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OPEN LETTER

Introducing patient-centric electronic medicine leaflets in the European Union

[version 1; peer review: 4 approved with reservations, 1 not approved]

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Abstract

Despite numerous advances in their content and structure over recent years, paper information leaflets for medicines are often hard to read for people with visual impairments, contain a lot of technical information, and people suffering from chronic conditions may find it challenging to identify all side-effects or dangers of taking a drug in their situation. Likewise, for people already taking different drugs, identifying contraindications may be time-intensive and easily overlooked, posing a risk for affected patients. Electronic product information (ePI), or eLeaflets, provide an opportunity for improvements in how patients interact with the information provided. We summarise opportunities of ePI and experiences from a co-creation process of such an app together with patients as part of the *Pharmaledger* project and put it into context of the current policy environment in the EU in light of EMA's key principles for the adoption of ePI in medicine. While more patient-friendly information remains a significant ask, ePI has the potential to make leaflets easier and quicker to read through search and zoom functions, provide a safe digital medicine cabinet employing blockchain technology, enables patients to identify falsified product boxes, receive real-time updates when a product expires or is being recalled by the manufacturer, and potentially even include a reminder function to increase adherence. We present a potential research agenda across disciplines for interested researchers. While many welcome the benefits of ePI, we urge policymakers to keep in mind that some groups, specifically people with low technical literacy, should not be left without

Open Peer Review

Approval Status ? ? ? ? ✗

	1	2	3	4	5
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Any reports and responses or comments on the article can be found at the end of the article.

alternatives. We recommend early initiatives to ensure a widespread understanding of how ePI works across populations while also taking this opportunity to use new insights to improve leaflets on paper.

Keywords
Electronic Product Information, ePI, eleaflet, patient involvement, patient engagement, blockchain, Health Policy, European Union



This article is included in the Health Sciences gateway.



This article is included in the Horizon 2020 gateway.



This article is included in the Healthcare and Policy collection.



This article is included in the Digital Health and Well-being collection.

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Plain language summary

The abstract has been reviewed by lay people and deemed suitable for non-experts.

Disclaimer

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Introduction

People need to be well-informed about their medicines. To ensure that medicinal drugs can be taken and prescribed safely, an immense amount of information has to accompany each product. The information currently comes in the form of a large, folded paper included with every product (paper information leaflet), which people read to differing extents (Raynor *et al.*, 2007) and interact with differently based on their situation. While someone without a chronic condition might simply want to learn if they can take a pill and later drive their car or have a glass of wine, someone receiving treatment for a severe or complex condition with multiple drugs would have to identify much more information to account for tolerability and interaction effects. Searching these large paper leaflets for the required information can be time-consuming and is not easily accessible for all: it is specifically challenging, for example, for people with visual impairments who often need tools such as magnifying glasses to read the leaflets (McMahon & Curtis, 2009). While the EU's Directive 2004/27/EC—which covers medical information provision—requires that information "must also be expressed in Braille format on the packaging [and] [t]he marketing authorisation holder shall ensure that the package information leaflet is made available on request from patients' organisations in formats appropriate for the blind and partially-sighted" (addition to Article 56a), it remains at least questionable whether citizens are aware of these options or make use of it. In this letter, we would like to raise awareness around the level of development of ePI (specifically the app developed by IMI Pharmaledger), as well as provide a brief overview of the current policy environment and the need for engaging the public in the further development and deployment of ePI.

Could a digital version of such leaflets improve the experience?

While digital literacy and smartphone access across the EU differ significantly by country (Van Kessel *et al.*, 2022), there is an ongoing and rapid digitalisation of health and care solutions, including medical information. The European Medicines Agency (EMA) refers to such digital versions of medicine leaflets as electronic Product Information (ePI; sometimes: eLeaflet) and defines this as any "authorised, statutory product information for medicines (*i.e.* summary of product characteristics, package leaflet and labelling) in a semi-structured format created using the common EU electronic standard. ePI is adapted for electronic handling and allows dissemination *via* the world wide web, e-platforms and print." (EMA, 2020a, p. 2). We share our insights concerning the development and co-creation of an ePI application (app) together with patients within the multistakeholder PharmaLedger project (https://pharmaledger.eu) and outline key considerations for future development and implementation. With this app, patients will be able to scan a 2D-barcode on a medicine box and receive the information contained on a paper leaflet, as well as offering additional features in the future which increase readability and safety. Through this scan, patients will also know immediately whether the drug has expired, if the box is an original (anti-counterfeiting check) and can be informed immediately in case of a batch-recall for the drug.

