

# Legal Approaches to New Psychoactive Substances: First Empirical Findings

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## Abstract

**Background:** Generic drug legislation, i.e., simultaneously banning groups of drugs, has been introduced worldwide to counteract the trade and use of emerging “new psychoactive substances” (NPSs) more effectively. **Summary:** The potential and de facto positive and negative effects of generic drug legislation have been described using an analysis based on documented evaluations of the experiences in the UK and Germany, supplemented with data from other publicly available sources. In particular, the effects of generic drug legislation on availability, use, sales, and overall health harms of NPS, and switches from NPS to traditional (classical) drugs are addressed. The results show that the introduction of generic drug legislation in the UK and Germany has enabled stricter regulation of NPS but has also led to some major harms within the domain of public health. Depending on the population considered, the rate of NPS use remained stable, slightly declined, or increased following the banning of NPS. Once banned, NPSs were more often purchased on the black market, often together with other (more harmful) drugs. Moreover, NPS-related harms did not reduce following the ban, and in some cases even increased. Finally, when harmful NPS, like potent synthetic opioids and cannabinoids, become substantially used and endanger public

health, legislators already have the legal means to ban the problem drug, thus overruling the need for a generic ban. **Key Messages:** Generic drug legislation may facilitate drug law enforcement, but it is not (very) effective in counteracting NPS use and it may increase NPS-related public health problems. It is concluded that, overall, the advantages of generic drug legislation are overshadowed by its serious disadvantages.

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## Introduction

New psychoactive substances (NPSs) are typically structural or functional analogies of traditional recreational drugs – with similar pharmaco-toxicological profiles to the drugs they are designed to mimic – and may be less or more harmful. Most NPSs, notably synthetic cannabinoid receptor agonists (SCRAs) and cathinones [1, 2], are usually only temporarily or sporadically available on the European Drug Market, creating challenges for the orthodox and relatively slow process of risk evaluation and drug control whereby only specific substances are prohibited. Therefore, to counteract the emergence of NPS and reduce NPS-related public health risks in a precautionary and more effective manner, several countries (including most European countries) have introduced generic drug

legislation (GDL) by which we mean here a pre-emptive ban on certain groups of drugs (however defined) [3, 4]. Several variants of GDL exist, including those focusing on generic definitions of a molecular core structure, and those defining NPS with reference to the physiological/psychopharmacological effect on the user.

The efficacy, advantages, and disadvantages of GDL have – to our knowledge – been evaluated in only two countries: the UK (Psychoactive Substances Act 2016; PSA) and Germany (“Neue-psychoaktive-Stoffe-Gesetz”; New Psychoactive Substances Law; NpSG). While these frameworks share some similarities (both create bans on NPS backed by criminal sanctions), the PSA defines a group of “psychoactive substances” according to the effect on the user, whereas the NpSG’s groups are based on precisely defined chemical families of substances including substitution patterns in parent molecules [3]. For more detail about the specific measures of the two NPS laws, we refer to the respective published NPS drug laws [5, 6].

Due to these and other qualitative differences between the two legal frameworks, we do not seek to directly compare them against one other. Instead, this article aims to augment previous research by considering the effects of GDL (broadly defined) in the only two European countries where such laws were evaluated. This article outlines the potential pros and cons of GDL, before critically discussing the effects of the PSA and NpSG with reference to the prevalence of NPS use; NPS sales; NPS-related harms; NPS users’ switch to traditional drugs; and NPS-related criminality. Global initiatives are then considered before a concluding discussion.

