’s level” (Brunt and Niesink 2011).

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