

Contents lists available at ScienceDirect

Exploratory Research in Clinical and Social Pharmacy

journal homepage: www.elsevier.com/locate/rcsop



Data-enriched edible pharmaceuticals (DEEPs): Patients' preferences, perceptions, and acceptability of new dosage forms and their digital aspects – An interview study



Meie Chao ^a, Natalja Genina ^a, Netta Beer ^a, Sofia Kälvemark Sporrong ^{a,b,*}

- Department of Pharmacy, University of Copenhagen, Universitetsparken 2, 2100 Copenhagen, Denmark
- ^b Department of Pharmacy, Uppsala University, Box 580, 751 23 Uppsala, Sweden

ARTICLE INFO

Keywords:
Personalized medicine
Additive manufacturing
QR-codes
Patient-designed medicine
Patient preferences
Oualitative interviews

ABSTRACT

Background: In the field of pharmaceuticals, there is a shift away from the traditional "one-size-fits-all" concept to a more patient-centered one. A potential approach to obtain personalized medicine is with printed Data-Enriched Edible Pharmaceuticals (DEEPs). DEEPs that are printed in the pattern of QR codes contain both the patient-tailored dose and data that can be used to give patients personalized drug information and combat counterfeit medicines.

Objectives: The study aims to explore patients' preferences, perceptions, and acceptability of DEEPs, and the digital aspects of them.

Methods: Thirteen participants, living in Denmark, were interviewed twice using a semi-structured approach. Interviews were conducted face-to-face or via video calls. The interviews were transcribed, translated, and analyzed using thematic coding analysis.

Results: The participants found it useful to participate in the design of their own medicine. The orodispersible nature of DEEPs and the possibility to select color, embedded images, flavors, and physical dimensions of DEEPs were considered beneficial for patients' adherence. Patients' personal preferences, convenience, and aesthetics were the main drivers for their favored design of DEEPs. The acceptability of digital healthcare in connection to DEEPs was found to be related to the participants' level of digital literacy.

Conclusions: The participants generally had a positive attitude towards DEEPs and the digital aspects of them. However, to accept digital healthcare in connection to DEEPs, it should be adaptable and easy to use for everyone. The combination of digital healthcare and on-demand fabricated DEEPs could potentially contribute to higher patient adherence and safety in the future.

1. Introduction

Since the completion of the Human Genome Project (HUGO) back in 2003, the focus on personalized medicine has become bigger than ever before. In 2018, 42% of the new molecular entities approved by the Food and Drug Administration (FDA), were under the category "personalized medicine". This indicates that current research is leaning more towards patient-tailored therapies instead of the traditional "one-size-fitsall", which has been the concept for decades. Besides the targeted design of drug molecules based on pharmacogenomics, personalized medicine also includes tailoring the dose, dosage form, and drug release kinetics of a drug product, and in addition customization of its physical appearance and functionality. The flexible opportunities regarding adjustment of the drug's appearance make it possible for patients to be co-designers of their medication when it comes to color, pattern, and more. This, in turn, can

be used to increase medication adherence by meeting patients' (e.g., polypharmacy patients) preferences and needs. $^{4-6}$

One promising way to achieve personalized medicine is by additive manufacturing (AM), which covers 2-dimensional (2DP) and 3-dimensional printing (3DP). AM is computer-controlled and offers on-demand manufacturing. In this means that the manufacturing process can be digitally well-controlled, and precise doses tailored for individual patients can be easily achieved. In this flexible when it comes to production sites, it can be produced in, for example, hospitals, pharmacies, or other locations. At the moment, there is only one 3D-printed drug product, Spritam developed by Aprecia, approved by the US Food and Drug Administration (FDA). It was approved in 2015 and is available on the market in fixed doses produced by mass manufacturing in the pharmaceutical industry.

