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Articles

Patients' involvement in the development of pharmaceutical products at pre-launch: problems experienced and how to resolve them

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Abstract

Background: Pharmaceutical products are developed for patients as the end-users. It has been advocated that patients should be involved in the development of such products. However, this is not the case as patients are usually not involved. To date, no study has investigated the involvement of patients at pre-launch stage of pharmaceutical products. Therefore, this study explored patients' involvement at this stage of pharmaceutical products development.

Methods: A survey of Market Access (MA) and Health Economic and Outcomes Research (HEOR) professionals at International Society for Pharmacoeconomics and Outcomes Research (ISPOR) Glasgow 2017 was carried out. Responses were examined using thematic and descriptive analyses to capture professionals' suggestions about involvement of patients at pre –launch stage and how to resolve issues identified.

Results: Results showed patients are not currently involved in this process, depriving them of benefits associated with involvement such as improved psychological well-being, health outcomes and drug safety. Participants advocated involvement of patients in the developments of pharmaceutical products. This may help improve adherence and quality of life in patients hence, ensuring effective use of pharmaceutical products.

Conclusion: Patients are to be involved at pre-launch stage of pharmaceutical product development. Their involvement can ensure adherence to early stage development regulations. This may facilitate effective networking among stakeholders. Whilst it is generally agreed that patients should be involved to ensure adherence to regulations, problems are experienced that could be resolved by effective communication; understanding of external issues and how to tackle them. Also, it may help with deeper understanding of issues important to patients.

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Market access; Pre-launch; Target products profile; Product development plan; Design of clinical trials; Food and Drug Administration.

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1. Introduction

Market access is defined as the method or process that will make sure that the right or the appropriate patients that would benefit from the development of any pharmaceutical product get quick and sustained or maintained access to such products at a fair price at the right time that such a product is needed (PMlive, 2012; Nowell, Norris, White, & Moules, 2017). Market access ensures the availability of pharmaceutical products with the development of appropriate value propositions, leading to their prescribing and uptake decisions by payers and patients with the aim of improving patient outcomes and optimising profitability for manufacturers (Odeyemi, 2014). Pharmaceutical products are developed with patients in mind as the end-users. A lot is being said by professionals in the pharmaceutical industry about what patients want without involving the patients in the process of pharmaceutical product development (Parsons et al., 2016). There has been a move in the pharmaceutical industry for patients' involvement in the development of pharmaceutical products as it is believed that this could help to improve the psychological well-being of the patients (Merlo, 2019). For example, Conversano et al. (2019) observed that patient feedback on mirtazapine, a noradrenergic and specific serotoninergic antidepressant, improved the effectiveness of the medication in reducing pain and improving quality of life (QoL) of the patients with depression and their psychological well-being. Although patients were not necessarily involved at pre-launch stage of the medication, however, they were involved at post-launch stage which highlights the importance of involving patients in the development of pharmaceutical products.

There are different stages of drug development consisting of pre-launch, peri-launch and the post-launch. This paper focuses on the pre-launch stage. The pre-launch stage has 3 phases usually consists of the development of Target Product Profile (TPP), Product Development Plan (PDP) and Design of Clinical Trials (DOCT) (Odeyemi, 2014). The TPP is best described as a roadmap for drug development, containing the formulation and product characteristics in pre-clinical and clinical studies – a comprehensive index for information on product development (CDER, 2007). The Food and Drug Administration (FDA) has a formal guidance document on how to develop the TPP (CDER, 2007). The PDP phase, the second phase, shows the list of activities involving completion, control and authorisation for process maintenance. Description of product benefit, detailed description of product, including market information, product-process specifications/ tolerance, financial and technological data used. The last phase in the pre-launch of pharmaceutical drug development is the design of clinical trials (DOCT), which is the third phase. It involves the maximisation of the value of a molecule usually with an efficient, systematic approach that merges real-world data and the patient perspective into the

