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Exploring multidisciplinary use of unlicensed medicines in primary and secondary care (EMULSION) study

Report to Funders

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NHS
Sunderland Clinical Commissioning Group

City Hospitals Sunderland NHS
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Acknowledgements

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We would also like to thank the organisations which enabled us to access these participants including City Hospitals Sunderland NHS Foundation Trust, NHS Sunderland Clinical Commissioning Group and Sunderland Local Pharmaceutical Committee.

Many thanks also goes to the UK Clinical Pharmacy Association, in particular Dr Sarah Carter and Pharmacy Research UK for their support and funding which allowed this project to take place and supported our development as early career researchers.

Study management

The steering group that was set up to oversee this study met at monthly intervals as set out in the original research proposal. Minutes are available from the study team on request.

Correspondence

If you would like any further information about this study, please contact the Chief Investigator, Gemma Donovan on gemma.donovan@sunderland.ac.uk or Co-Lead Investigator Lindsay Parkin on lindsay.parkin@sunderland.ac.uk

Background

An unlicensed medicine (ULM) is a product which does not have a marketing authorisation from the MHRA. ULMs include Specials, food supplements and imported medicines. They have not undergone the same regulatory processes as licensed medicines, including rigorous assessment of safety and efficacy. How and why prescribers choose to initiate these medicines, pharmacists source them and patients use them has never been explored.

Aim and objectives

- To explore the use of unlicensed medicines across primary and secondary care from the perspectives of prescribers, pharmacists and patients
  - To conduct an analysis of guidance documentation designed to support the use of unlicensed medicines
  - To describe experiences of prescribing, dispensing and taking ULMs
  - To explore perceptions of risks and benefits associated with ULMs
  - To identify concerns around use of ULMs
  - To discover any perceived improvements to ULM use in the NHS

Methods

This project incorporated three phases; an analysis of guidance documentation in existence in the UK to support the use of unlicensed medicines, qualitative exploration of the use of unlicensed medicines using face-to-face semi-structured interviews with prescribers, pharmacists and patients sampled across secondary care and focus groups to report the findings of the interviews and gather further data on the themes which were identified.

Guideline analysis

The guideline analysis included documentation from both primary and secondary care which was obtained from a combination of database searches and the use of a 'Call for guidance' which was distributed amongst local and national networks. The analysis incorporated both thematic analysis of the content of the guidance documentation and an assessment of quality using the AGREE II tool.

Qualitative study

A grounded theory approach was taken with the qualitative phases, using theoretical sampling to identify subsequent participants to interview and using constant comparison to develop themes from across the data sample. Participants were drawn from City Hospitals Sunderland NHS Foundation Trust, NHS Sunderland Clinical Commissioning Group and the wider NIHR North East and North Cumbria Local Clinical Research Network.

Ethical approval was obtained from the NHS West Yorkshire Research Ethics Committee and the University of Sunderland Research Ethics Committee. The IRAS reference is 15/YH/0191. This study was accepted onto the NIHR Health Services and Delivery portfolio (Reference number: 162518).

Results

Guideline analysis

With the use of thematic analysis it was revealed that the content varied across the sectors and between individual organisations. There were numerous themes which emerged during the analysis from which parent themes were elicited (Table 1). It also highlighted a potential lack of guidance documentation in primary care, including the community pharmacy setting due to the small number of submissions from these settings. The quality of the guidance documentation was also very varied according to the AGREE II scoring tool (Figure 1).

Parent theme	Sub-themes
Responsibility around the use of unlicensed medicines	Understanding the definitions around unlicensed medicines Awareness of patients and professionals when using an unlicensed medicine Responsibilities of individuals and organisations involved in using unlicensed medicines References to the guidance and legislation which informed guidance documentation
Operational issues with using unlicensed medicines	Selecting the pharmaceutical formulation Role of the pharmacist and the wider pharmacy team in managing the use of unlicensed medicines Patient involvement Stages of using an unlicensed medicine Continuing treatment
Risk versus benefit	Evidence to support use of unlicensed medicines Place of unlicensed medicines in the treatment of a patient and potential alternatives Describing and assessing risk Reporting of errors and adverse effects associated with unlicensed medicines
Controlling the use of unlicensed medicines	Costs associated with unlicensed medicines Audit of unlicensed medicines use Restricting use of unlicensed medicines Organisational decision making surrounding unlicensed medicines