Developing ePI together with patients

Including patient perspectives in eHealth development can help provide different types of value; namely, identifying unmet needs, better usability and desirability, better fit into the patient journey, better adoption, better health outcomes, advocacy and trust, a sense of purpose, and better health equity and access (Jacob *et al.*, 2022). To identify and better understand the needs and priorities for an ePI app, we conducted a series of five workshops with a group of patients recruited by the European Patients' Forum (EPF) and the European Forum for Good Clinical Practice (EFGCP) (Figure 1). These sessions were led by industry partners, with support from EPF staff (Hunt *et al.*, 2022). The group consisted of eight people from different countries directly or indirectly affected

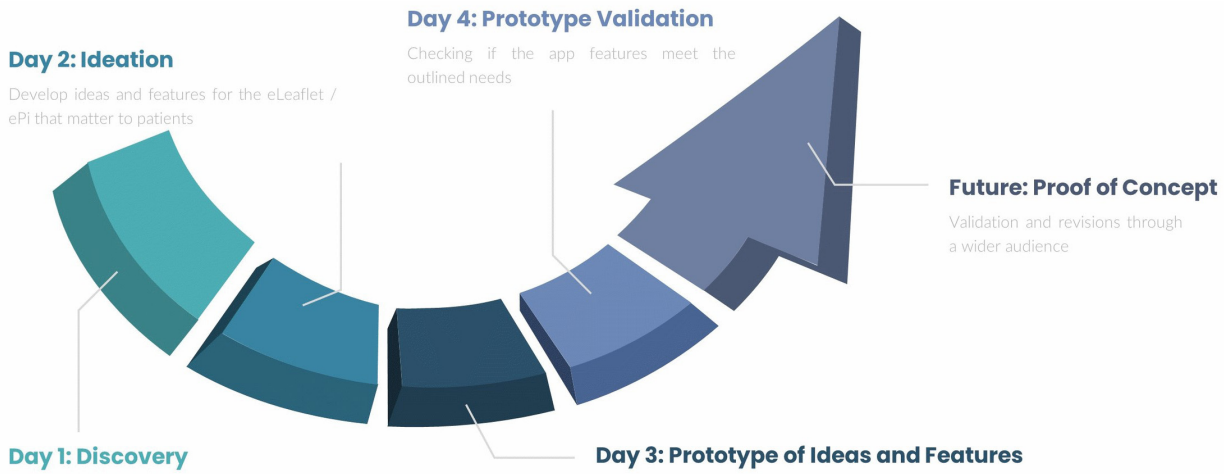

Figure 1. ePI development workshops with patients.

by various disease areas (five female, three male), including two co-authors of this paper. More user-friendly information arose as the key ask from these workshops, together with a need for well-described contraindications with other drugs, automatically updated information on the medicine and side-effects, intuitive formatting and easily readable text, as well as specific information on how and when to take medicine.

The input from the first four workshops was taken into account for the development of the PharmaLedger ePI app, and a fifth, follow-up workshop focused on the usability of the beta version of the lite app, a web-based version with limited functionality accessible through a browser. While there is no need to install the app—lowering barriers for accessibility—it requires the scanning of two codes printed on the box: one to access the web app (QR Code), and another to access the medical information (2D Code). This caused some confusion among testers and is an important consideration in practice. Details on these workshops have been described in publicly available webinars (Jarke *et al.*, 2022a, Jarke *et al.*, 2022b, Hunt *et al.*, 2022) and the forthcoming press release by the Pharmaledger Association (unpublished report). The data and brief description of the workshops can also be found in our accompanying open repository (Jarke, 2023).