clinical trial design process (Sendyona, Odeyemi, & Maman, 2016). With a well-designed protocol, clinical trials can be executed with greater confidence and predictability, with shorter timelines, and will ultimately create evidence of value to stakeholders (Odeyemi, 2014). In the United Kingdom (UK), in advance of any clinical trial, the company will have to apply for a clinical trial application (CTA) from the Medicines and Healthcare products Regulatory Agency (MHRA). Medical and scientific experts assess preliminary research to decide if testing in humans can go ahead (Torjesen, 2015). A number of pharmaceutical companies carry out these activities without involving patients or when patients are involved very few of them are probably in the clinical trials and not from pre-clinical stage.

Patient-Focused Drug Development (PFDD) is a new initiative from the Food and Drug Administration (FDA) in the USA intended to bring patient perspectives into an earlier stage of product development (CDER, 2007). The goal is for patients to provide context for benefit-risk assessments and review decision making, and to input their feedback in the development of new assessment tools, study endpoints, and risk communications (Perfetto, Burke, Oehrlein, & Epstein, 2015). Safety and efficacy of pharmaceutical products especially drugs, are sensitive issues as users who are patients want to be sure that the products that they are taking or using are actually safe and effective for use with no or minimal side effects (Alshammari, 2016). The most effective way to ensure safety and efficacy is by involving patients in the development of these products so that patients using these products can provide feedback to the manufacturers regarding possible side effects to ensure safety and efficacy (NIHR, 2020). Hence, involving patients in the development of pharmaceutical products may help to ensure the safety and efficacy of such products thereby improving the psychological well-being of the patients.

Feedback relating to side effects of pharmaceutical products to patients is taking seriously in some fields like psychology where the study of the side effect of drugs and how it affects psychological functioning of patients is referred to as pharmacopsychology as introduced by Kraepelin who was a pioneer of scientific understanding of psychiatry and psychopharmacology. Fava et al. (2014) and Fava, Tomba, & Bech, (2017) noted that a drug effect such as sedation or motor stimulation may be considered adverse for one patient, and yet therapeutic and desired for another patient. Within the same patient, it may be of value at one stage of patients illness and adverse at a later stage. Hence, it is important to involve patients in the development of pharmaceutical products as their feedback might help with psychological well-being of patients and quality of life (Cosci, Guidi, Tomba, & Fava, 2019). Fava et al (2014) and Fava, Tomba, & Bech, (2017) also emphasised the behavioural toxicity meaning that taking some drugs could cause changes in patient's mood, patients perceptual, cognitive and other

human functions that could limit the ability of the patients taking such drugs to affect patient's well-being.

These problems can be managed by, observing patients in a clinical setting suggesting the importance of involving patients in the development of pharmaceutical products (Cosci, Guidi, Tomba, & Fava, 2019; Fava et al., 2014; Li & Li, 2018; Tomba, Guidi, & Fava, 2018).

Another benefit of involving patients in the development of pharmaceutical products is the issue of adherence It has been reported that psychological factors such as behaviour can negatively affect disorders or symptoms such as pain and make these worse and may influence the psychic integration of disease, adaptation, compliance and adherence (Mirdrikvand et al., 2019; Settineri, Frisone, Merlo, Geraci, & Martino, 2019), this has resulted to the integration of clinical psychology and its role in medical settings such as drug development and use, thereby helping to offer a substantial contribution to a deep evaluation of patients (Merlo, 2019).

Pre-launch stage could be perceived as the most important stage in the development of pharmaceutical products as all planning and strategy of drug development for the whole life cycle should be considered at this stage. In addition, the manufacturers need to ensure that a developed product provides a solution to the target market problems (CDER, 2007). Awareness of developed pharmaceutical products, readiness, validation, signups and effectiveness are done at this stage. It is possible for pharmaceutical products to go through all the medical trial process, regulatory checks and business plan and still fail when brought to market (Wiering, Boer, & Delnoij, 2017). In order to avoid this outcome, involving end users (patients) at this stage may be beneficial; contrary to prior understanding (Torjesen, 2015). It would be good practice to incorporate the patient viewpoint into all the processes at pre-launch stage. The study also examined the possible issues/problems associated with involving patients at pre-launch stage of pharmaceutical development, and how to resolve issues associated with involving patients.

