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Assessing the impact of laws controlling the online availability of 25I-NBOMe, AH-7921, MDPV and MXE – outcomes of a semi-automated e-shop monitoring

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Abstract

Aims: The indicator of availability has been used in the risk assessment (RA) of new psychoactive substances (NPS). This paper aims to examine the pre- and post-control availability of 25I-NBOMe, AH-7921, MDPV and MXE, which were assessed by the EMCDDA. *Methods*: Data were collected by a semi-automated software tool (I-TREND SASF) on e-shops in national languages (Czech, French, Dutch, Polish and English) that offered shipping of these compounds into the respective countries; frequency analysis was used. *Findings*: The number of e-shops selling these substances decreased between III/2014 and XII/2015 (except for AH-7921). Both increases and decreases were found on the country-level for all the compounds (except for an overall decrease for MXE). In one instance an NPS disappeared from this market in 2015 (25I-NBOMe in NL); 25I-NBOMe and AH-7921 in France and AH-7921 in Poland appeared for the first time in 2015. The shops listing AH-7921, 25I-NBOMe and MDPV in XII/2015 ranked higher in terms of "popularity" than in III/2014. The IP addresses were more likely to be outside the EU in 2015 than in 2014. *Conclusions*: We found no evidence that national-level compound bans contributed to the changes in online NPS markets. Indicators of the accessibility, availability, popularity, and IP origin should be considered in RA. Data triangulation with street markets and the darknet is needed as well as more research into the "displacement" and "replacement" effects of control laws.

Keywords

New psychoactive substances, risk assessment, online shops, availability, drug control

History

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Introduction

The availability of psychoactive substances and analysis of drug market activity are important indicators that help to understand the supply of illicit drugs and to design policies to reduce it (EMCDDA & Europol, 2007). Drug seizures, together with information on drug prices, purity at the street level, and the composition of seised samples (mainly sourced from the police and customs) can provide a multi-dimensional view of drug availability as a whole, especially if combined with user-sourced drug sample analysis as in the case of the Dutch Drug Information and Monitoring System (further DIMS) (Brunt & Niesink, 2011). Data on drug availability is routinely collected e.g. within the REITOX (Réseau Européen d'Information sur les Drogues et les Toxicomanies) network. Nevertheless, in countries where there is no systematic collection of data and/or drug samples from drug users and drug sellers, the police-sourced information on drug markets might be representative of law enforcement activity rather than of the behaviour of illicit market players (Blumstein, 1993; Caulkins, 2007; Tonry, 1995).

Monitoring the online market in psychoactive substances

Increasing use of the internet by both drug users and sellers has opened up a new space for more accurate monitoring of a specific drug market segment – the online indexed (surface) market in psychoactive substances. Web monitoring activities are considered vital in order to gain a better understanding of the phenomena of new psychoactive substances (NPS) (Corazza et al., 2013, 2012a,b). Specifically, the monitoring of online markets, unlike information about drug supply on ''traditional'' drug markets, offers a picture of all the psychoactive substances being offered in real time, and of their characteristics.

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A vast number of outlets have appeared on the surface web (publicly available online web pages), selling (mostly) NPS that are not controlled, also sold as ''legal highs'', ''bath salts'', or ''research chemicals'' (Newcombe, 2009; Vardakou, Pistos, & Spiliopoulou, 2011). Online markets selling NPS have been subjected to several research enquiries. Schmidt and colleagues evaluated the accessibility of ''legal highs'' via the internet by UK-based retailers and found 39 unique websites with 1308 products (Schmidt et al., 2011). Meyers and colleagues conducted research on the availability of ''bath salts'' in online shops on the surface web (we refer to them further as *e-shops*); 31 websites were found globally (Meyers et al., 2015). Some e-shops also exist in a grey area by restricting purchase options to trusted members via password-protected platforms (Martinez, Kmetonyova, & Belackova, 2016). Unlike smart shops or head shops (Ryall & Butler, 2011), online retailers can service user populations across regions and countries.

For the sale of illegal psychoactive substances, online markets on the so-called ''darknet'' provide access to a variety of illicit goods (Barratt, 2012; Barratt & Aldridge, 2016; Van Hout & Bingham, 2013, 2014). These online spaces can only be accessed through IP-anonymising software, and those that operate as marketplaces use a decentralised electronic currency (the bitcoin) which is difficult to track (Nakamoto, 2008; Soska & Christin, 2015). One of the most renowned darknet market places for illicit goods was Silk Road, which opened in 2011 and closed by the end of 2014, following a police intervention (Barratt, Ferris, & Winstock, 2014). NPS can also be found in these markets, although to a much smaller extent than illegal goods (Barratt et al., 2014; Van Buskirk, Naicker, Roxburgh, Bruno, & Burns, 2016).

