The Novel Psychoactive Substances in the UK Project: empirical and conceptual review work to produce research recommendations

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Scientific summary

Background

The Advisory Council on the Misuse of Drugs (ACMD) defined novel psychoactive substances (NPS) as: *"psychoactive drugs which are not prohibited by the United Nations Single Convention on Narcotic Drugs or by the Misuse of Drugs Act 1971, and which people in the UK are seeking for intoxicant use".* NPS use provides grounds for concern including: technological advances that outstrip legal controls; cheap availability through the internet as well as from traditional drug dealers; high levels of cultural acceptability of NPS use in the UK by international standards; large uncertainties surrounding the identity of individual substances purchased online and on the streets. Even when a new substance is clearly and accurately identified, there may be very little information on effects, the risks posed by use, and how these may be reduced. There are systems in place for monitoring the emergence of new drugs nationally and internationally. The key UK policy development has been the implementation of the Psychoactive Substances Act in the spring of 2016. Although the research literature is developing rapidly, it is unclear how far the NPS phenomenon has been considered in explicitly public health terms, and therefore also unclear is the extent to which existing evidence is able to inform public health responses.

Objectives

Three specific objectives of the NPS-UK project were to:

1. Summarise and evaluate what is known about NPS use, related harms and responses.
2. Develop a dedicated conceptual framework for a public health approach to NPS use.
3. Make recommendations on key evidence gaps and priorities for future research.

Methods

The project comprised two main study components: a review of existing research (objective 1), and the development of a conceptual framework (objective 2). The conceptual framework

was developed in part to assist with the narrative synthesis of the data from the empirical review. It was then used for the construction of a robust assessment of key evidence gaps and research priorities, and articulation of the key issues facing public health intervention research (objective 3).

Evidence synthesis

Electronic databases were searched between 1st January 2006 and 29th June 2016 inclusive: MEDLINE, Embase, PsycINFO and Science Citation Index. Searches for grey literature included a google search for “novel psychoactive substances”, “new psychoactive substances”, and “legal highs”; hand searching of relevant UK and US websites; and contacting experts. Primary studies, secondary studies involving the analysis and interpretation of primary research, and discussion papers with data on NPS use, problems or responses, and published in English language, were included.

We conducted a scoping review of all relevant material to map the available evidence. We used these data to conduct an evidence gap analysis based on a set of *a priori* research questions. The literature as a whole was judged to be at such an early stage of development that the benefits of conducting detailed risk of bias assessments were not justified. The evidence gap analysis informed decision-making on the selection of bodies of evidence for narrative synthesis. The four selected areas were those pragmatically judged most promising for syntheses (for example, in terms of UK relevance and sufficient depth of data) that would support the development of research recommendations.

Conceptual framework development

This work was done iteratively in two main stages. We began by examining the nature of contemporary evidence-informed public health, and possible similarities between NPS and other complex multi-sectoral public health challenges, as well as with tobacco, alcohol and illicit drug use. We then developed a preliminary hypothetical public health approach to NPS. We identified possible research data needs to complete the first stage of this work. We then utilised this Stage 1 version to interpret the data from the empirical review. Following the

completion of the review work, we updated the conceptual framework in light of the empirical data in Stage 2. Because of the early stage of development of the empirical literature we made few substantive changes to the conceptual framework, and exercised caution in using it as a basis for research recommendations.

Research recommendations & public involvement

Research recommendations were developed from two distinct data sources. Firstly, research recommendations made by authors of primary studies in the existing literature selected for narrative synthesis were thematically coded. Secondly, we used the conceptual framework (developed prior to the review work and informed by wider public health sources of evidence) developed by the authors to identify what may be missing from this literature. Data from these two sources were then combined. Both earlier parts of the process and the research recommendations themselves were discussed in public engagement work involving policy makers, researchers and Novel psychoactive substance (NPS) users and user carers as stakeholders in informing the study design and processes, interpreting the findings, and validating the study recommendations.

Results

Scoping review

995 in total studies met the inclusion criteria. We mapped, and made extensive use of cross-tabulation to characterise the literature according to a set of analytic categories developed *a priori*. We also assessed evidence gaps in the literature according to *a priori* research questions to prioritize which research areas should be synthesised in more detail. We found little data on social and other risk factors, population-level risk factors, harms associated with long term NPS use, provision and effectiveness of prevention interventions, and treatment outcomes for NPS users. We undertook more detailed narrative syntheses as follows on: surveys on the prevalence and patterns of NPS use in the UK; UK qualitative studies on the patterns and harms associated with NPS use; systematic reviews (largely comprising data on harms associated with NPS use); and evaluations of policy responses to NPS use.