### Potential Advantages and Disadvantages of GDL

Legally speaking, the main advantage of GDL is that the list of prohibited drugs does not require continuous risk evaluation and legislative updating when new NPS emerge. This theoretically enables law enforcement agencies to immediately seize new NPS and efficiently prosecute those involved in their production and supply. However, definitions of NPS which relate to the psychoactive effect on the user can cause interpretive problems and create obstacles for law enforcement, as it can be difficult conclusively to say what effect a specific chemical will have, even with expert advice. Additionally, banning entire families of chemicals may hinder legitimate medical and industrial research [7], including designing safer recreational drugs and drugs with therapeutic applicability. Even where GDL provides specific exemptions for scientific research, qualitative evidence shows that the existence of a serious criminal offence

disincentivises institutions and individuals from conducting research with banned compounds [8, 9]. Moreover, in contrast to orthodox drug legislation, banning substances via GDL implies absence of a risk evaluation of the substance in question, arguably creating a legislative focus on improved drug enforcement instead of public health [10].

GDL arguably plays an important symbolic function in discouraging NPS use and thereby reducing NPS-related harms. Introducing GDL may increase awareness of NPS’ potential adverse health effects and/or remove the motivation to use drugs that are not illegal. However, measuring the prevalence of NPS use is difficult as: (1) the NPS market strongly fluctuates with new NPS appearing and disappearing within 1 year; (2) users are often unaware which specific NPS they use; and (3) certain groups such as the homeless are not captured in prevalence surveys. Determination of NPS-related harm is also difficult because – as a definitional group – “NPS” includes myriad substances with greatly variable (and especially in the long-term, often unknown) toxicological effects. For instance, opioid-type NPS and SCRA’s carry significant health risks, whereas cathinones are far less harmful. Additionally, the data on NPS-specific harms are of generally low validity because many NPS users are polydrug users [10–12], consuming different drugs concomitantly, which obfuscates accurate diagnoses. Although reported numbers of fatal/non-fatal incidents can be used to estimate the (changes in) a drug’s public health impact [13], NPS-related cases often refer to small samples and are not usually toxicologically confirmed because hospital drug screens cannot detect all NPS. Finally, NPS’ legal status may play only a minor role in users’ decisions to use NPS [11], and therefore the symbolic function of GDL has previously been criticised in general and specific terms [8, 14].

### Evaluation 1: The UK’s PSA

Table 1 summarises the following evaluation. The PSA came into force on May 23, 2016. Subject to limited exemptions such as food, ethyl-alcohol, caffeine, nicotine, and already-controlled drugs, the PSA’s definition of a “psychoactive substance” is any substance “which is capable of producing a psychoactive effect . . . if, by stimulating or depressing the person’s central nervous system, it affects the person’s mental functioning or emotional state.”

The UK Home Office Report (HOR) on the effects of the PSA was published in November 2018, i.e., 18 months after its introduction [15]. It concluded that, overall, the PSA had achieved its main goals of: (1) ending NPS sales;

**Table 1.** Summary of observed effects following the introduction of generic drug legislation

Parameter	UK, England-Wales, or Scotland	Germany
Legal availability	Decrease	Decrease
Use prevalence	Decrease in adults and 16–24 year olds but minor increase in vulnerable users including children and prison inmates	No change in adults but increase in adolescents/young adults and inmates in prisons
NPS-related intoxications	No evidence for decrease in analytically confirmed SCRA hospitalisations *	Decrease but invalid data **
NPS-related DRD	Increase	Decrease
Addiction treatment demand for NPS-related problems	No change in adults, large decline in youngsters (<18 yrs.), and increased among the homeless	No change
Sales of NPS	Shift to street markets and dark web cryptomarkets	Reduced quality of NPS and shift to street markets and Internet
NPS-related criminality	Insufficient data but increased supply of NPS by organised criminal groups	Increase in possession and trafficking-related offences <sup>#</sup>

\*SCRA, synthetic cannabinoid receptor agonist, \*\* Most cases were not analytically confirmed; mainly due to polydrug use.  
<sup>#</sup> Concerns “first generation” drugs regulated by Betäubungsmittelgesetz (BtMG); number of offences regulated by NpSG increased by 495 in 2017 and 771 in 2021.

(2) ending the game of cat and mouse whereby new NPS emerged faster than the government could ban them; (3) reducing NPS use; and (4) reducing NPS-related harms. More recently, Burgess [8] evaluated the PSA and the HOR’s conclusions, criticising the latter’s findings and arguing that the PSA has, in fact, failed to achieve most of its goals.