Monitoring of NPS availability at the European level

The standardised attempts to assess online availability at the European level began as unstructured searches through popular search engines for the purpose of the risk assessment (RA) of several NPS, such as 2C-T-2, 2C-T-7 or GHB (EMCDDA, 2002, 2004).

Since 2006, the EMCDDA has been conducting multilingual surveys called ''snapshots'' in which six specific NPS-related search strings are entered into three web search engines in each country, with the URLs of the e-shops that are identified being collected along with information about the site and the products for sale (Hillebrand, Olszewski, & Sedefov, 2010). For instance, the 2011 snapshot was carried out in 18 languages and found 631 e-shops offering NPS for sale (EMCDDA, 2012).

The EMCDDA snapshot methodology has been used, for example, to show a decrease in the availability and price of AMT over a six-month period (Wood & Dargan, 2014), to demonstrate the greater availability of a controlled substance than those that are not controlled (Nizar, Dargan, & Wood, 2015) and to perform international comparisons of NPS prices (Vermette-Marcotte, Dargan, Archer, Gosselin, & Wood, 2014). Since 2011, the outcomes of the snapshot survey have been included in the RA of NPS conducted by the EMCDDA (2009).

RA and the availability of NPS

RA is a structural evidence-based activity aiming to objectively collect relevant information about the potential risks posed by psychoactive substances and to assess risk quantitatively (Caulkins, Reuter, & Coulson, 2011), providing a background for informed decisions by policy makers, regulatory bodies, and stakeholders in drug services (Drapalova, Grund, & Belackova, 2016; Fitch et al., 2003; Mounteney, 2009; Rhodes, Stimson, Fitch, Ball, & Renton, 1999).

Globally, the risks of newly emerged substances are assessed by the Expert Committee on Drug Dependence of the World Health Organisation (WHO, 2010). On a European level, RAs are performed by the Scientific Committee of the European Monitoring Centre for Drugs and Drug Addiction (EMCDDA, 2009). Since 1998, the EMCDDA has performed 19 RAs, of which 17 have suggested control measures at the European level.

The RA process collects data to assess the amount and probability of harm in several dimensions, including biological, psychological, social, and economic harms to individuals, groups and societies. The data about the availability of NPS is primarily assessed within the category of ''Public health risks'' where it concerns the availability and quality of a new psychoactive substance on the market (purity, adulterants, etc.) and the populations and settings where it is obtained and used. Secondly, the availability of NPS is considered under ''Options for control and possible consequences of the control measures'', where, additionally, the prices of NPS are assessed alongside the potential impact of NPS control (EMCDDA, 2009).

In the process of providing information about the risks in a timely manner for evidence-based policy decisions, RA procedures are challenged by the large number of newly emerging substances and by their rapid turnover (Drapalova et al., 2016; Winstock & Ramsey, 2010). It is thus crucial to obtain real-time data in order for RA procedures to be accurate and to correspond to the situation on the NPS market.

Aims

This paper assesses the online availability of four NPS that were subjected to RA by the EMCDDA in the period from January 28th, 2014 to April 28th, 2014 (Mounteney & Griffiths, 2014). These were 25I-NBOMe (EMCDDA, 2014c), AH-7921 (EMCDDA, 2014d), MDPV (EMCDDA, 2014a) and methoxetamine (EMCDDA, 2014b), further referred to as MXE As an outcome of the RA, EU member states were required to control these compounds before October 2nd, 2015 (EC, 2015).

Table 1 shows when the countries in this analysis, the I-TREND project partners – the Czech Republic (CZ), France (FR), the Netherlands (NL), Poland (PL) and the United Kingdom (the UK) – adopted control of the four NPS. It shows that all the countries banned the four compounds by the required time, and that several countries had banned some of the compounds even prior to the council decision (FR and the UK had banned them all except for AH-7921; MDPV had been controlled in all the I-TREND countries except for NL).

Q7 Table 1. Control of the four NPS in project partner countries.

	Czech Republic	France	Netherlands	Poland	United Kingdom
25I-NBOMe	1.10.2015	***24.9.2013***	1.7.2015	1.7.2015	***10.6.2013***
AH-7921	1.10.2015	***24.9.2013***	1.7.2015	1.7.2015	1.1.2015
MXE	1.10.2015	***5.8.2013***	1.7.2015	1.7.2015	***5.4.2012***
MDPV	***6.4.2011***	***27.7.2012***	1.7.2015	***8.6.2011***	***16.4.2010***

This paper aims to evaluate the impact of both the EU-level decision and national-level control measures on the indicators of online accessibility and availability of the four NPS, on the country of origin of their IP addresses, and on the ''popularity'' ranking of these e-shops. The paper also discusses the relevance of these different indicators to RA procedures.