2. Methods

2.1 Data collection and inclusion criteria

A questionnaire survey was carried out to achieve the aims of this study. The questionnaire was developed and piloted with five participants to ensure that the questions asked were appropriate. Ethical approval was obtained from the Manchester Metropolitan University (MMU). The questionnaire was administered at the International Society for Pharmacoeconomics and Outcomes Research (ISPOR) Glasgow conference to 104 participants; professionals from various backgrounds. All professionals who attended the ISPOR Conference, who were willing to participate in the study and completed at least 50% of their questionnaire were included.

Those whose questionnaires were not completed up to 50% were excluded. The questionnaire asked about their perspective of how involved patients should be at the pre-launch stage.

Participants were also asked about any problems that could arise if patients were involved, and they were requested to provide their views on how the problems identified can be resolved. Participants were required to respond to the following questions for each of the pre-launch stages: (1) How involved should the patient be in the development of pharmaceutical products? (2) What are the problems associated with involving patients at this stage? (3) How can the problems experienced as a result of involving patients be resolved?

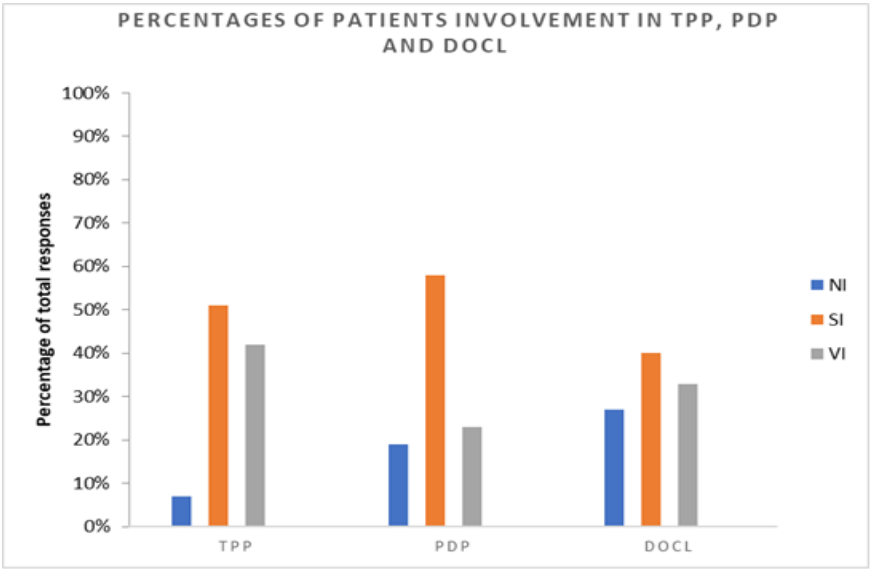
2.2 Thematic analysis

Thematic analysis was used to identify perceptions of patient involvement in the development of pharmaceutical products, problems involved and how to resolve problems experienced at pre-launch stage (Nowell, Norris, White, & Moules, 2017). Responses were categorised according to their theme for analysis. For question (1), the responses were given the following theme: NI - Not involved (0-1), SI - Somewhat involved (2-3), VI - Very involved (4-5). Questions (2) and (3) responses by the participants were analysed under the following themes: Communication, Cost, Effectiveness, External, Quality of life and Safety.