### NPS Use

#### General Population

The Scottish Crime and Justice Survey asked adults whether they had used “legal highs” (NPS) before and after the PSA introduction. Prevalence decreased significantly from 0.39% in 2014/15–0.26% in 2019/20 [16, 17]. The Crime Survey for England and Wales also reported a significant decrease among adults aged 16–54 from 0.9% in 2014/15–0.4% in 2021/22, and in 16–24 year olds from 2.8% to 0.9% [18].

#### Vulnerable Subpopulations

The HOR noted no statistically significant pre/post-PSA change in NPS use among UK youngsters aged 11–15 [15]. NPS use remained largely unchanged among predominantly English users aged under 25 [19]. A 2018 Scottish Government survey indicated a small increase in 15-year-olds using and being offered NPS compared to 2015 [20, 21].

NPS use in UK prisons remains a major problem post-PSA [22, 23]. The percentage of positive results from random mandatory drug tests (rMDTs) for non-NPS drugs was relatively stable over several years, but when

NPS were included the total positive drug tests rose from 9.3% in the 12 months before March 2017 (before the inclusion of NPS in the national rates) to 21.3% in the 12 months before March 2018. NPS were present in 60% of all positive samples in March 2018 [24].

The HOR noted mixed findings on NPS prevalence among the homeless. However, the UK Advisory Council on the Misuse of Drugs and the European Monitoring Centre on Drugs and Drug Addiction (EMCDDA) reported high levels of UK homeless NPS use post-PSA [25, 26]. Additionally, adults presenting for NPS treatment in England with a housing problem increased from 32% in 2015/16 to approximately 45% in 2017/18 (and has since remained stable), while overall treatment numbers have decreased [27], suggesting increased problematic NPS use among the homeless post-PSA. Whether NPS use is a symptom, cause, or both of homelessness is unclear [8], and evaluation of homeless NPS prevalence is complicated by an apparent spike in English, Welsh, and Northern Irish rough sleeping levels in 2017/18, i.e., about 2 years after the enactment of the PSA [28].

#### NPS Sales

Over the preceding decade, face-to-face purchases of illicit substances from individuals or headshops (retailers selling drug paraphernalia and NPS) have been gradually displaced by internet-based sales. The precise impact of GDL on this is unclear [29]. In 2013, there were some 250 brick-and-mortar headshops and 100–150 online UK NPS vendors [30]. Post-PSA, most visible sales of NPS from physical headshops ceased (and many online

suppliers) closed down or stopped UK NPS sales [15, 31]. Nonetheless, headshops and the internet remained important sources of NPS post-PSA, and the number of people obtaining NPS from a stranger/street dealer significantly increased [15]. The internet (particularly the dark web) may now be a platform for marketing NPS [32], and NPS are now easily ordered via e-commerce. By “pushing” NPS sales to street markets and the internet, the PSA may have encouraged increased use among vulnerable populations including adolescents and the homeless [15], thus increasing harms among them [33, 34]. Furthermore, the closure of headshops has precipitated negative changes including aggressive sales/delivery practices among dealers, lower and unstable NPS quality, and increased potency of NPS [34]. Some discrepancies were also noted between the goals stated in the HOR and those stated pre-enactment. For example, the HOR stated the PSA’s goal was to end open sales, but the Act was intended to curb open and clandestine sales [30].

#### NPS-Related Intoxications

Enquiries made by health professionals to the UK National Poisons Information Service about NPS declined post-PSA but had already been on a downward trajectory pre-PSA [35]. A recent study of toxicologically confirmed UK SCRA hospitalisations found no clear evidence of an upward or downward trend in the rates of severe intoxications [36]. Since 2014/15 there has been a declining trend in psychostimulant-related hospitalisations in England [37], but the specific psychostimulants are not identified in the data and presumably include many non-NPS stimulants. There is some evidence of increased NPS-related ambulance call-outs post-PSA [8], and the integration of SCRAs into the existing street market has probably increased demand for drug-related emergency services [34].