Methodology

A semi-automated shop-finder software (I-TREND SASF), developed within the I-TREND project and adopted to the five project partner languages (CZ, FR, PL, NL and UK), searched the surface web for the four compound names (25I-NBOMe, AH-7921, MDPV and MXE) shortly before their RA by the EMCDDA (March 22nd, 2014) and 21 months later (December 29th, 2015); the latter date was almost two months after the control measures were supposed to have been adopted by all EU member states.

Data collection using the I-TREND semi-automatic shop-finder (I-TREND SASF)

I-TREND SASF performs online searches based on the EMCDDA snapshot methodology – see the background section and EMCDDA (2009) – with the modification that it stores only a limited number of outcomes ($n = 100$ in this study) for each search engine and set of key words. The advantage over the snapshot methodology is that I-TREND SASF can search the internet periodically or at any ''ad hoc'' moment while building upon human-assisted categorisation from its previous searches. This means that once a search outcome (a web page) has been approved by the administrator as an actual e-shop (rather than a discussion board or another web page irrelevant to the purpose of the search), it is classified as such in any further searches (and irrelevant outcomes are excluded in any further searches too). This makes the use of I-TREND SASF time-saving in comparison to the EMCDDA snapshot. Further on, several characteristics of the ''approved'' e-shops are retrieved automatically and stored (e.g. IP address unique identifier, country code, popularity ranking). Last but not least, with the use of I-TREND SASF, it has been possible to isolate unique e-shops (i.e. to exclude any URLs which serve to display one e-shop under multiple links); only ''unique'' e-shops are presented in this analysis. Further information about the methodology can be found elsewhere (Martinez et al., 2016).

An ad hoc search by I-TREND SASF was conducted for the purpose of this research in III/2014 (the first point) and in XII/2015 (the second point) using the three most ''popular'' search engines in each I-TREND project partner country (e.g. Google.pl, Yahoo.fr, Seznam.cz; the selection was made with the use of online ranking web pages such as alexa.com, pageranking.org and checkpagerank.net). The search phrases used in this research consisted of several terms identifying e-shops in national languages (''basket/trolley/shopping cart'', ''buy'' and ''price'') and of the four compound names that were subject to this analysis (25I-NBOMe, AH-7921, MDPV and MXE). At each point in time, the e-shops were further checked in order to verify that the compounds of interest were available at the e-shop, were in stock, and could be shipped into the country for which the shop was identified.

Data analysis

A frequency analysis was carried out, focussing on the changes between the two monitoring points. The first indicator that was examined was the number of outcomes (e-shops selling NPS in national languages) per substance and country (referred to as ''accessibility''), together with the overall ''availability'' of the selected NPS in each of the countries (whether or not e-shops selling the compound were found in a country-level search).

The second indicator subjected to analysis was the publicly available country code of the e-shop's IP address, which indicates the country in which the online shop was technically hosted (the location of the ''server''); the physical location of the vendor might be different, however.

The third indicator was the global ranking of the e-shop according to www.alexa.com, which represented the site's ''popularity''. Alexa.com was chosen because it listed more characteristics of the webpages we identified as e-shops selling NPS than other ranking systems; another benefit was that it displayed separate results for sub-domains (e.g. nsd.webshop.com and nps.webshop.com rather than just webshop.com). The rank was calculated by Alexa.com using a combination of the average number of daily visitors to the site and page views on the site over three-month periods, based on the records from internet users with the Alexa device installed (Kamerer, 2013). The most popular online sites (Facebook, Google) rank close to 1; the top 1% of popular pages ranks < 2,000,000. I-TREND SAFS automatically downloaded the rank of each of the approved e-shops, if available. For the purpose of this analysis, the rank values of the web pages identified by I-TREND SAFS were divided into five categories based on the percentile distribution of the entire sample rank in 2014 (VERY HIGH – below 100, HIGH – 100th to 2 mil, MIDDLE – 2 to 5 mil, LOW – 5 to 10 mil, and VERY LOW – more than 10 mil). A high rank not only suggests that the page is popular, but also implies a higher likelihood that the web page will be displayed as a search outcome.