3. Results

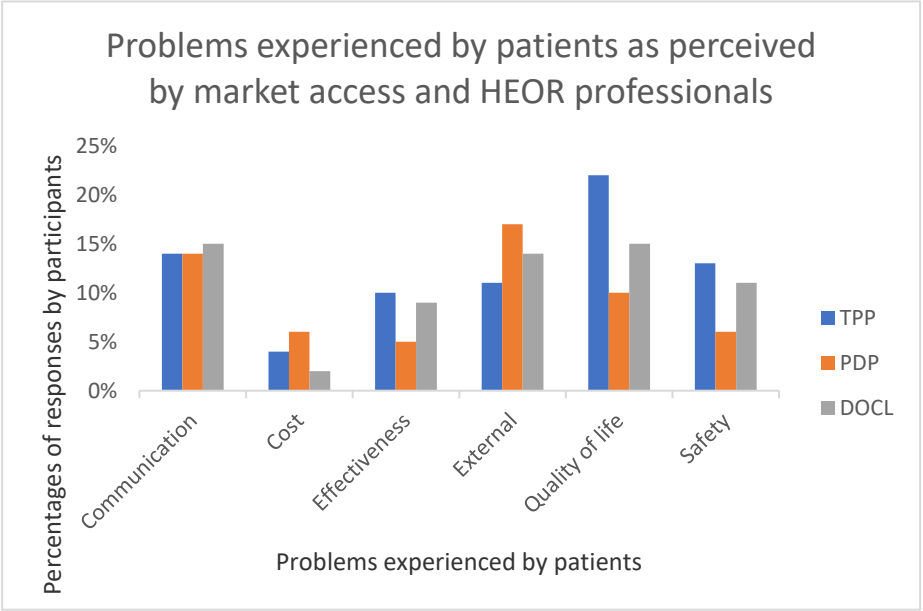
Question (1). (Analysed in Figure 1) How involved should patients be in the development of pharmaceutical products? At TPP, 42% participants believed that patients should be very involved (VI) and 51% stated that patients should be somewhat involved (SI), whilst 7% believed that they should not be involved (NI). This meant that the majority of the participants were in support of patients being involved in the early development of pharmaceutical products as 93% out of the 104 participants are in favour of patient involvement. At PDP stage, 23% participants agreed that patients should be very involved (VI) and 58% believed that they should be somewhat involved (SI); however, 19 % stated that they should not be involved (NI). There was a reduction in the number of participants in favour of patient involvement at this stage as 81% out of the 102 participants at this stage were in support of patients' involvement. At DOCT stage, 33% participants at the ISPOR conference stated that patients should be very involved (VI) and 40% believed patients should be somewhat involved (SI), while 27% believed patients should not be involved (NI) in this stage and 73% out of the 103 participants were in favour of patient involvement. The requirements for patient involvement as perceived by the professionals surveyed were eminent at the 3 levels of pre-launch that is TPP to PDP and DOCT.