The future of ePI in Europe

Direct input from patients in the development process is key to developing a patient-centric app. In addition to gaining specific insights, patient inclusion and testing provide invaluable knowledge on how people interact with an app in real life and reveal issues that a static dataset cannot. For example, the best meta-analysis would not have told us that a warning logo may not be perceived as such at all: where the developers had chosen an icon that they found to be similar to a nuclear warning sign, one user was wondering why there was a "flower symbol" popping up on the app. Different conditions can affect the flow of the process. During the workshop, we found out that shaky hands, in combination with using older phones, lower the chances of successfully scanning the 2D matrix code. On the other hand, a different code—the QR code leading to the app itself—was still easily scannable under the same conditions. We recommend the continued inclusion of patients and users in the future development of ePI and outline more insights from workshops and related sessions hosted with different stakeholders (Hunt *et al.*, 2022; Jarke *et al.*, 2022a; Jarke *et al.*, 2022b).

ePI will not solve all issues with medicine leaflets

There are many aspects of information leaflets in general that can be improved (Medina-Córdoba *et al.*, 2021; Young *et al.*, 2017). Despite its potential, ePI is not a silver bullet to address all existing issues with medicine leaflets. Our consultations outlined above, and a survey from 2021 suggest people often find information leaflets too complex and sometimes overwhelming (PFMD, 2021). Simplifying medical information is difficult and has wide-ranging ethical, regulatory, and legal implications. It requires extensive research to protect the safety of those taking medicine. While a worthwhile endeavour, the complexity of information does not simply vanish by going digital, and additional efforts are required to help patients understand the information more easily.

Without certainty about levels of digital literacy in patients and being sure everyone benefits equally, paper leaflets will need to be kept alongside electronic versions to avoid new inequalities in health and care. Many people still prefer paper in a hypothetical scenario when given a choice, specifically among people over 40 years old (PFMD, 2021). One scenario accounting for this could be on-demand printing, meaning boxes would come without information leaflets, but pharmacists can print them if patients request them. While previous research has identified some support for such a scenario (Hammar *et al.,* 2016), no data exists on openness from pharmacists to such a solution, and there is a risk of patients who would benefit from a paper information leaflet not taking up the offer due to being hesitant in social interaction.

Advantages of ePI

Nevertheless, an ePI app has the potential to provide a set of highly beneficial functions, including a search function helping to find relevant information more quickly, specifically for side-effects, tolerability, drug-to-drug interactions, as well as a zoom-in function or read-aloud function for people with visual impairment. Information can technically be available in multiple languages.

The global trade of counterfeit medicines is currently estimated to create USD 4.4 billion in illegal revenue, causing massive financial damage to EU governments and legitimate businesses. Of greater concern are the issues directly related to ill health: a model from the OECD estimates that globally 7,2000 to 16,9000 children annually die from pneumonia because they are not treated with proper medicine but counterfeit products (OECD & EUIPO, n.d.). Adding a feature to an ePI app that identifies whether a box is an original can enable patients or carers to spot fake products easily. Further, a batch recall notification feature on personal mobile devices can help communicate the recall and therefore safety of patients. Lastly, having a digital medicine cabinet—an overview of which medicines a user is currently taking and took in the past—could come with a feature in the future that cross-checks the adverse effects of taking these drugs together and issues a warning. Likewise, evidence from behavioural sciences shows that reminders about when to take medication are quite effective in increasing medicine adherence (Jarke *et al.*, 2021; Tran *et al.*, 2014; Zhao *et al.*, 2019), and future versions may include such a function.

Data privacy

The more complex an ePI app becomes and the more features it brings, the more data it also has to process. This data needs to be kept secure and it has to be ensured that patients are not identifiable, a key concern also prevalent in the workshops with patients. At the moment, using a distributed ledger technology such as blockchain, where the data is not stored centrally seems to be the safest option, but it also comes with legal constraints, as it remains unclear if and to what extent the EU General Data Protection Regulation applies where there is no clear data owner (Kayhan, 2022). While blockchain is rising in popularity, it is still an emerging field, and many important questions are emerging alongside. This includes considerations regarding patient data ownership, concerns about how sensitive information should be managed, and who should have access to it.