Findings

At the first monitoring point (III/2014), 66 e-shops identified for the project partner countries were selling at least one of the four NPS subjected to RA. At the second point (XII/2015), 33 e-shops were selling one or more of the four compounds (half of the shops found at the first monitoring point). These were all active unique e-shops (all parallel or duplicate shops, e.g. the same shop under multiple URLs, had been removed).

A total of nine of these e-shops were identified in both III/2014 and XII/2015. This means that 57 e-shops that had been selling the four compounds at the first monitoring point were ''dead'', meaning they ceased to exist ($n = 43$), were no longer selling any products ($n = 11$), were not offering any of the four substances, or appeared in the 101st or a further search outcome at the second monitoring point ($n = 6$). It also shows that 24 new e-shops selling these compounds appeared at the second monitoring point. Out of the 66 outcomes in III/2014 and 33 in XII/2015, several were identified within search outcomes for more than one I-TREND country (four in 2014, seven in 2015).

As a result of the decrease in the overall number of shops selling the four compounds, their accessibility was thus lowered significantly within the five EU countries in XII/2015. Interestingly, as will be discussed further, several compounds were identified in country-specific searches at the second point that were not originally available at the first point. This suggests that in some cases, the availability of these compounds actually increased.

Fluctuations in availability and accessibility

The highest number of e-shops across both monitoring points that was selling at least one of the compounds (accessibility across countries) was found in the UK ($n = 43$ in III/2014, $n = 17$ in XII/2015); however, this was also the largest decrease in the number of relevant e-shops that occurred (−61%). The second largest number of e-shops was found for PL ($n = 17$ in III/2014, $n = 13$ in XII/2015), with a somehow smaller rate of decrease (−24%) compared to the UK. A remarkably lower number of e-shops selling the four NPS of interest was found in the searches in FR ($n = 4$ in III/2014, $n = 6$ in XII/2015), in NL ($n = 5$ in III/2014, $n = 4$ in XII/2015), and in CZ ($n = 3$ in III/2014, $n = 4$ in XII/2015). An overview of the e-shops per country is provided in Figure 1.

When accessibility per compound is looked at, the most widely-marketed NPS in our sample was MXE, with 44 e-shops selling the compound in III/2014 and 20 in XII/2015 (on a per-country basis, it was the most widely-marketed compound in the UK, PL, FR and CZ in III/2014 and in the UK, FR, PL and NL in XII/2015), followed by MDPV (the most widely-marketed in NL and FR in III/2014 and in CZ and NL in XII/2015), followed by 25I-NBOMe and followed by AH-7921; see Table 2.

Across all the countries, the number of e-shops selling MXE decreased over the monitoring period. There was also a noticeable decrease in the number of e-shops selling the other compounds, and yet this varied between the individual countries and compounds (both increases and decreases occurred). This finding is discussed in detail below.

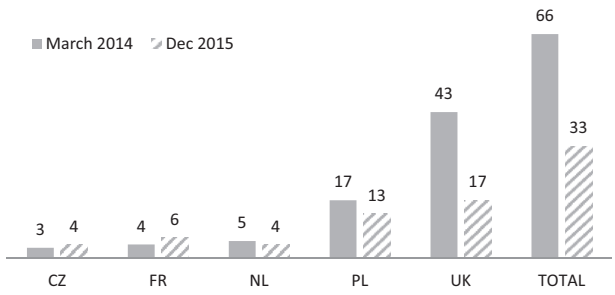

Figure 1. Number of e-shops per country listing at least one compound assessed in 2014 and 2015.

Over the monitoring period, the number of shops selling MDPV decreased in some countries (FR, NL, the UK) and increased in others (CZ, PL). Online searches during XII/2015 found that 25I-NBOMe was no longer stocked in NL, and the number of UK e-shops selling it had decreased. No change in the number of shops selling 25I-NBOMe was detected either in the PL search or in CZ (where it never appeared).

AH-7921 was the least widely-marketed substance of the four. While AH-7921 never appeared in the CZ and NL searches, it was identified in the PL and FR search in XII/2015 for the first time. Additionally, the number of e-shops selling the compound in the UK ($n = 6$) remained consistent at the two monitoring points.

This shows that despite overall decreases in accessibility, in some cases the availability of the compounds per country increased (AH-7921 in FR and PL, 25I-NBOMe in FR) or remained the same (all the compounds that were available per country in III/2014 remained so in XII/2015, except for 25I-NBOMe in NL, which was no longer available in XII/2015).

Country of e-shop domain origin (IP address)

In terms of the e-shops' IP addresses identified in III/2014, most of them were located in a US domain ($n = 20$, 30% of all

Table 2. Number of shops listing particular NPS per I-TREND project country.