Data-enriched edible pharmaceuticals (DEEPs) have been proposed as new solid dosage forms that are manufactured by AM, where an ink

^{*} Corresponding author at: Department of Pharmacy, University of Copenhagen, Universitetsparken 2, 2100 Copenhagen, Denmark. E-mail addresses: natalja.genina@sund.ku.dk (N. Genina), sofia.kalvemark-sporrong@farmaci.uu.se (S. Kälvemark Sporrong).

formulation, containing an active pharmaceutical ingredient (API), is imprinted in the pattern of Quick Response (QR) codes on edible orodispersible 'paper' (substrate). 14-16 The QR encoded pattern containing the patient-tailored dose (i.e., the API) can be manufactured on-demand, and at the same time the QR code pattern encapsulates unique patient information that can be used for traceability and instantaneous on-dose verification of a single dosage form. The latter is a term used for a method that can verify an individual dosage form as an original drug product, even when removed from the primary and/or secondary packaging. 17 According to the World Health Organization (WHO), more than 10% of the global medicine market consists of counterfeit and falsified medicine, and in Asia, Africa, and the Middle East, it makes up 20% to 30% of the medicine market. 17 One way to combat counterfeit medicine could be to use new dosage forms with digital aspects like DEEPs. 15 Moreover, patients with swallowing problems, such as many in the pediatric and geriatric groups, can benefit from DEEPs as they disperse in the mouth without a need to swallow a large object. 18,19

This type of solid dosage form with digital elements is also closely linked to digital healthcare and self-monitoring, where patients can monitor critical health parameters longitudinally and unobtrusively by, for example, wearable digital devices and a smartphone.³ For example, the smartphone can be used as a "sensor for medication adherence" as it can act as a reminder or engagement service to avoid missing a dose or double dosing. It could also act as a tool for processing and displaying parameters received from wearable devices, such as pulse meters and/or oxygen saturation monitors. This information can be digitally shared with healthcare professionals for follow-up purposes and for tracking drug intake. A DEEP with an embedded QR code can contain patient-tailored and patientcollected information that is useful, and digitally as well as real-time accessible for both patients and healthcare professionals, on their demand, and in the desired format (e.g., language, specific information). Furthermore, a daily drug update can be recorded and monitored by scanning the DEEP with a smartphone and sharing this information on an online platform. This available and processed information could help healthcare professionals to have a better treatment overview and make informed decisions for subsequent treatment options that would ultimately result in better therapeutic outcomes.³ Fig. 1 illustrates the concept behind the potential implementation of DEEP in a real-world scenario.

Digital healthcare has the potential to improve issues with non-adherence. ^{20,21} However, a challenge for digital healthcare is that it relies on the engagement of healthcare professionals and patients in order to be successful. Age and level of digital literacy are important factors for patients' willingness to self-monitor and accept digital healthcare. UNESCO defines digital literacy as: "a set of basic skills which include the use and production of digital media, information processing and retrieval, participation in social networks for creation and sharing of knowledge, and a wide range of professional computing skills". ²² Geriatric patients are considered to be the most likely group to question digital healthcare and self-monitoring due to low digital literacy. ²³

To fully achieve patient adherence to and satisfaction with new dosage forms and the possible use of digital healthcare, it is important to gain knowledge about patients' needs and concerns. ⁶ The aim of this study was

to explore the preferences, perceptions, and acceptability of DEEPs as new dosage forms, and the acceptability of digital healthcare among different patient groups in Denmark.

2. Material and methods

To explore the preferences, perceptions, and acceptability of DEEPs, a qualitative approach with semi-structured interviews was used.

2.1. Setting and participants

Maximum variation sampling (i.e. striving for a wide variety of participants/perspectives) was used to explore different dimensions of the topic.²⁴ Characteristics like age, medical and social background were considered to achieve this, including persons with different cultural backgrounds and parents. Initially, participants who experienced problems with their medicines were recruited, thereafter, participants with a foreign background, participants representing the geriatric group, and parents of the pediatric group. These groups were recruited as they potentially either would have difficulties with DEEPs (e.g. language, culture) or be relevant groups for using DEEPs (difficulties with swallowing, need for monitoring). Inclusion criteria for participants were that they were 18 years or older, resided in Denmark, and used at least one prescribed oral medicine daily. For the parents, the criterion was that they had given their children at least one oral prescription medicine. Recruitment was done through snowballing, starting from the researchers' networks, however, none of the participants had personal relations with the researchers.