Figure1. Patient involvement at pre-launch stage



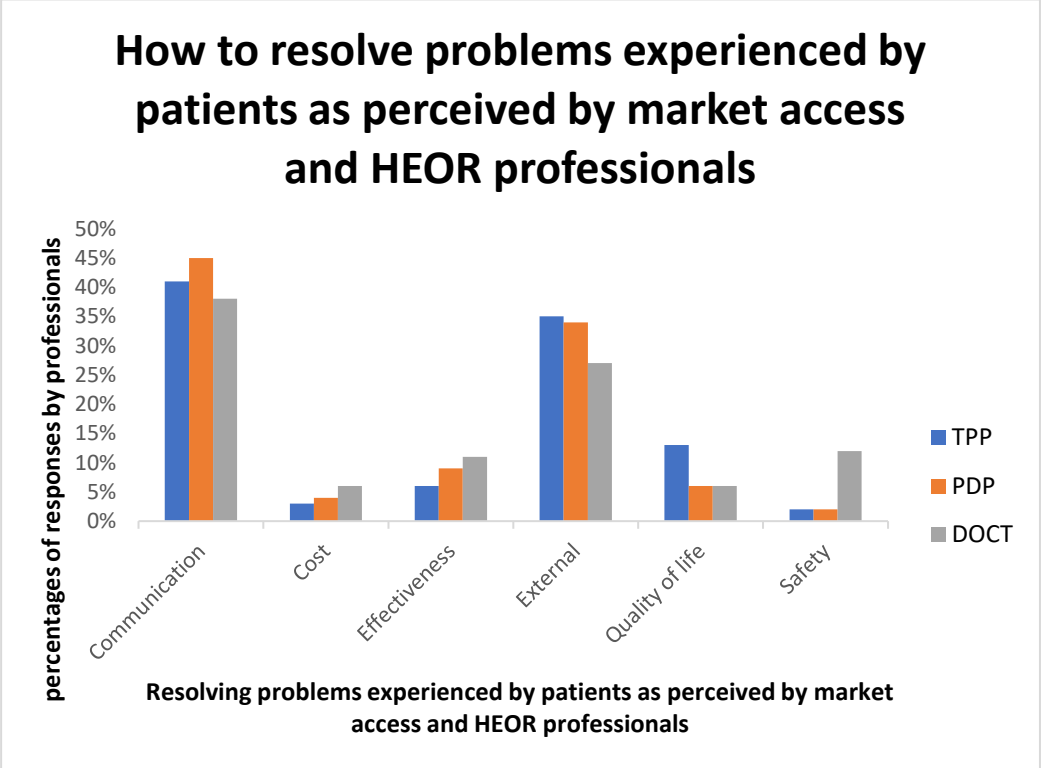
Question (2) (Analysed in Figure 2) Problems associated with involving patients in the development of pharmaceutical products. For TPP, the results showed that patients experienced problems with QoL 22% with safety 13% and with communication-related issues 14%. Patient involvement is therefore associated with problems with QoL, communication and safety, so involving patients at this stage may help to mitigate later issues and potentially improve health outcomes for patients. Similarly, 15% communication issues were identified for PDP 14% and DOCT was 15%; hence, these were recurrent issues as they were present across all of the stages. In addition, external factors, such as working with stakeholders, were also identified for PDP 17%, for DOCT 14% and for TPP 11%. Moreover, QoL issues 15% and external factors 14% were issues also identified for DOCT.

Figure 2. Problems experienced by involving patients at pre-launch



Question (3) (Analysed in Figure 3) examined how problems experienced by involving patients at the early stage of development (pre-launch) could be resolved. The results showed that communication was the main resolution method suggested as a way forward for issues experienced at all three stages i.e. communication with results as follows: TPP 41%, PDP 45% and DOCT 38%. Other resolution methods suggested based on this study included working on external issues, which is external factors (such as working with stakeholders) experienced by involving patients at pre-launch stages. Results for external factors were as follows: TPP 35%, PDP 34% and DOCT 27%. QoL was identified as a problem at TPP stage 13%, and at DOCT stage, also at this stage safety was 12% and effectiveness 11% were suggested as resolute for issues experienced by involving patients at pre-launch stage.

Figure 3. How to resolve problems experienced by patients



Accessible summary:

1. No previous study has investigated patients' involvement in the development of pharmaceutical products at pre-launch stage, the problems arising from their involvement and how to resolve those problems.

1.1. This study investigated and showed the impact on health outcomes, psychological well-being of involving patients at pre-launch, problems encountered, and an insight into how to resolve them.

1.1.1. The results of this study can be used by policy makers, healthcare professionals and stakeholders to guide process development and provide insight into how to involve patients effectively in pharmaceutical product development.

4. Discussions

This is the first study to explore the involvement of patients in the development of pharmaceutical products at pre-launch: problems experienced and how to resolve them. This study examined how these problems experienced as a result of involving patients at pre-launch stage can be resolved (Wiering, Boer, & Delnoij, 2017). It also examined the problems that could arise from this, such as communication, QoL and safety; these findings are in line with their study by Cosci, Guidi, Tomba, & Fava (2019) and Merlo (2019). It has provided insight into the importance of involving patients in the development of pharmaceutical products such as improvement in QoL of patients when the stakeholders (patients) are involved in the development of pharmaceutical products. Li & Li, (2018) showed that when patients, physicians and pharmacists work collaboratively it improve patients' QoL, psychological well-being and reduce medication-related adverse effects.