Get ready and leave no one behind

In their key principles for ePI for human medicines, EMA's first principle outlines how any ePI app needs to primarily benefit public health (EMA, 2020b). This notion should always be at the forefront of any further developments of ePI and its implementation. By conducting several focus group sessions with patients and industry we understand that patients have priorities which are not easily incorporated into the ePI envisioned by the EMA, such as more user-friendly information. Independent of how exactly a final ePI app will look like, it will be necessary to involve all stakeholders in the process: to ensure the development of a successful implementation of ePI, we encourage the consultation of healthcare practitioners, pharmacists, and, of course, patients and the general population, as the industry moves from a paper-based to a digital system. We suggest continuing this involvement and preparing the public soon, as apps might soon be commonplace. Such involvement should also be accompanied by rigorous evaluation. To avoid reinventing the wheel and foster cooperation in the development of ePI across sectors, the establishment of the Pharmaledger Association (https://pharmaledger.org) as a not-for-profit non-governmental organisation that brings together members of the project consortium and other stakeholders from the healthcare sector is already a promising step. In addition, connections should also be made to relevant initiatives that work to improve the content of ePI (*e.g. Gravitate Health:* https://www.gravitatehealth.eu) and efforts in developing quality standards for health apps, such as *Label2Enable* (Hoogendoorn *et al.,* 2023). Understanding the use of product information will allow for evidence-based conversations with regulators and other stakeholders to suggest changes to the future of ePI to make the data more human-centric. A comprehensive, interdisciplinary research agenda could benefit implementation greatly. We provide an initial, non-exhaustive overview of potential research questions based on our own internal discussion and a brief, non-representative survey among the PharmaLedger consortium and social media followers of EPF in Table 1 for consideration.

Table 1. Opportunities for research.

Research area	Areas for investigation / Research questions
Health sciences and medicine	Pharmacists' perspective on the adoption and use; Systematic review and country comparison of existing print-on-demand practices in different countries; How can patient data (the medicine cabinet) be used to their direct benefit?; Is it accessible to people with disabilities?
Social, behavioural, and educational sciences	Ongoing evaluation of usability; Understanding of leaflets by users (both digital and paper) Interventions to increase understanding and uptake (e.g. through nudges and boosts); Acceptance by stakeholder groups; Predicting adoption of e-PI apps (what and how to target when proposing change); Best practices in roll-out; What aspects of ePI make people read the leaflets if they don't read paper leaflets; Traits/types of people using vs not-using ePI or paper leaflets in general; How to communicate and educate people on the technology (specifically for people with low digital or health literacy)
Economics and finance	Models for financing ePI apps; How to fund costs for print-on-demand?
Policy, public administration, regulatory science	Comparison of infrastructure for using ePI between countries; After rollout and adoption: Rhetoric and practice - is there a gap?; Equity: do some groups may benefit less and why + identifying countermeasures
Law	Readiness of legal systems for adoption; GDPR compliance; Legal considerations for adoptions in non-EU countries; Does ePI pose any unidentified ethical challenges?
Technology	Use of Blockchain for digital medicine cabinets; Can patients be informed about new research regarding the drug?; Can eleaflets highlight information for specific groups (*e.g.* age, gender, chronic disease) - also relevant for legal research; Can the blockchain technology used for the app made be more environmentally sustainable; Are there alternative technologies to blockchain?

Given the recent and fast developments around ePI, we conceived this paper to make stakeholders, specifically researchers, aware of the advanced stage the technology and policies are already in. We hope that this short overview piece brings further stakeholders into the process and urges those involved to identify and consider special needs of disadvantaged people or those living with disabilities. It appears evident that paper leaflets should not disappear immediately while certain groups are still reliant on them and important steps have been taken in recent years to improve them, specifically through EMA's Readability Guideline (EMA, 2009). In addition, active patient input has increasingly been sought to improve design and readability (CIOMS, 2022). The emerging body of research around ePI should be seen as an opportunity to gain insights on improving leaflets generally, including those on paper. ePI is not a silver bullet to solve all existing problems with paper leaflets—however, we urge regulators and decision-makers to use the momentum to further improve the understandability of leaflet content—in all formats, digital and paper.

Ethics and consent

Ethical approval and consent were not required.

Data availability

Underlying data

No underlying data are associated with this article.

Extended data

Open Science Framework: ePI Workshop Summary with Data.docx

https://doi.org/10.17605/OSF.IO/APN8B (Jarke, 2023).

Data are available under the terms of the Creative Commons Attribution 4.0 International license (CC-BY 4.0).

The data on patient workshops referenced in this article can be found in the open repository, and have previously been provided and discussed in PharmaLedger's 3rd Open Webinar "Making ePI a Reality: The User Journey", the Patient Engagement Open Forum session "Electronic medicine leaflets – What do patients want?", as well as during the EPF Congress 2022 session "ePI – How Patients Benefit From a Digital Version of Medicine Leaflets". An upcoming press release by the Pharmaledger Association will share these insights with a wider audience.