A recruiting post was sent to potential participants on Facebook Messenger, email, or handed out physically. The participants received no incentives for participation.

2.2. Ethical considerations

Individuals who were interested in participating in the study received an information letter describing the study and the interview process. A consent form was sent by email or handed out physically at the interview. The participants had the opportunity to ask questions before the interviews started, were promised anonymity, and gave their permission to audio recording of the interviews. The interviews were voluntary, and participants were given the opportunity to withdraw their consent at any time.

The processing of personal data in this study was approved by The Faculty of Health and Medical Sciences (no.: 514-0504/20-3000) in accordance with the rules of the General Data Protection Regulation (Regulation 2016/679).

2.3. Data collection and analysis

To make it convenient and give the participants time to reflect, the interviews were divided into 2 rounds due to the length and the extensive number of questions. The interview guide for the first interview was developed from the study aim and earlier research. It investigated participants' medical backgrounds, preferences, and perceptions towards personalized

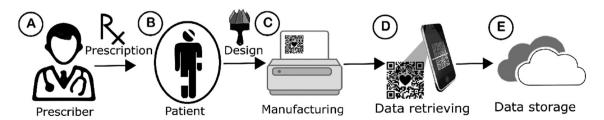


Fig. 1. Illustration of the concept behind the potential implementation of data-enriched edible pharmaceuticals (DEEPs): (A) a healthcare professional prescribes the medicine; (B) a patient has an opportunity to co-design his/her medicine; (C) customized medicine (DEEP) is manufactured, for instance, in the compounding pharmacy; (D) secured data retrieving from a DEEP with the use of a smartphone; (E) secured data storage, where only authorized parties have access.

DEEPs as a potential dosage form. Topics in the interview guide included issues with current medicines, flavors, visuals, and possibilities with DEEPs compared to current medicines. In addition, pictures of DEEP prototypes in different sizes, shapes, colors, patterns with and without incorporated images were shown to the participants to visualize the concept (see Fig. 2). The interview guide for the second interview investigated participants' attitudes towards digital health, and preferences for a potential app in connection with DEEPs. ^{23,25} Also, pictures of potential app features were shown (see Fig. 3). To further explore digital literacy, questions about what phone and (health) apps the participants used were asked, for example, "Which phone do you have?" and "Which health apps do you use?". No modifications were made to the interview guides regardless of the adult participants' background. For the interviews with parents, the interview guides were revised to get answers about their children's use of medicine.

Between the 2 interviews, participants' preferred DEEPs (sizes, shapes, colors, type of patterns) from the first interview were printed out and shown in the second interview. For those participants, who wanted both interviews conducted on the same day, several DEEPs were printed out on edible paper beforehand, to give them an opportunity to see some examples. The interviews were conducted by the first author, who at the time was a master's student in pharmacy, on Skype or face-to-face, and audio recorded with Voice Memos on Mac OS and iPhone. All data were transcribed verbatim in the language used in the interview, in Word 2020 (Microsoft). A thematic coding analysis was done, by the first author, supervised by the last author (a social scientist experienced in qualitative research), using the six phases proposed by Braun and Clarke. 26 Digital literacy was determined by an overall analysis of the participants' answers, with emphasis on questions on phones, apps, and the responses to the potential app they were shown at the second interview. High or low digital literacy was decided based on UNESCO's definition (see Introduction). All authors (second and third authors have backgrounds in pharmacy and global health, respectively) discussed the preliminary analyses during data collection and the final analysis after data collection. NVivo 12 (Mac) was used during data analysis, and relevant quotes originally in other languages were translated into English.

3. Results

Interviews were conducted between March and August 2020. Six participants were interviewed on 2 different days with 1–7 days between each interview, while 7 participants wanted both interviews to be conducted on the same day. Interviews with 5 participants were conducted face-to-face, the remaining online. Interviews were conducted in one of the languages the interviewer could speak (8 in Danish, 2 in English, and 3 in another language) and lasted from 44 to 106 min per participant.