Table 1: Thematic analysis: generated themes

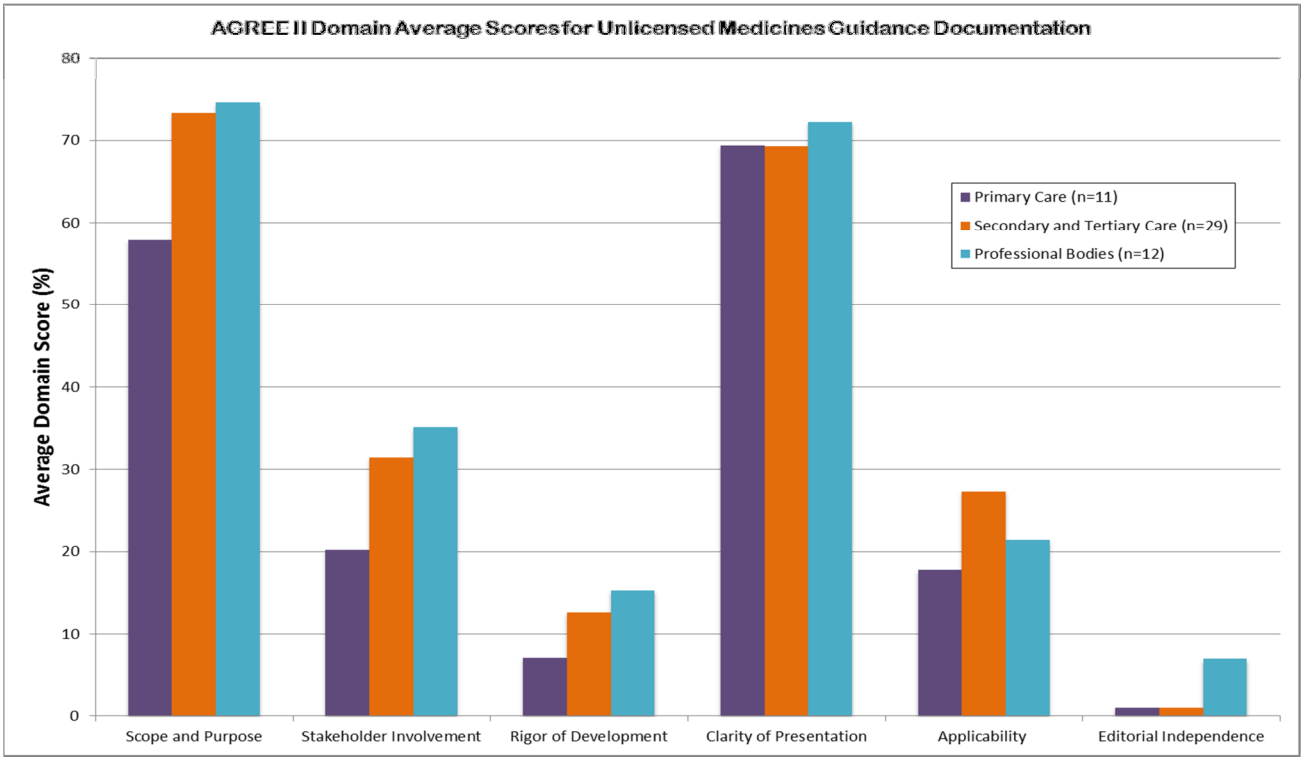

Figure 1: AGREE II domain scores for guidance documentation

Qualitative study

Several themes were identified across the data by healthcare professionals and patients in primary and secondary care, including:

- Healthcare professionals' awareness of when they were using an ULM and their definition of an ULM
- Perceptions of safety of ULMs was elicited, including the lack of safety and efficacy data compared to licensed products and the perceived under-reporting of adverse effects
- Provision of information and whether patients were likely to be informed about the unlicensed status of their medicines, who the person to inform them should be and what information patients would want
- The place of unlicensed medicine use in the clinical management of a patient, including whether licensed alternatives were tried first
- Trust as an important aspect in the use of unlicensed medicines. This was apparent throughout the interviews and between all actors

Lack of education and training for healthcare professionals around what an ULM is and the associated implications with their use, coupled with a lack of information seems to perpetuate problems identified in the use of ULMs. Cost implications associated with ULMs was a strong theme among primary care participants, however, many secondary care participants lacked an awareness of the associated costs which could lead to under-utilisation of viable alternatives.

Costly and burdensome regulatory processes for medicines licensing were often cited for the use of ULMs and seemed to legitimise their routine use in practice.

Discussion

The lack of marketing authorisation creates many issues in the use of ULMs, including a lack of access to information and reduced intelligence around their safety and efficacy. Despite this they are generally perceived as safe. The regulatory implications of using ULMs and the potential variability between products, does not seem to be well understood. Consideration of how the patient will use the medication and the provision of suitable written information seems to be inconsistently considered. There is a need for training and the development of mutually agreed standards on the use of ULMs to be created to inform a more consistent approach to their use by both healthcare professionals and patients.

Whilst pharmacists seem to have a greater knowledge of unlicensed medicines and consider many aspects of their use in comparison to their non-pharmacist colleagues, they were often more reluctant to inform patients that they were taking an unlicensed medicine and to discuss the implications of this. This was in part due to concerns around damaging the patient-prescriber relationship and a perception of this being a role for the prescriber. This perception was also captured among patient participants. However, patient participants also expressed that the pharmacist who dispenses the medicine should also inform them at the point of giving out the prescription. Although patient participants they also acknowledged that this could cause problems if the prescriber had not previously informed the patient.