Acknowledgements

We would like to thank the other members of the Pharmaledger Patient Advisory Group whose input to the workshops informed this paper substantially: Margit Paul, Gregor Cuzak, Marta Morato, Outi Saramäki, and Lotte Klim. We also express our gratitude to Charles Vesley, who led the initial four workshops, as well as Patrick Maher for his input at that stage.

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Open Peer Review

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Version 1

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Diana A. van Riet-Nales
Department of Chemical Pharmaceutical Assessments, Medicines Evaluation Board (MEB), Utrecht, The Netherlands

The paper does not go into enough detail about the full complexity of the product information (i.e. the package leaflet, SmPC and product label). It should be acknowledged that the PI is not only intended to provide information driven by patient and consumer needs, but also by the needs of industry and/or regulators to ensure that users can make well informed decisions about the prescription, dispensation and use of the product in real world clinical pratice.

For this article, the open letter format does not enable an evaluation of its conclusion without reading many references, which I consider a major limitation.

Please find attached some comments that may be of help in revising the paper.

Abstract

1. It is not the paper that is making leaflets difficult to read. It is just the leaflets themselves that are difficult to read, either on paper or as a pdf on screen.
2. The leaflets are not only but for example difficult to read for people with visual impairments.
3. A chronic condition is not necessarily a problem in identifying a contraindication in a leaflet. People may have several chronic conditions and still be capable to so so, whereas people with just one short term condition may not. What matters in the end is what a patient can or cannot read, understand and process in combination with the complexity and number of package leaflets to consider.
4. Please acknowledge that the list of ePI advantages is not exhaustive and use the word for example.

Introduction

1. You may consider avoiding the word drug all over the paper and adopt the EU wording (active substance, medicine, medicinal product, package leaflet, product (not paper)

information leaflet.). This makes it clearer that the word drug is used in the context of a medicine and not substance abuse.
2. A package leaflet is not only about what people want to learn, but also what they would need to know and respect when prescribing, dispensing or using the product to ensure its safety and efficacy.
3. It is an understatement that package leaflets are only difficult to read for people with visual impairments. A lack of adequate health literacy is another important barrier.

Could a digital version of such leaflets improve the experience?

1. The letter would improve if the authors would choose whether they want to focus on visual impairments, or on any impairment hindering adequate reading, understanding and processing (adherence) to the product information, especially as the next paragraph starts with eHealth in general.

Developing epI together with patients

1. The letter is difficult to read on its own and would benefit from more information on the methods section. For example, why would a group of eight people be sufficient for the workshops, especially considering the wide heterogeneity of the participants and the fact that two of eight (25%) of the authors were part of the group?. It is stated that four/five workshops were held. All with the same 8 people? Or 4/5*8=32/40 different participants?

The future of ePI in Europe

1. The section raises the question to which extent knowledge from human factor design was used during the development of the app. You may wish to explain.

ePI will not solve all issues with medicine leaflets

1. I am not sure that simplifying medical information is the only real difficulty. Please address the difficulty of providing targeted information to any user from those with low health literacy requiring rather short and simple information to those that expect information to be complete and at an academic level.
2. The question arises if on demand printing could be a real problem-solving strategy as it would require consumers and patients to indicate that they want a paper version which may first of all be considered as a burden to the dispenser and secondly be associated with the shame of not being able to use digital tools.

Advantages of ePI

1. You focus on the benefit of an ePI for people with visual impairments. A read-out function may also be relevant for people with limited reading skills.
2. Please underpin that the reference to children and pneumonia is only an example

Data privacy

1. Would data manipulation also be a risk?

Get ready and leave no one behind

1. A healthcare professional includes a pharmacist.
2. It is not clear how the research areas connect to the earlier workshops / focus groups . Were academic professionals involved in the translation of focus group discussions into these research questions?

3. What makes it evident that paper leaflets should not disappear immediately? If it is the same people with impaired digital skills that are now not reading the package leaflet, it would not make any difference. Please discuss.
4. The last line speaks about content. Content is not only about what it already in the package leaflet and might be considered too much or too difficult, but also about what is not in the package leaflet and may be considered essential by health care professionals, patients and consumers in order to address real world clinical practices. Please be informed that this aspect has been discussed in the context of e.g. the EMA reflection paper on the pharmaceutical development of medicines for use in the older population.