3.1. Characteristics of the participants

Thirteen participants from different regions in Denmark were interviewed. Eleven of them used oral medicine daily and 2 of the participants were parents, who had given oral medicine to their children. The age of the participants ranged from 21 to 78 years, and they used between 1 and 7 different prescribed medicines. The parents had children in the ages 1–8 years and had given them 1 to 3 different oral prescription medicines before the interviews. See Table 1 for participant characteristics.

3.2. Patient designed DEEPs

3.2.1. Orodispersible formulation and flavors

Participants expressed that the orodispersible formulation seemed to be more comfortable to take than their current medicine. Especially the parents and participants, who had indicated that they had swallowing difficulties, found the orodispersible dosage forms valuable.

"It's very good, especially when you take a lot of pills as I do. It's much better [that it dissolves in the mouth]. I'm so tired of swallowing the pills" (P11).

Most of the participants preferred berry-like flavors (strawberry, raspberry, or blackcurrant), and citrus flavors like lemon, orange, or lime. The berrylike flavors were all chosen due to a positive taste experience from candy and other medicines. The participants, who chose the citrus flavors, all expressed that the citrus flavors were the most refreshing flavors for medicine. Other participants also noted that more flavors should be available for daily medicine takers instead of just one flavor.

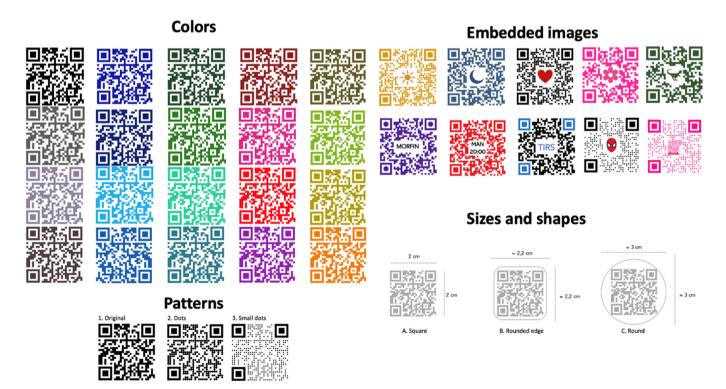


Fig. 2. The visual features of the potential DEEPs. MORFIN = Morphine; MAN 20:00 = Monday 8 pm; TIRS = Tuesday.

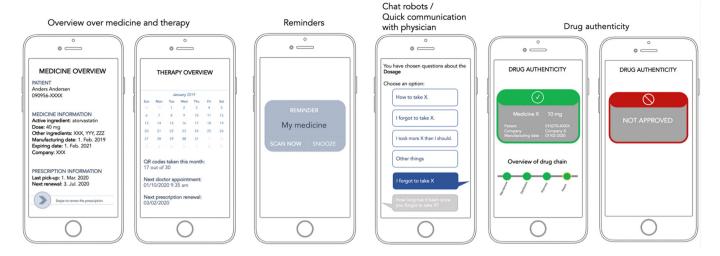


Fig. 3. Examples of features of a potential app.

Table 1Participant characteristics (Letter P refers to the adult participant and his/her number (1 to 11), whereas the parents are referred to as Parent 1 or 2.