Prescribers often described using pharmacists as a source of information and advice for the use of unlicensed medicines, either in the hospital pharmacy department, as part of medicines information services, as GP practice pharmacists or local community pharmacists. There was a

desire across the settings for prescribers and pharmacists to work more closely together to ensure that an unlicensed medicine was the most suitable option for the patient and to ensure that an appropriate medicine was supplied.

There seems to be inconsistency in whether patients are informed about the unlicensed status of the medicines. The qualitative work found that some patients were not informed, where others were very well informed. This is in contrast to the guideline analysis which contained a plethora of references to informed consent around initiation of an unlicensed product. However, the lack of written information for the patient highlighted in the guideline analysis was also echoed in the qualitative work, and so this may be an area for further work.

Patients expressed a desire to be informed of the unlicensed status of their medicine, including why the medicine was unlicensed and what the implication of this was for them. It was also highlighted that unlicensed medicines are not supplied with a patient information leaflet. A standard set of information leaflets for the most commonly used unlicensed medicines as well as a generic leaflet on what an unlicensed medicine was, was often cited as a desirable resource for healthcare professionals and patients. Patients also wanted to receive information verbally.

A training need was highlighted in the qualitative work and the lack of consistent standards was highlighted in the guideline analysis. There is therefore a need for training and the development of core standards on the use of ULM in order to inform a more uniform approach to their use. As pharmacists become increasingly integrated into general practice and secondary care settings, and expand their roles to become prescribers it could be that unlicensed medicines are an area in which pharmacists take a specialised role.

There is a lack of transparency around who writes guidance on ULM and on what foundations they base their recommendations. Many seemed to be written by pharmacists; the qualitative work demonstrated that pharmacists are a source of information frequently utilised by other healthcare professionals, therefore it would seem appropriate for them to lead on guidance development. However, this raises the question as to whether a lack of multidisciplinary and patient involvement perpetuates the lack of awareness of unlicensed medicines outside the pharmacy profession.

There was little documentation from community pharmacy or the primary care sector. It is not clear if this is due to a lack of guidance or a lack of submission to the project for analysis. However, the lack of references to any sort of guidance in the primary care qualitative work reflects this finding and this is an issue that potentially needs to be addressed. It is worth noting that the RPS recently updated its guidance on Specials which may improve this.

Conclusion

Unlicensed medicines form part of prescribing practice involving many different healthcare professionals and patients. However, their unlicensed status means that many of the tools that are traditionally available to support clinical decision making and patient use are lacking.

However, ULMs were often paralleled with licensed medicines by both healthcare professional and patient participants, indicating that the licensing status of the product appears to have little impact on decision making and processes for use. This is reflected by the fact that prescribers are not always aware that they have prescribed an unlicensed product or what the potential implications of prescribing them are. Pharmacists appear to have a wider working knowledge than their medical and nurse colleagues of ULMs and the potential implications of their use. They are often referred to for medicines information and advice. However, despite this, pharmacists seem reluctant to discuss the licensing status of medicines with patients and prescribers in the absence of a good pharmacist - prescriber relationship. Patients expressed a desire to know the rationale behind why an unlicensed medicine was chosen and wanted to have parity of access to information to that of licensed medicines.

Dissemination of findings

Peer-reviewed publications
Published:
Donovan, G., Parkin, L., Wilkes, S (2015) 'Special unlicensed medicines: what we do and do not know about them' *British Journal of General Practice*

In preparation for submission:
Donovan, G., Parkin, L., Brierley-Jones, L., Wilkes, S (draft) 'Special unlicensed medicines use in the UK: A guideline analysis' Target publication: *European Journal of Clinical Pharmacology*

Publications planned:
Methods paper on a grounded theory approach across settings using two independent researchers and a combination of interviews and focus groups. Target publication: *Health Services Research*

Qualitative study exploring the use of unlicensed medicines across primary and secondary care from the perspectives of prescribers, pharmacists and patients. Target publication: *BMC Health Services Research* (open access)

Conferences
Poster presentations
Unlicensed medicines use in the UK: A systematic review and quality assessment of published guidelines, UKCPA Autumn Symposium, November 2015

Abstract submissions
What is the quality and content of published UK guidelines on the use of unlicensed medicines?
Society for Academic Primary Care, July 2016 (submitted for poster presentation)

How are unlicensed medicines used in practice by prescribers, pharmacists and patients across primary and secondary care?
Society for Academic Primary Care, July 2016 (submitted for oral presentation)

Exploring the use of unlicensed medicines across primary and secondary care from the perspectives of prescribers, pharmacists and patients: A qualitative study
Royal Pharmaceutical Society Conference, September 2016

Exploring the use of unlicensed medicines across primary and secondary care from the perspectives of prescribers, pharmacists and patients: A qualitative study
UKCPA Autumn Symposium, 2016 (oral presentation)

Study Blog (http://wp.sunderland.ac.uk/emulsionstudy)
A blog has been established for this project which incorporates both the study progress and support for other early careers researchers. This will continue to be updated until the end of December 2016.