Is the rationale for the Open Letter provided in sufficient detail? (Please consider whether existing challenges in the field are outlined clearly and whether the purpose of the letter is explained)
Partly

Does the article adequately reference differing views and opinions?
Partly

Are all factual statements correct, and are statements and arguments made adequately supported by citations?
Partly

Is the Open Letter written in accessible language? (Please consider whether all subject-specific terms, concepts and abbreviations are explained)
Partly

Where applicable, are recommendations and next steps explained clearly for others to follow? (Please consider whether others in the research community would be able to implement guidelines or recommendations and/or constructively engage in the debate)
Partly

Competing Interests: I am an EMA expert and e.g. rapporteur for the EMA reflection paper on the pharmaceutical development of medicines for use in the older population

Reviewer Expertise: Regulation

I confirm that I have read this submission and believe that I have an appropriate level of expertise to state that I do not consider it to be of an acceptable scientific standard, for reasons outlined above.

Reviewer Report 14 August 2024

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?

David K. Raynor
School of Healthcare, University of Leeds, Leeds, England, UK

Rationale
Information for patients about medicines is fast moving area, and this open letter is timely.

The letter would be strengthened by making it more clear that the arguments relate specifically to mandatory leaflets about medicines in the EU (mandated by regulators and produced by the pharma companies) - rather than leaflets and patient information available from other sources.

Related to this, it would be useful if the letter clarified the terminology used. The reader needs to know that mandatory information leaflets are referred to by Regulators as ‘Package Leaflets’ (PL). However, in common parlance they are called ‘patient information leaflets’ (PIL). In contrast, the introduction to the letter refers to ‘paper information leaflet’.

It needs to be clearer that the EMA’s electronic patient information (ePI) project relates only to putting existing mandated text in package leaflets in a format adapted for electronic handling, enabling wider use of regulator-validated medicines information in various e-formats and platforms.The mandated text must remain the same.

There is insufficient differentiation between the usability of the **text in the information** and the usability of the **electronic medium** through which the information is accessed. This is a critical difference. In respect to the former, no mention is made that all mandated leaflets in Europe have to undergo a process of ‘user testing’ with laypeople, to make sure that they are "clear, legible and easy to use'.

Accessible language
The letter is not written always in accessible language, for example ‘people suffering from chronic conditions’ rather than ‘people with long-term illnesses’ and use of the term ‘contraindications’. There are also many long sentences, which would benefit less proficient readers by being split and possibly bulleted.

Differing views and opinions
The letter should mention the comprehensive review of package leaflets commissioned by the EMA in the mid-2010s, carried out by the universities of Utrecht and Leeds. This needs to be referenced, along with the main findings from this review related to electronic medicine leaflets. This review was the stimulus for the EMA’s ePI project. I was a co-author on this review.
Assessment of current shortcomings in the summary of product characteristics (SmPC) and the package leaflet (PIL) (europa.eu)

Factual statements and arguments
The section under "Developing ePI together with patients" mentions a series of five workshops with ‘eight people from different countries affected by various disease areas’. However, the reader

would benefit from knowing whether these participants were ‘expert patients’ (such as those contributing to the work of patient organisations) and who may not be representative of the average person. More clarity is needed about these workshops, and how they were undertaken. For example, participants are referred to as ‘testers’ – was there any formal testing undertaken?

Some readers may not be aware that the leaflets for all approved medicines in Europe are available on the EMA website and the national regulatory authority websites.

Recommendations and next steps
Although the opportunities for research are articulated, the textual information about recommendations, and the next steps, could be more clearly numbered or bulleted.

Other points

- Some statements need clarification, for example in the abstract "while more patient friendly information remains a significant ask..."
- Also in the abstract is the phrase "...provide a safe digital medicine cabinet employing blockchain technology". This may not be understood by many readers.
- In the section, under ‘The future of ePI in Europe’, an example is described of a warning logo or icon that was misunderstood. It would be useful for the readers if that icon was reproduced in the letter.

Is the rationale for the Open Letter provided in sufficient detail? (Please consider whether existing challenges in the field are outlined clearly and whether the purpose of the letter is explained)
Partly

Does the article adequately reference differing views and opinions?
Partly

Are all factual statements correct, and are statements and arguments made adequately supported by citations?
Yes

Is the Open Letter written in accessible language? (Please consider whether all subject-specific terms, concepts and abbreviations are explained)
Partly

Where applicable, are recommendations and next steps explained clearly for others to follow? (Please consider whether others in the research community would be able to implement guidelines or recommendations and/or constructively engage in the debate)
Partly

Competing Interests: Academic advisor to Luto Research which develops, refines and tests health information materials. Co-chair of the Patient Safety Communication Advisory Panel of Bayer AG.