These changes cannot be causally attributed to the PSA with certainty. Enquiries to the National Poisons Information Service may have declined as medical professionals have become more familiar with common NPS, and the trends in hospital statistics often predate the PSA and are complicated by obscure definitions/grouping of drug types. The HOR’s claim that the PSA’s goal of reducing NPS-related harms “has been achieved in the main” [15] may be true for NPS-related non-fatal incidents, but as shown below this cannot be said for NPS-related deaths.

#### NPS-Related Drug-Related Deaths

Pre-PSA, the number of NPS-related related death (DRD) in the UK was relatively low. Although there were 68 NPS-related DRD in 2012, many of these were actually caused by substances already controlled under

the Misuse of Drugs Act 1971 and not by the NPS which became subject to the PSA 4 years later [38, 39].

Scottish NPS-related DRD rates had gradually increased since the 1990s but skyrocketed following the PSA’s introduction from 74 in 2015 (pre-PSA) to 286 in 2016; 337 in 2017; and 575 in 2018. The latest figures show that NPS-related DRD reached 825 in 2021, accounting for 62% of all Scottish DRD. In about 65% of these, a benzodiazepine-type NPS (“street benzos,” e.g., etizolam) was implicated in combination with (classical) opioids [40, 41]. It is important to note that the reduced prescribing of benzodiazepines by doctors (which predated the PSA) may have encouraged demand for “street benzos” [42]. NPS-related DRD in England and Wales halved in the year following the PSA’s introduction from 123 in 2016 to 62 in 2017 but have since climbed to 258 in 2021 [43]. In England, Wales and Northern Ireland, NPS-related DRD increased by 222% in the 3 years post-PSA compared to the preceding 3 years, while non-NPS DRD increased by only 8% over the same period [44]. The number of deaths where SCRAs (as well as benzodiazepines) was implicated and/or detected post-mortem have steeply increased post-PSA [43, 45].

These increased DRD rates could be variously attributable to the higher incidence of polydrug use, higher UK prevalence of licit/illicit opioids, and/or deteriorations in the coverage and quality of addiction services [41], but the PSA has evidently failed to reduce NPS-related DRD. Lastly, it is worth noting that the claim policymakers often advance that all NPS are dangerous as they are often implicated in DRD [15] could be misguided, or at least paints in too-broad brushstrokes. For example, in the (common) cases of DRDs involving co-use of benzodiazepine-type NPS and opioids, the opioid likely caused the death rather than the less toxic NPS.

#### NPS-Related Addiction Treatment

The HOR noted a post-PSA decline in the number of patients entering treatment for NPS-related problems [15]. The number of under 18 s in treatment in England for NPS as a primary substance declined by 90% between 2015/16 and 2020/21 [46]. Between 2014/15 and 2015/16 (pre-PSA) the number of patients (all ages) in treatment for NPS-related problems in England rose from 1154 to 2042, but rates have since roughly stabilised at 2014/15 levels, with 1186 in 2021/22 [47]. This suggests that the PSA may have prevented a continued upward trend, but has not been successful in reversing it [47, 48]. However (as noted above), the number of those with housing problems undergoing treatment for NPS-related problems rose sharply post-PSA: of all patients entering

treatment, those with NPS-related problems had the highest proportion of housing needs, increasing from 19.2% in 2013/14 to 41.9% in 2021/22 [47].