	CZ	FR	NL	PL	UK	Total[d]
25I-NBOMe[b]						
03–2014	0	0	2	3	15	**20**
12–2015	0	1	0	3	5	**9**
TREND[a]	0	First time	Remove	No change	–	–
AH-7921						
03–2014	0	0	0	0	6	**6**
12–2015	0	1	0	1	6	**6**
TREND[a]	0	First time	0	First time	No change	**No change**
MDPV						
03–2014	2	4	5	4	22	**31**
12–2015	4	2	3	5	5	**12**
TREND[a]	+	–	–	+	–	–
MXE[c]						
03–2014	3	4	4	14	25	**44**
12–2015	1	3	3	8	10	**20**
TREND[a]	–	–	–	–	–	–
Total						
03–2014	3	4	5	17	43	**66**
12–2015	4	6	4	13	17	**33**
TREND[a]	+	+	–	–	–	–

[a]Changes in accessibility per country and compound are marked as – decrease, + increase or ''no change''. Changes in availability per country and compound are marked as ''First time'', ''remove''; there is no sign for ''no change'' in availability. Where a compound wasn't available in either of the periods, it is marked as ''0''.

[b]An additional shop (UK) that was listing the substance was identified by the tool in 2015, but was found to be out of order, and thus is excluded from the figures.

[c]Out of stock in two additional shops (PL, UK) in 2015 and two other shops listing the substance were identified (UK, NL), but were found to be out of order in 2015, and thus they were excluded from the figures.

[d]The totals are lower than the sum in both the columns and rows, as several e-shops were identified in more than one country and were selling more than one compound.

shops), a Dutch domain ($n = 11$, 17%) or a domain in another EU country ($n = 12$, 18%); see Figure 2. That said, the majority of the IP addresses selling NPS compounds in III/2014 were based in EU countries ($n = 38$, 58%). This was a higher share than in XII/2015 ($n = 16$, 49%). During the second monitoring period, the ratio of e-shop domains located in the US increased notably ($n = 15$, 45%); see Figure 2.

E-shop popularity

An Alexa Global Ranking was available for 66% of the shops identified in III/2014 ($n = 44$) and 58% of the shops identified in XII/2015 ($n = 19$), i.e. they were visited by internet users with the Alexa device installed on their browsers; the results below are discussed for those e-shops only (see Figure 3).

In III/2014, more than a quarter of the e-shops selling the NPS of our interest ranked among the very high (7%, $n = 3$) or high (18%, $n = 8$) distributions, i.e. 25% of the shops ranked ''high'' or above; in XII/2015, a similar proportion of the e-shops ranked among the most popular (''high'' = 26%, $n = 5$). Nevertheless, a greater proportion of e-shops selling the four compounds at the second monitoring point were ranked ''low'' or ''very low'' (36% in III/2014, 52% in XII/2015). While the ranking of the most numerous e-shops selling MXE decreased between III/2014 and XII/2015 (from 33% to 27% ranking ''high'' or above), for the e-shops selling all other compounds it increased (from 24% to 29% ''high'' or above in MDPV, 38% to 48% in AH-7921, and 3% to 48% in 25I-NBOMe). It should be pointed out, though, that the shops with the highest ranking proportions overall were those selling AH-7921 and 25I-NBOMe in XII/2015; the shops selling AH-7921 in III/2014 also had the highest ranking among all the shops in that period.

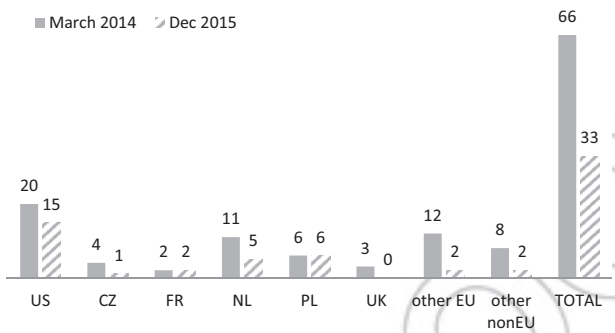

Figure 2. IP address of e-shops selling the compound in March 2014 and December 2015.

Discussion

We assessed the indicators of online availability for four NPS (25I-NBOMe, AH-7921, MDPV and MXE) that were subjected to RA by the scientific committee of the EMCDDA and suggested for control by EU member states. We retrieved data before their European-level RA (March 22nd, 2014) and two months after their control had become mandatory (December 29th, 2015); several compounds were, however, already controlled prior to the first monitoring point in some I-TREND project countries (all of them in FR, all except AH-7921 in the UK, and MDPV in CZ and PL).