Narrative synthesis

UK survey data

We identified 29 studies. The most robust nationally representative data was for mephedrone (Crime Survey for England and Wales (CSEW) and the Scottish Crime and Justice Survey (SCJS) have been conducting national surveys since 2010-2011). Lifetime mephedrone use is uncommon in adults (approximately 1-2%) but is about two to three times more prevalent in men than women, and also young adults compared with older adults. Prevalence rates of recent mephedrone use are declining substantially. Nationally representative data on NPS use as a whole and on particular NPS other than mephedrone are less developed, and comparisons across years are not yet possible. Nationally representative surveys of school children have found similar low prevalence for mephedrone use and NPS as a whole. Data on particular sentinel populations likely to be at greater risk of NPS are growing, though remain quite limited. The key contributions are the collation of existing UK survey data from multiple sources on multiple substances, and drawing attention to the diversity of prevalence rates and issues in interpreting reported findings.

Systematic reviews

Systematic reviews (n=10) mainly comprised summaries of clinical presentation data. Side effects of NPS were wide ranging, with psychiatric, cardiovascular, renal and gastrointestinal symptoms being the most commonly reported. Treatment of these effects appears to mostly involve observation and supportive care, and in severe cases may require hospitalization. We did not find population-level data on acute health harms with dedicated attention to prevalence and policy issues, or data on chronic health or social harms in a longitudinal context.

Qualitative studies of novel psychoactive substance in the UK

Qualitative studies on NPS use in the UK (n=7) are at an early stage of development. Existing studies show potential to provide useful information on issues such as drug effects and reasons for, and patterns of, use. Qualitative studies may make useful contributions to

behavioural epidemiological studies, and studies of drug market functioning and policy issues.

Responses to novel psychoactive substance use and problems/harms

Quantitative studies (n=17) evaluated the effects of legislative prohibitions of NPS use or supply on a number of outcomes including access, use, healthcare utilization and self-reported exposure and toxicity. Reductions in use, presentations or other outcomes were generally observed, though not always. Studies typically utilized simple counts of routinely collected data, particularly poison centre and hospital admissions data. Study designs were mainly before and after comparisons, without controls, which limits the basis for attribution of effects. Examination of the utility of routinely collected NPS data in different settings is needed and sources of information bias, and to evaluate pharmacovigilance and other data.

Conceptual framework

Stage 1

Our conceptual framework seeks to build upon concepts and approaches developed for drug use in general, as well as evidence-informed responses to other public health challenges which may be viewed as sharing similar features. Many contemporary public health challenges (such as health effects of climate change or obesity) are commonly conceptualised as requiring complex adaptive system changes that differ through the life-course. NPS may also be regarded in this way.

We provide a conceptual map of key individual-level risks and harms due to NPS adapted from those developed for other forms of drug use (*see Figure 1*). Apart from acute effects, most forms of risk of harm accumulate over time with continuing use. Harms to individuals, whether they are health-specific or wider harms, are strongly shaped by environmental and contextual influences, dynamically interacting with life-course stages. Intervention targets for prevention extend beyond those proximal to acts of drug use, as attention is warranted to social structural influences that shape individual risk. Other drug use, both licit and illicit, is

expected to be implicated in production of harm where other drugs are being used, and it will be rare that none are.

Problems also manifest themselves at levels beyond the individual user, for example involving family members and local communities. Harms to society include the costs of health care, crime and law enforcement. Health impacts incurred by NPS users can be aggregated with measures of physical and/or mental health, lost Quality Adjusted Life Years (QALYs).

Stage 2

The empirical review findings indicated that the existing literature, although large, is at an early stage of development, and there is currently meagre data to inform directly what we hypothesised to be an evidence-informed public health strategic response to NPS. The hypothesised needs for research to inform public health responses have not yet been met. The conceptual framework itself was thus not significantly altered in Stage 2, as we found no reason to make major changes. We took account of the hypothesised nature of our conceptual data in making research recommendations.