#### Switch to Other Drugs

Corresponding with the HOR's statement that some NPS users switched (back) from SCRAAs to (safer) natural cannabis post-PSA [15], NPS users appear to have gradually returned to "traditional" stimulants such as MDMA (ecstasy) and cocaine. Particularly among (but not limited to) vulnerable users, there is evidence of a switch from NPS to traditional drugs due to the increased price of NPS [49, 50]. As previously noted, national UK surveys reported a decline in NPS use among 16–24 year olds, while the use of both cocaine and MDMA (somewhat) increased between 2015/16 and 2018/19: powder cocaine from 4.4% to 6.2% and MDMA from 4.5% to 4.7% [18]. Additionally, a UK wastewater analysis study conducted between 2014 and 2018 found a post-PSA increase in traditional drug consumption, especially of cocaine and ketamine, which the authors suggested indicated a shift away from NPS – although the study did not seek to analyse contemporary NPS, focusing only on mephedrone which was controlled under the Misuse of Drugs Act 1971 in 2010 and thus never controlled by the PSA [51]. However, as correctly acknowledged by the HOR, due to a lack of determinative information on the extent to which NPS users have switched to other substances it is not possible to say whether the PSA has led to an overall reduction in drug-related harm [15].

#### Criminality

Whereas pre-PSA there was "little evidence of NPS use driving crime and disorder" [30, 52], and the EMCDDA and Europol found no evidence for involvement of established organised criminal groups in the NPS trade [53], a merging of markets has occurred post-PSA whereby organised criminal groups now supply NPS in addition to traditional drugs [34]. Combined with the apparent switch from NPS to traditional drugs like cannabis, ecstasy, heroin, and cocaine, this implies an increase in serious and organised crime. Almost immediately after the PSA came into force, the UK National Crime Agency identified "county lines" dealing in NPS. This is where criminal gangs exploit vulnerable people to expand from cities to smaller towns and is linked to intimidation, serious physical violence, the use of firearms, human trafficking, and child sexual exploitation [54]. However, the HOR found no evidence of increased NPS-related violence and/or acquisitive crime due to the lower availability and increased prices of NPS [15].

## Evaluation 2: The German NpSG

Table 1 summarises the following evaluation. The NpSG came into force on November 21, 2016. The NpSG batch-wise bans seven chemical families of NPS, each defined by a specified chemical "backbone," plus their possible chemical substituents. The NpSG was evaluated by the "Institut für Therapieforschung," Munich (Institute for Therapy Research, IFT), and its findings were reported by Kraus et al. [55] in 2019, i.e., nearly 3 years post-NpSG introduction. In contrast to the HOR's findings in relation to the PSA, Kraus et al. [55] noted few positive effects of the NpSG. The German evaluation was, however, less detailed than the HOR, and focused primarily on the prevalence of NPS use, acute intoxication rates, forensic psychiatry, and violations of the NpSG.

#### NPS Use

##### General Population

In Germany, two surveys among 9,204 (in 2015) and 9,267 (in 2018) adults aged 18–64 showed stable rates of NPS use at 0.9% and, thus, no effect of the NpSG [56].

##### Vulnerable Subpopulations

Between 2015 and 2019, NPS use among those aged 12–25 increased from 0.0% to 0.3–1.5% [55, 57]. Like in the UK, NPS use is popular in German prisons. Between 2016 and 2018, the most-used drugs by German prisoners were SCRAAs (86–97%) [55]. For SCRAAs, a urine positive rate of 48% (of 927 samples) was reported in German prisons in 2015/16, which post-NpSG (2017–2018) decreased to 30% (of 1,877 samples), although at the last time point in the study (2018) the rate rose again to 35% [55]. The German evaluation report presented no data on the prevalence of NPS use among the homeless.

#### NPS Sales

Headshops still exist in Germany post-NpSG but are no longer allowed to sell NPS. Users have now switched to other sources. A survey of 663 NPS users showed that since the NpSG's introduction, only 6% purchased NPS from headshops, whereas 61% obtained NPS through the internet [58]. The IFT evaluation found that while street dealers were a minor source of NPS in 2016, accounting for 15% of sales, by 2017 they had become the main source of NPS with 56% of sales, which rose to 72% in 2019 [55]. German NPS users reported that the introduction of the NpSG was accompanied by a reduction in the quality of NPS [55, 56], which may have contributed to an increasingly negative image of NPS use [55]. This reduction in quality encouraged German users to reduce their use of (certain) NPS,

switch to other (potentially more dangerous) NPS, return to traditional drugs, and/or change their supply channel (mostly to the online and street markets). Therefore, closing headshops may have contributed to a reduction of the availability and sale of NPS (one of the NpSG's intended goals), but it appears that at least some NPS sales have shifted to (dangerous) clandestine markets.