Developments in accessibility and availability and impact of control

Essentially, the overall number of e-shops selling these substances identified on the surface web decreased substantially for the I-TREND project countries (decrease in ''accessibility''); this also applied on a per country basis, except for France, where there were more shops identified in III/2015 than in XII/2014. Decreases in the number of e-shops offering MXE were observed across all four country searches; the number of e-shops selling 25I-NBOMe also decreased in the UK and the number of MDPV selling shops decreased in FR, NL and the UK.

On the other hand, there was only one instance in which an individual compound completely disappeared from the market during the second monitoring point (25I-NBOMe in NL). In three cases, substances were found in national language searches in XII/2015 (25I-NBOMe in FR and AH-7921 in FR

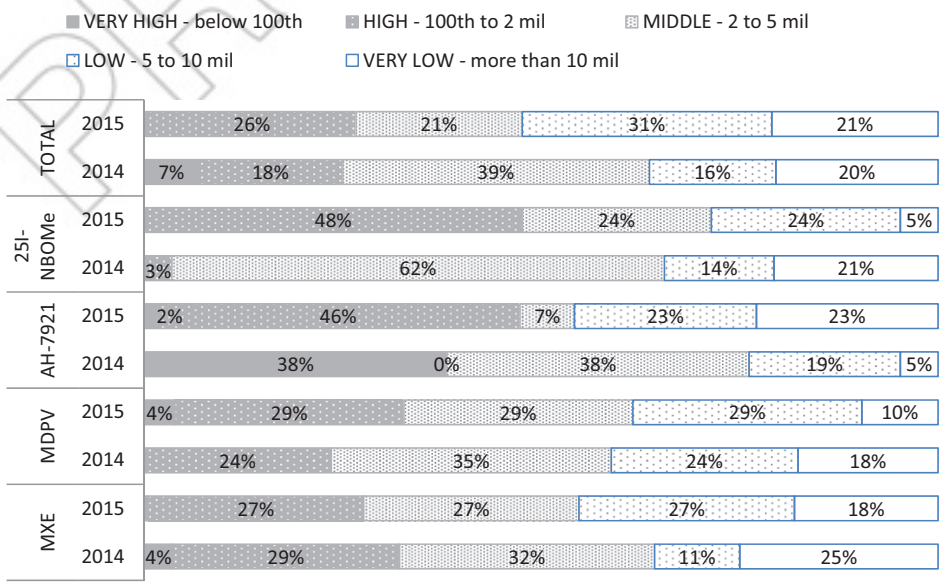

Figure 3. Alexa global ranking of the e-shops selling the four compounds in 2014 and 2015 (only e-shops where the ranking was available).

and PL), but they did not originally appear there in III/2014 (an increase in ''availability''). In two cases, the number of e-shops offering a particular compound in a given country increased (MDPV in CZ and PL). All four compounds could be found in the UK throughout both points; the number of shops offering AH-7921 in the UK and 25I-NBOMe in PL did not change during the monitoring period.

First, this indicates that the responses of online vendors to control measures varied across the five countries; this is expressed in the outcome of online searches of the internet using selected key words in the five national languages. It also suggests that despite decreases in accessibility (the number of e-shops listing or selling a particular compound), the availability of some compounds per country could increase (FR, PL) or remain the same (PL, UK). Additionally, the relative ''popularity'' evidently increased for the e-shops listing all compounds except for MXE, suggesting that those shops had become more heavily accessed by internet users in XII/2015.

When looking at the impact of country-level bans on the accessibility and availability of the four compounds, they appear to be rather limited. The number of e-shops identified through country-level searches decreased by more than half in the UK (from $n = 43$ to $n = 17$) in XII/2015. The UK had previously legislated against all three compounds where the decrease occurred (prior to the first monitoring point), whereas the decrease in the number of e-shops selling the compounds in countries where legislation was introduced in between the monitoring points was much lower (from $n = 17$ to $n = 14$ in PL) or increased slightly (from $n = 3$ to $n = 4$ in CZ).

When one looks at the trends per compound, the only country where a substance disappeared from the national-level searches after it was banned was NL (in the case of 25I-NBOMe). In this respect, NL stands out of the sample, similarly to the way it does with policies and their outcomes in other drugs (MacCoun & Reuter, 1997; Reinarman, Cohen, & Kaal, 2004).