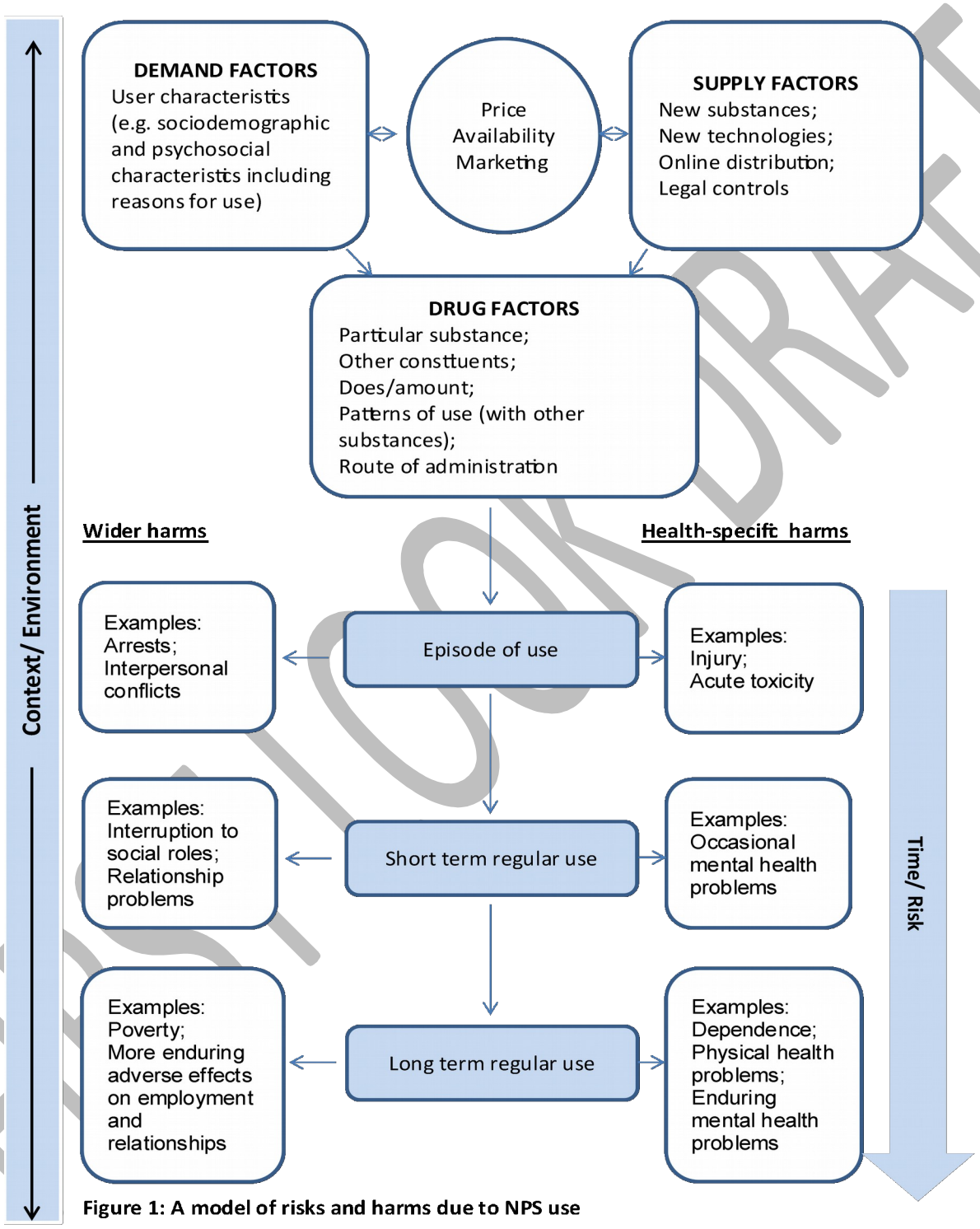

Figure 1: A model of risks and harms due to NPS use

Public involvement

Public involvement activities had demonstrable value in validating our study design, findings and research recommendations. The project was successful in engaging with policy makers and researchers at different stages of the research process. However, we were less successful with NPS user involvement, in part because the short term nature of the project offered restricted scope for investment in building relationships with NPS users over time.

Conclusions

There are 20 research recommendations presented as the principal conclusions of this study, of which there are 9 key recommendations as follows:

Pharmacology related research

1. Evaluate the effectiveness and sustainability of the existing pharmacovigilance system for NPS and the effects of planned innovations.
2. Evaluate the pharmacological, toxicological and related scientific base needed to inform the pharmacovigilance and public health surveillance systems.

Epidemiology and related research

3. Evaluate the effectiveness and sustainability of the existing public health surveillance system for monitoring NPS markets and other new online drug trends. This evaluation should cover monitoring actions, both quantitative and qualitative research, and associated commissioning arrangements, and be cognisant of opportunities for innovations such as test-purchasing new brands online as they become available.
4. Develop the behavioural epidemiology and related science of patterns and correlates of NPS use and problems in the context of alcohol, tobacco and other drug involvements.
5. Use cohort study designs to better understand the determinants of NPS use and related physical health, mental health and psychosocial problems, and how patterns of involvement and consequences change over time.

Interventions

6. Develop the science of prevention of NPS and other drug use. This should include evaluation of existing interventions and the development and evaluation of novel interventions addressing both proximal and distal determinants of NPS and related drug use, and how risks should be communicated to different groups.
7. Evaluate the public health impacts of legislative prohibitions of NPS use or supply, and other major policy initiatives.

Recommendations for research commissioners

8. Consider using the research recommendations presented here as a possible basis for conducting a formal research priority setting exercise using consensus development methods (such as those developed by the James Lind Alliance).
9. Evaluate existing strategic provision for, and develop as necessary, a long term planning system for research on NPS and other drug use.

Study registration

The systematic review element of this study is registered as PROSPERO CRD42016026415.

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