Reviewer Expertise: How to develop, refine and test health information materials.

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard, however I have significant reservations, as outlined above.

Reviewer Report 30 November 2023

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?

Golda Cohen
Université d'Angers, Angers, France

In this open letter promoting accessibility of medicine leaflets, authors present an opportunity of using a software application currently under development, ePI, which offers a range of functionalities, such as leaflet translation, zooming and a reminder system. The document emphasizes the inclusion of patients in the development of this application, an approach already implemented using focus groups. In addition, authors question stakeholders implications for further research on accessibility on medicine leaflets. However, some elements could be clarified, as mentioned below:

Abstract

1. ePI is developed to encourage the understandability of medicine leaflets for almost everyone. However, the first sentence draws attention to targeted populations: people with visual impairments, and people with chronic conditions. This sentence could be more inclusive, knowing that readability of medicine leaflets appears to be an issue to most individuals (for a sociological approach, see Akrich, 1995).

2. Authors report features designed to make information more accessible. One of these features proposes a "reminders about when to take medication" system. However, while research corroborates the potential effectiveness of this feature, authors do not specify how it works. Would it be based on user settings? Is care professionals/peers would be allowed to help?

Main body of text

1. Authors reported that some participants misinterpretated a warning sign using ePI. What was the purpose of this sign? How did they choose it? How did they solve the issue? There is a wild literature on health pictograms to improve the adherence of medicine which could help to avoid these misinterpretations (see the recent chapter from Dowse (2022) about designing, evaluating, and applying pictograms in pharmacy practice research)

2. The efficiency of ePI seems to rely on users' digital literacy. Considering the importance of this

ability, authors may write a paragraph about this topic.

3. Grey typo in figure 1 is too bright.

4. Were people over 65 included in the focus group? This population is more likely to consume medicines than the others, yet they also tend to suffer from e-Exclusion (Hetzner & al., 2014). The accessibility of ePI for seniors particularly should be considered.

5.The focus group is composed of 8 participants, including two co-authors. How were the co-authors involved? Participatory or non-participatory observation? How did authors prevent methodological biases?

Is the rationale for the Open Letter provided in sufficient detail? (Please consider whether existing challenges in the field are outlined clearly and whether the purpose of the letter is explained)
Partly

Does the article adequately reference differing views and opinions?
Yes

Are all factual statements correct, and are statements and arguments made adequately supported by citations?
Yes

Is the Open Letter written in accessible language? (Please consider whether all subject-specific terms, concepts and abbreviations are explained)
Yes

Where applicable, are recommendations and next steps explained clearly for others to follow? (Please consider whether others in the research community would be able to implement guidelines or recommendations and/or constructively engage in the debate)
Partly

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Iconography, social representations, health pictograms, health literacy, communication

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard, however I have significant reservations, as outlined above.

Reviewer Report 30 November 2023

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Pauline May
East Lancashire Hospitals NHS Trust, Blackburn, England, UK

This Open Letter outlines preliminary work involving stakeholders and patient/public advisors, into the possible formation of an application for electronic product information for medicines. The letter describes a series of workshops with patients and industry partners to help identify appropriate features of the application and to evaluate and revise the proposed application. The risks and benefits of electronic product information are outlined and a summary of recommendations for future research in this area is included.

The following comments are suggested amendments to the letter.

The abstract contains sentences that are long and complex. A plain language summary could be included, despite the statement that the abstract has been deemed suitable for non-experts. I suggest either editing the abstract to ensure that sentences are not unnecessarily long, or including a plain-language summary.

Need to define EMA in the abstract.

Figure 1: There could be more clarity/explanation as to what was involved in each of the workshops. Please also include details as to who was involved in the 5th workshop, was this with the original group or a wider audience?

The Future of EPI in Europe: Under this heading the authors describe outcomes of the workshops and possible problems with the app, should this be in the section above?

Advantages of ePI: numbers in this section need reviewing: 7,2000 and 16,9000.

Get ready to leave no-one behind: 'as apps might soon be commonplace' Are apps not already commonplace?

Table 1

Please review the following sentences: Do some groups may benefit less and why?

Can the blockchain technology used for the app made be more environmentally sustainable?