In fact, 25I-NMOBe and AH-7921 were newly offered on the FR online market in XII/2015 despite the fact that they had already been banned in 2013, prior to the monitoring beginning. The number of e-shops selling MDPV increased between III/2014 and XII/2015 for CZ and PL, where MDPV was already banned in 2011. Remarkably, in PL, one compound appeared in online searches only after it was banned (AH-7921). From this we can conclude that in some countries, the compounds were made available online despite being made illegal.

The results here give reason to believe that the shift to non-European IP addresses (from the EU countries to the US and non-EU countries), although it has no influence on availability or accessibility to users, can be seen as an outcome of the broader control measures on the European or international level. In this respect, it is noteworthy that 116 NPS were put under control in China, a likely producing country of NPS (Van Buskirk et al., 2016), on October 1st, 2015. It is plausible to assume that this has contributed to an overall decrease in the number of e-shops offering the four compounds in this analysis, and possibly to a greater extent than the individual bans in destination countries.

Displacement to other markets and replacement of compounds

In order to assess the full impact of regulation on the availability of the four compounds, further inquiry is needed in terms of finding out whether the substances that were less widely marketed online increasingly appeared on the ''darknet'' after they were controlled or on other street-level illegal markets in Europe, referred to as ''displacement effect'' (Aldridge & Decary-Hetu, 2016) and whether substitutes for them emerged (''replacement effect''). Evidence on ''displacement'' and ''replacement'' can offer insights into unintended consequences of NPS control laws, described previously in relation to drug prohibition (Benson, 2009; MacCoun, 1993; Thornton, 2007).

When it comes to the ''displacement'' of the four substances on the darknet, an assessment made by the Cyprus National Focal Point suggests that only two substances (25I-NBOMe and MXE) were sold in the period between June and October 2015, the former to a greater extent than the latter (EMCDDA, 2015b); the sale of 25I-NBOMe on the darknet had already been reported in 2013 (Caldicott, Bright, & Barratt, 2013). Both 25I-NBOMe and MXE, at the same time, happened to experience a large decrease in the number of outlets selling them on the surface web (see Table 3), and 25I-NBOMe ceased to be sold by NL e-shops after the ban. MDPV, however, was not found in darknet market places at all (it had been banned in most countries prior to the first monitoring point, and the number of shops offering it had decreased almost threefold by the second point). This suggests that some compounds continued to be sold on the darknet after the ban and others never appeared there.

MDPV was largely seen on street markets and among injecting drug users in Europe in 2010 and 2011, prior to several country-level bans, and has somehow persisted since (EMCDDA, 2015a; Rácz et al., 2015). There is insufficient evidence to reach a clear conclusion on the occurrence of MDPV on street markets within the I-TREND project partner countries. In the Netherlands, MDPV has been a topic of discussion among potential drug users in drug fora since at least 2007 (DHPForum.nl, date of reference June 16, 2016) and was first handed in for chemical analysis at the Dutch Drugs Information and Monitoring System (DIMS) in 2010, about five years before it was banned. However, some level of increased user interest was found in the Czech Republic during 2014, when MDPV was discussed among the participants in Czech online fora for the first time despite the fact that it had been prohibited in 2011.

With respect to the ''replacement effect'', i.e. the extent to which alternative new substances to these four NPS are emerging (EMCDDA, 2009), previous analysis of new synthetic cannabinoid mixtures demonstrated that the compounds were exchanged as a response to legislative changes (Dresen et al., 2010; Kikura-Hanajiri, Uchiyama, Kawamura, & Goda, 2014). Also, quantitative analysis of online fora has provided insights into a decrease in discussions of particular compounds on online boards after they were banned, and an increase in the discussion of other compounds, but such developments are difficult to attribute to the effect of a compound being banned (Ledberg, 2015). Notwithstanding

that the compounds in our analysis have themselves been offered as ''replacement'' at some point (Corazza et al., 2012a,b).

Several indicators of ''replacement'' could be found in both the qualitative and quantitative data collected through the I-TREND project. For instance, in the Czech Republic, the participants in online discussion fora hypothesised that several compounds could be a good substitute, given that MXE was banned (Drapalova & Belackova, 2016). Among the compounds which appeared in discussions on international fora as possible substitutes were MXP, MXM, 3-MeO-PCP, 4-MeO PCP, 3-MeO-PCE, Ephenidine and Diphenidine.

When it comes to the ''replacement'' effect on the supply side of the market, several of the e-shops that were active in December 2015 were offering an ''analogue to MXE'' being MXP ($n = 4$), others were offering ''replacement for MXE'' being deschloroketamine ($n = 2$), and some were offering either of the two without any reference to MXE ($n = 4$). Out of these e-shops that were offering either of the two ''analogues'', several were offering MXE at the same time ($n = 4$), while others did not have MXE in stock or were not listing it at all at that time ($n = 6$).