| Participant | Age (years) *age of child | Gender (gender of child) | Occupation | Type of oral medicines (Tablets per day) | Digital literacy |
|-------------|------------------------------|-----------------------------|------------|---------------------------------------------------------------------------------------------------------------------------|---------------------|
| P1 | 21 | Female | Student | Hormonal oral contraceptives, antihistamines (2) | High |
| P2 | 65 | Male | Work | Cholesterol-lowering (3) | High |
| P3 | 26 | Female | Student | Hormonal oral contraceptives (1) | High |
| P4 | 49 | Female | Work | Antidepressants, antibiotics, antihistamines (3+) | Low |
| P5 | 24 | Female | Work | Hormonal oral contraceptives, antacids (2+) | High |
| P6 | 71 | Male | Retired | VKA, beta-blocker (3+) | High |
| P7 | 62 | Female | Retired | Cholesterol-lowering, oral antidiabetic, ACE-inhibitor, antiplatelet, antihistamine, high dose vitamin, analgesics $(7+)$ | Low |
| P8 | 75 | Male | Retired | Cholesterol-lowering, ARBs, anticoagulant (3) | Low |
| P9 | 73 | Male | Retired | Oral antidiabetic (1) | Low |
| P10 | 72 | Female | Retired | VKA, antihormone, beta-blocker, calcium (5+) | Low |
| P11 | 78 | Female | Retired | Cholesterol-lowering, antiplatelet, oral antidiabetic, laxative, ACE-inhibitor $(10+)$ | Low |
| Parent 1 | 1* | Female (*girl) | Work | Analgesics (not relevant) | High |
| Parent 2 | 2* and 8* | Male (*2 girls) | Work | Antibiotics, analgesics (not relevant) | High |

Abbreviations: VKA = Vitamin K antagonists; ARBs = Angiotensin II Receptor Blockers; ACE-inhibitors = Angiotensin-Converting Enzyme inhibitors.

"You could make like different variants with several flavors depending on if you have to take it [the medicine] daily, like all the time and over many years. It could happen that you will get tired of just one flavor" (P3).

3.2.2. The physical appearance of DEEPs

A majority of the participants preferred the DEEP to have a rounded edge rather than completely squared as a regular QR code (see Fig. 2). The rounded edges were experienced as more user-friendly and an adherence factor, as some of the participants were concerned about the sharp edges on a square. Furthermore, the size of the dosage form was found to be critical, and should, according to the participants, not be bigger than the tongue, despite the orodispersible properties of DEEPs. Therefore, a size of 2×2 cm² was perceived as being optimal.

All the participants preferred either a blue or a red pattern of QR codes in DEEPs except for one participant who chose a pink color (see Figs. 2 and 4). The main reason for choosing blue was as it was perceived as neutral. A few also associated it with the evening. The participants who chose red selected it due to easy recognition and personal preferences. They expressed that it was the "clearest" of the shown colors (see Figs. 2 and 4). It was also noticed that 3 out of 4 participants, who chose red, had a non-Danish background. However, some found red and other colors unacceptable and associated them with being too "funky", "candy-like" and "toxic". Dark

colors such as brown and black reminded some of the participants of feces and poison and were therefore not chosen. Another concern about the colors was whether or not they would make stains on the tongue due to the presence of dye in the printed QR code pattern. The parents chose green and pink for their children based on the favorite colors of the children.

According to the participants, the patterns of the QR code should either be the original pattern or the small dots (see Figs. 2 and 4). Participants' main reason for choosing the original pattern was the recognizable patterns, and for the small dots it was aesthetics. The dots were perceived as more modern and good-looking than the other two patterns. The participants perceived the small dots as the pattern with the lowest ink concentration and thereby a lower risk of adverse drug reactions (ADRs) and stains on the tongue.

The majority of the participants found an embedded image on a DEEP to be useful, especially images of heart, sun, moon, and text (see Figs. 2 and 4). The heart was chosen by several of the participants because it was representative of "life". Participants who wanted a text on the DEEPs, for example, time, day, or initials, perceived it as a useful element - an extra help to remind them when to take their medicine. This was especially true for participants, who took their medicine irregularly. One parent perceived characters, such as Peppa Pig, as a good way to help and give a good

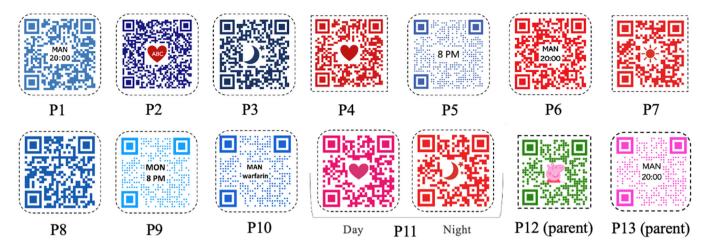


Fig. 4. Participants' preferences for the appearance of the DEEPs. MAN 20:00 = Monday 8 pm.

experience for her child when taking medicine. In contrast, the other parent was against images of cartoon characters on the DEEPs as it, for him, was associated with toys and should not be mixed with medicine.