The study revealed that patient involvement could help to address problems in the development of pharmaceutical products and enhance timely access to appropriate products for end users. By including patients, it may help to facilitate interaction and communication among the various sponsors/stakeholders such payers, manufacturers, regulators and healthcare providers (Sendyona, Odeyemi, & Maman, 2016). These authors would advise that policy-makers are to further investigate this area, as greater understanding between sponsors on the needs or preferences of patients could lead to improvements in patient adherence, persistence, and satisfaction (Jimmy & Jose, 2011); ultimately improving clinical and QoL outcomes and psychological well-being.

External bodies or stakeholders, such as the regulatory bodies, should work more with patients based on the findings of the current study to address the gap between unmet needs for new interventions for diseases. Communication was the key resolution method suggested for addressing patient issues in early stage development of pharmaceutical products. As a result, patients should be informed about their involvement and role in early phase development (Jimmy, & Jose, 2011).

4.1 Strengths

This study is the first to examine the perceptions of involving patients in the development of pharmaceutical products. To date no study on the involvement of patients at pre-launch of

pharmaceutical product development exist; this is the first study on patients' (end users') interest and involvement in the development of pharmaceutical products. Therefore, the findings of the present study have added to the current level of knowledge in this area (Lowe et al., 2016).

The study involved participants who worked directly with patients in the design and development of pharmaceutical products, and in most cases make decisions for patients. Therefore, it is important to understand their views towards patient involvement (Schuhmacher, Gassmann, & Hinder, 2016). This may help to inform the development of these products to improve access and patient outcomes.

Participants were recruited at ISPOR Europe so participants were from all parts of the world, giving a comprehensive representation of participants from various countries and in the world. The findings of the study provided some insight into pharmaceutical products development in the world, hence enhancing the validity and transferability of the findings (Yilmaz, 2013).

Participants were able to express themselves freely at their own time without pressure from the researcher which made it possible for them to express themselves freely without been restricted (Questback, 2015).

4.2 Limitations of the study:

The study only involved professionals from the following backgrounds: pharmaceutical industry, academic, health professionals, policy makers, payer, health technology assessment bodies and consultants in health economics and outcomes research and not patients. This meant that professionals and lay men who do not work in the industry were excluded from this particular study. Hence, future studies should examine the perception of patients by involving them directly so as to have a full representation of their interest (Sacristan et al., 2016).

The current study was conducted in the English language hence participants who do not speak English were excluded from the study (Newington & Metcalfe, 2014). People who do not speak English might have different opinions from the sample of participants in the current study.

Participants were also given a questionnaire to complete with options to choose from i.e. survey. This can be a limitation as their responses might have been different if they were interviewed or asked open questions about this study (Bowling, 2005).

Responses to some of the questions were done in the participant's own time. This meant that they were given time to complete the questionnaire without the researcher being with them. The participants' responses to the questions asked might have been different if the researcher was with them as we normally have in interviews for most qualitative interviews (Nowell, Norris, White, & Moules, 2017).

5. Conclusions

Patients are to be involved in early stage of pharmaceutical products development that is pre – launch stage. There are issues experienced as a result of involving patients at pre- launch stage such as external factors which is working with stakeholders. Other issues are communication among stakeholders and problems with patient's quality of life. The main resolute to resolving issues experienced as a result of involving patients at pre-launch stage are communication among stakeholders and working effectively with external factors.

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Abbreviations

CDER – Centre for drug evaluation and research

CTA – Clinical trial application

DOCT – Design of clinical trials

FDA – Food and Drug Administration

ISPOR - International Society for Pharmacoeconomics and Outcomes Research

MHRA – Medicine and Healthcare products Regulatory Agency

MMU – Manchester Metropolitan University

NI – Not involved

PDP – product development plan

QoL – Quality of life

SI – Somewhat involved

TPP – Target products profile

VI – Very involved

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