Use Question marks for all questions - consistency.

Is the rationale for the Open Letter provided in sufficient detail? (Please consider whether existing challenges in the field are outlined clearly and whether the purpose of the letter is explained)

Yes

Does the article adequately reference differing views and opinions?
Yes

Are all factual statements correct, and are statements and arguments made adequately supported by citations?
Yes

Is the Open Letter written in accessible language? (Please consider whether all subject-specific terms, concepts and abbreviations are explained)
Partly

Where applicable, are recommendations and next steps explained clearly for others to follow? (Please consider whether others in the research community would be able to implement guidelines or recommendations and/or constructively engage in the debate)
Yes

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Health literacy, musculoskeletal physiotherapy, health equity, qualitative research

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard, however I have significant reservations, as outlined above.

Reviewer Report 12 July 2023

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Amber Young
University of Otago, Dunedin, Otago, New Zealand

This Open Letter describes a research into development of an application for patients to use to read electronic information leaflets about their medicines. The Letter described background research undertaken in focus groups with eight participants to identify their needs and preferences for digital information. The authors provide a comprehensive table of recommendations for further research required around the development of this technology. The argument for digital leaflets and the benefits of an app is strong, yet some potential downsides have also been identified which is important when developing new technologies. There are some comments below that could be considered for updating this Letter.

Abstract:

1. The first sentence is quite long, could this be split into two?

2. The sentence beginning “Likewise, for people already taking different drugs….” Requires some clarification. Do you mean looking for interactions between their medications?

3. Review ‘enables’ or ‘enable’ patients to identify falsified product?

4. What do you mean by ‘understanding of how ePI works across populations’? Is this how different population groups engage with ePI?

Main body of text:

1. Consider reviewing opening sentence. I do not think the PIL ensures that medicines are prescribed safely as they are aimed at patient use rather than prescribers.

2. The statement “…someone receiving treatment for a severe or complex condition with multiple drugs would have to identify much more information…” should be revised. People would not have to but might want to identify much more information.

3. Please indicate how a patient would scan the 2D-barcode – would they need a smartphone device?

4. I like the figure, but find the light grey font quite difficult to read. Consider making this darker.

5. It is not common practice to include co-authors or members of the research team as part of the participant cohort, particularly where there may be conflicts of interest. Including patients from outside of the research group as co-authors is appropriate. Please clarify. Additionally, it would be good to gather information from a larger group as the potential cohort is very diverse with different needs and priorities – although I note this is outside the scope of an open letter.

6. An Open Letter should not include new data and analysis, although I see that these data have been presented in webinars and available in an open repository – is that sufficient?

7. The first paragraph under ‘The future of ePI in Europe’ seems to be more suited being under ‘Developing ePI together with patients’ as it is about considerations when developing ePI and what was found in your research.

8. You mention printing leaflets on request. There are numerous downsides to this, some listed, but also consider cost to the pharmacy and added time for this function and patients not knowing this could be an option – particularly concerning for those who do not have good health literacy.

9. The information about counterfeit medicines is alarming. The feature to detect counterfeit medicines is good. However, I would argue it should not be on the patient to determine if their prescribed medicines are counterfeit, but should lie with the medicine procurement agencies.

10. You mention a digital medicine cabinet – would this be built by patients scanning in all of their medicines? Could it be linked to a health record? Would they need to scan each medicine box/bottle every time they get a new one? This could become bothersome for patients.

11. Table 1 has a small typo - Equity: do some groups may benefit less and why + identifying countermeasures. Also consider in the table the legality/ethics around data management and privacy.

Ethics and consent:

Ethical approval and consent would be needed for those who participated in the focus group sessions.

Is the rationale for the Open Letter provided in sufficient detail? (Please consider whether existing challenges in the field are outlined clearly and whether the purpose of the letter is explained)
Yes

Does the article adequately reference differing views and opinions?
Yes

Are all factual statements correct, and are statements and arguments made adequately supported by citations?
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Is the Open Letter written in accessible language? (Please consider whether all subject-specific terms, concepts and abbreviations are explained)
Yes

Where applicable, are recommendations and next steps explained clearly for others to follow? (Please consider whether others in the research community would be able to implement guidelines or recommendations and/or constructively engage in the debate)
Yes

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Pharmacy, health equity, medicine and health information, communication about medicines, qualitative research

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard, however I have significant reservations, as outlined above.