This together suggests that while new substances are emerging on the market, attributing them to a particular compound or even its ban is a complex issue. In order to measure the full consequences of compound control, more conceptualisation and firm criteria for ''replacement'' need to be set up and a comprehensive research design would be needed to capture this effect.

Limitations and methodological considerations

One of the limitations of attributing an effect to country-level bans is the lack of measures that could indicate the level of control enforcement in time and across the countries, which has been a limitation of many studies in the arena of drug policy (Ritter, Livingston, Chalmers, Berends, & Reuter, 2016).

Another limitation on assessing the effectiveness of a ban on certain compounds in terms of limiting their online availability is that the e-shops in this study cannot be seen as specifically ''Czech'', ''Polish'' or ''French'', as a simple translation of the e-shop or some of its pages would make it appear in the search for a different country (or language). Also, the cross-border nature of NPS e-shops can best be demonstrated through UK searches, as many NPS users in the EU use English to make their online purchases despite it is not their native language (Drapalova & Belackova, 2016). Thus, the UK search outcomes might as well be sensitive to EU-level or international legislative developments or to individual bans in other EU countries than to the legislation in the UK.

A number of methodological decisions have been made around the indicators used in this analysis, and these have to be considered in future research. The number of e-shops (an indicator of ''accessibility'') will depend on whether the researchers chose to consider all the search outcomes achieved using selected key words or whether they exclude some of them if they are not properly translated. Additionally, numerous e-shops chose to be displayed under a multitude of URLs, in order to maximise their online visibility; the number of unique shops (presented in this paper) could be as low as 67% of the total search outcomes; see (Martinez et al., 2016). Thus, the figures will differ according to whether only unique e-shops are presented or not. Additionally, when one is searching for e-shops offering particular compounds, the actual availability of these compounds should be verified directly on the e-shop web pages, alongside country-level shipping restrictions on these compounds.

All the steps described above were taken in this analysis, thus reducing the number of search outcomes. The rather low number of outcomes does not permit the analysis of e.g. the statistical significance of the observed trends. This ''small sample'' limitation is most apparent with regard to the ''low-profile'' compounds (25I-NBOMe, AH-7921), which yielded probably the most striking patterns of online availability, accessibility and popularity (in terms of having newly appeared in countries that had banned them or of being relatively highly ranked by Alexa).

Additionally, a number of technical features of online searches administered through conventional search engines (e.g. Google.com) were beyond our control. Thus, the findings have to be understood within the scope of their volatile nature.

Finally, it was beyond the scope of this study to test whether the product would actually arrive when ordered, or whether it would contain the compound which was advertised. Some of the vendors could, in fact, be a scam, and substances which appeared to be available to purchase might never reach their buyers.

Conclusions

This analysis suggests that when it comes to the online market with NPS, the power of policies introducing national-level control laws is limited. In some countries, the online ''availability'' of selected NPS increased after control measures were introduced (where the compounds were newly offered) and mostly, fluctuations in availability and accessibility of the e-shops with NPS in this research did not seem to be linked to national-level bans. It is possible that the national-level control laws within the EU have shifted some e-shops' IP addresses away from the EU – which matters little to the consumers. A decrease in ''accessibility'' of the four compounds, as measured by the number of e-shops offering them, didn't correspond to the national-level bans, but could have been influenced by other control laws, such as those in producing countries. Lastly, e-shops seemed to counterbalance their low or decreased numbers by their rather high ''popularity''; this suggests that even if the number of e-shops decreases, those that remain are likely to be visited more by the consumers.

This analysis has pointed to the range of indicators that are feasible and meaningful for the purpose of RA procedures and in evaluating the impact of control measures (accessibility, availability and popularity). Semi-automated monitoring tools not only offer the possibility of collecting all these efficiently, but also allow timely information to be collected. It is, however, important to triangulate the monitoring of the surface e-shops with data from other sources. While it is

apparent that some compounds appear on other markets too and that alternative substances to those under control are emerging, it remains a challenge to further conceptualise and measure the ''displacement'' and ''replacement'' effects. This would help to go beyond the scope of the present paper in assessing whether and to which extent emergence of new, potentially harmful compounds is associated with control laws as their ''unintended effect''.

Assessing the impact of laws controlling the online availability of 25I-NBOMe, AH-7921, MDPV and MXE – outcomes of a semi-automated e-shop monitoring

Declaration of interest

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