Most participants found the opportunity of designing the appearance of their own medicine useful. Several participants said that it would be a way for them to remember the medicine because they would feel like being part of the development of it. All participants saw the possibility of a dose tailored to their needs, as a positive opportunity and the biggest advantage of DEEPs. It was seen as a solution to avoid ADRs and unnecessary doses, which participants viewed as helpful for both patients and health care professionals.

The possible price of a DEEP was an important factor for the participants. Only a few participants would choose the DEEP if it was more expensive than their current medicine. Especially participants who were retired or birth control pill users would not choose it if the price was higher. This was due to financial reasons and not enough advantages of the DEEPs as compared to existing solutions, respectively. The participants expressed that the price was one way for patients to successfully accept the product.

"People may be conservative, but something that stops people from being conservative is money" (P13).

3.3. Digital healthcare

All except one of the participants had a smartphone with a camera and internet access. Despite this, 6 of the participants could be categorized as having low digital literacy as they lacked fundamental skills regarding a smartphone, such as entering digital platforms, and processing and retrieving information. Some of them had to receive help from friends and family to get access to apps. Even though the majority of these 6 persons could use basic functions such as calling and messaging, none of them understood how to do more advanced functions like installing an app on the smartphone. One participant did not know how to enter the camera function.

The acceptability of digital healthcare was strongly connected to the participants' level of digital literacy. It was mainly the older participants and immigrants that did not fully accept or were in control of digital healthcare. Both groups were found to be more prone to deny digital healthcare due to language barriers and/or incapability of self-monitoring.

3.4. App features and self-monitoring

The majority of the participants found the shown examples of potential app functions useful (see Fig. 3), however, a few of the participants with low digital literacy had trouble understanding what it was. Medicine overviews and reminders were the 2 most chosen features. A suggested chat robot was the least preferred. Some of the participants, who got blood tests several times a year, also suggested an overview of the test results in

the potential app. Other functions that were mentioned to be helpful, were online patient information leaflets and language options.

As for the QR codes, some were unsure about the use of the code, to begin with, but they all understood the concept at the end of the interviews. The participants viewed the QR code as an extra safety since the code was unique and could contain information tailored for the individual. However, most of the participants did not want to scan the QR code on the DEEP every time they took the medicine.

Regarding drug authenticity, the majority of the participants expressed they had trust in the Danish drug regulations and the pharmacies. However, when asked about a function that could verify the authenticity of a drug, it was accepted by all participants except one. Especially participants, who came from or had worked in another country, found the drug authenticity function useful. None of the participants would, however, use the function as a part of their daily routine. Hence, it was perceived more as an extra supplement rather than actual help.

One of the most common requests for the potential app was that it should not be an extra app "floating around" on the phone, but preferably be part of, or interact with, already existing health apps. Furthermore, a general perception was that it was essential for the app to be simple and user-friendly. Despite the different preferences, the majority of the participants accepted the use of a potential app, although they thought it should be voluntary and possible to deselect.

"It would be fine to have an app. It would also be fine not to have it. There shouldn't be a demand to use it. If Mr. Jensen doesn't want to use it or can't use it, it should not ruin his medical treatment" (Parent 2).

The participants found a potential app to be time-saving for both patients and health care professionals. Especially, if more self-monitoring could be included in the therapy, it would be an advantage according to several participants with self-monitoring experience. Some participants were concerned about the lack of personal contact if more interaction between the patient and healthcare provider took place digitally. For some of the elderly participants, the digitalization of health care was also perceived as dehumanizing.