#### NPS-Related Intoxications

The total number of German DRD between 2016 and 2019 was stable at around 1300, but the proportion of DRD in which NPS was involved (including in combination with other drugs) significantly decreased from 5.7% to 1.4%. DRDs where NPS were the sole drug involved also decreased, from 2.6% to 0.6% [59, 60]. Nine deaths involving SCRA were reported in 2020 [2]. However, like the HOR, the German evaluation concluded it is impossible to know whether the NpSG resulted in an overall reduction in drug-related harm [55].

#### NPS-Related Addiction Treatment

In Germany, the number of people entering treatment for NPS-related problems is presumably underestimated. Data from addiction services (outpatient and inpatient counselling and treatment) indicated no change in demand of people with NPS-related problems between 2016 and 2018, i.e., since the introduction of the NpSG [55]. In virtually all cases where NPS are mentioned, NPS use was not the primary diagnosis for entering addiction treatment, but rather it was co-use of NPS (mainly SCRA) with traditional drugs within the preceding 12 months [55].

#### Switch to Other Drugs

The NpSG did have an impact on NPS users' behaviour. For example, novel substances have emerged circumventing the NpSG, which – according to users – has led some users to reduce NPS use and others to adopt more hazardous consumption patterns [56]. When German NPS users were asked what impact the introduction of the NpSG would have on their future consumer behaviour, 78% expected that the rate of traditional drug use would remain the same and 5% thought it would decrease. The use of NPS was expected to remain the same or decrease according to 72% and 27% of respondents, respectively [55]. Actual pre/post changes in NPS use after the introduction of the NpSG were not assessed.

#### Criminality

Simple possession of NPS for personal use outside custodial settings is not a criminal offence under the PSA, whereas under the NpSG simple possession of NPS is

prohibited, only by administrative law, i.e., possession of NPS is formally forbidden but is not enforced [55]. However, per the German Narcotics Act (BtMG; “Betäubungsmittelgesetz”), a prohibitive law following the orthodox approach of banning individual substances, possession of “first generation” NPS such as the SCRA JWH-018, benzylpiperazine, and mephedrone is illegal and is still enforced. In 2021, a total of 361,048 drug-related convictions (78% dealing/possession-related) were reported in Germany [60]. NPS-related offences increased between 2020 and 2021. For NPS controlled under the BtMG, possession-related offences increased between 2018–2021 from 2,609 to 2,925 and trafficking offences increased from 293 to 726. Notably, the number of NpSG violations increased from 361 in 2018 to 771 in 2021 [56, 60].

### Conclusion Based on the Two Evaluations

The evaluations of GDL in the UK and Germany show that these legal approaches have enabled stricter regulation of NPS but have largely failed to reduce NPS-related harms (Table 1). Depending on the population considered, the rate of NPS use remained stable, slightly declined, or increased following the GDL. Once banned, NPS are more often purchased on the black market, often together with traditional drugs. In the UK, no conclusive downward trend in severe NPS intoxications was observed post-PSA, but NPS-related intoxications seem to have decreased in Germany. Since the PSA's introduction, there has been a significant and sustained increase in homeless people undergoing treatment for NPS-related problems. In the UK, the number of NPS-related DRDs has steeply increased since the PSA, though other factors may have contributed to this. In Germany, the number of NPS-related DRDs was and remains very low.

#### Global Initiatives

In 2019, China introduced GDL to restrict the production and trafficking of illicitly manufactured fentanyl (IMF) and their analogues, 1 year after scheduling two specific fentanyl precursors [61]. This measure prompted a drastic reduction in direct shipments of IMFs from China to the USA, but it did not stop the IMF-fuelled opioid crisis in North America, mainly because: (1) these NPS are often purchased and shipped in untraceable small quantities [62]; (2) IMF shipments were rerouted through Mexico [63, 64]; (3) some fentanyl precursors needed for the synthesis of therapeutic drug were exempted [65]; and (4) IMF production and trafficking was taken over by crime syndicates

[66] in countries including India and Myanmar [65]. A 2019 UNODC report noted that IMFs were identified in samples sold as heroin in cryptomarkets from a variety of European vendors [67]. Interestingly, no new IMFs were detected in Europe in 2021 [2].

Neicun et al. [59] recently evaluated the effectiveness of different legal approaches in preventing NPS use and NPS-related acute poisonings and fatal overdoses between 2008 and 2019. Their analysis showed that regardless of the regulatory model adopted, policy measures implemented across 10 European countries have not been particularly effective. Conversely, they have been accompanied by increased levels of toxicity and health harms for users. The study also found that scheduling individual substances was the most effective means of preventing NPS use, at least in the short term. Collectively, these observations indicate that the production and market availability of NPS is a global, complex, and disruptive issue which cannot be stopped by GDL, although it may have some effect on drug trafficking from NPS-producing countries.

#### *Limitations of the Study*

Before moving to the discussion we wish to reiterate the limitations of this study. Firstly, both empirical evaluations that were reported here refer to different forms of GDL, albeit both laws have similar goals and there is overlap in the substances proscribed. Secondly, the effects described here relate to two populations with differences in demography, drug use patterns, and socio-economic determinants. For these reasons, as noted in the Introduction, we are not comparing the PSA and NpSG with one another but describing the pros and cons of different types of GDL. Thirdly, while these two empirical evaluations offer some of the best available evidence, general populations surveys and hospital statistics have known reliability issues. More thorough and accurate evidence gathering for all drug use is needed. A major limitation of this study is that the effects have been evaluated in two different populations which show differences in demography, drug use pattern, and social-economic determinants.

### **Discussion and Conclusions**

To summarise, we have shown that the introduction of GDL in the UK and Germany had some intended positive (legal) effects but also some serious negative (public health) effects (Table 1). With respect to NPS, GDL was selected as a key strategy to primarily reduce the availability of NPS. GDL does indeed enable more efficient drug enforcement due to its precautionary approach

of pre-emptively banning all NPS. Unfortunately, the introduction of GDL increased the prevalence of use in certain vulnerable groups in the UK and Germany, though in the general adult population NPS use decreased or remained stable, respectively. It seems that the availability of NPS was not affected, likely because legal sales of NPS were replaced by illegal sales via street dealers and e-commerce. The evaluations performed in the UK and Germany showed that the goals directed at harm reduction were either not or only partly accomplished, and some serious public health outcomes were seen post-PSA.

Certain NPSs, like IMFs and potent SCRA, are evidently more harmful than their parent compounds heroin and THC, respectively. Indeed, opioids are implicated in the majority of DRD in the USA and Europe [68, 69], so the partial success of national efforts to limit their production in and trafficking from China and India should not be readily dismissed. However, as outlined here, despite the legal benefits of GDL, it is no panacea for NPS regulation and carries important public health risks. We, therefore, propose that alternative options should be pursued and studied. NPS control laws can only be optimised by allocating sufficient resources to overcome the knowledge gaps due to the limitations of datasets on NPS prevalence, harm, etc., which hamper a meaningful evaluation of a particular law's impact.

Finally, one may question the importance of NPS, which has preoccupied drug policymakers as a dominant and distinct theme [70] and why policymakers seem to oversell the effects of NPS control laws. NPSs are arguably an over-estimated phenomenon with only a few molecules having established in niche markets and only among small specific groups [71]. In conclusion, it seems somewhat incongruous to focus so exclusively on strengthening law enforcement at the expense of harm in the public health domain, which puts doubt on the added value of generic drug laws.

### **Conflict of Interest Statement**

The authors have no conflicts of interest to declare.

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### **Author Contributions**

J.A. led on the drafting of the manuscript. N.B. and W.B. submitted substantive input and feedback.

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