"...in this case, it could be detrimental because I believe in personal contact./
.../ We are humans and relations should not be related to a machine but should
be personal like the meeting we are having now. I think it's a part of the joy of living and being realistic. So, there are many things we cannot perceive from electronic information, but only personally" (P9).

4. Discussion

4.1. The physical appearance of DEEPs

The patients' possibility to influence the design of the DEEP was perceived positively by the majority of the participants, suggesting that an influence on their own treatment may lead to better adherence and treatment outcomes.⁶ The preferences, perceptions, and acceptability towards the appearances of the DEEPs were related to the participants' personal preferences and convenience. The colors seemed to affect the participants' acceptability indirectly. Studies have shown that the color of medicines has different meanings depending on the culture.²⁷ In this study, the selection of red color for DEEP by non-Danish patients emphasizes the influence of the cultural background on the patients' preferences.

Findings from the study showed that the orodispersible nature of DEEPs was perceived as an advantage by all participants. In recent studies, it was found that orodispersible and chewable dosage forms were preferred over conventional solid oral dosage forms, such as tablets, among children. ^{28,29} This suggests that orodispersible dosage forms like DEEPs could contribute to more convenience for all patients, although especially the pediatric and geriatric groups as they more often experience problems with their current medicine, such as swallowing issues and lack of precise doses. ^{3,28–30}

4.2. Digital health

Acceptability of digital healthcare and potential self-monitoring was strongly connected with the participants' level of digital literacy. It was seen that mainly the older participants and participants with a foreign background had challenges accepting digital healthcare. This could be a problem as the older group is one of the biggest medicine consumers, and their acceptability of digital healthcare is therefore crucial. ³¹

Similar to other studies, participants, who had the experience of self-monitoring, were highly accepting of it and felt confident with the use of digital devices. ³² The participants' acceptability towards self-monitoring could also be related to the feeling of being in control of morbidities. ³³ In contrast, participants, who did not want to self-monitor, had concerns about conducting for example health measurements. For the geriatric group, it was also associated with fear of missing personal contact. This might also explain why the chat robot function was the least preferred feature in a potential app. It has also been shown that geriatric patients are open to digital healthcare, as long as it does not replace face-to-face meetings. ²³ This suggests that, because of the diversity in digital literacy, it is important to support patients with low digital literacy or lack of interest in for example self-monitoring, in order to implement digital devices in the healthcare regimen. ²³

An important factor for the participants was to not have an extra app with separate functions, but an app collaborating with already existing healthcare apps. Also, the patients' low willingness to scan every QR code might challenge the self-reporting of a routine drug intake and on-dose drug verification possibility that DEEPs with QR codes offer. ^{15,17} Even though a drug authenticity function might not be as relevant for the Danish population (counterfeit medicines are rare in Denmark), it could still benefit other populations where the extent of counterfeit and falsified medicine is greater. ³⁴

Several studies point in the direction that personalized medicine, including DEEPs and related apps, will be more expensive than conventional medicine. ^{35–37} Even though the participants found DEEPs beneficial in several ways, the price was a factor that could change their acceptance of them. The price acceptance depended strongly on the individual participant's social and economic background, and most of them did not want to pay more than what they were used to. This could potentially contribute to health disparities in a society, depending on the health care system. ³⁷ Furthermore, studies have shown that on average, Android users in the US have a lower income than iPhone Operating System (iOS) users. ³⁷ Hence, to avoid further disparity, any QR code-related applications should be inclusive of any system related to patients' digital devices.

The participants had opinions on the things they were asked about, even though some of it, for example, the concept of DEEPs, was new to them. This shows both the feasibility and the importance of including the patient perspective in all phases of the development and implementation of personalized medicine using new techniques and digital healthcare. This can help developers achieve positive outcomes for patients.^{23,38}

4.3. Limitations

A limitation of this study was that the participants could not taste nor see the final dosage forms. They only saw a prototype version due to the COVID-19 lockdown and the inability to access the laboratories in time. Therefore, the answers were based on associations with other medicines that they had taken in the past. The final dosage forms were more flexible than the prototype. ¹⁵ Moreover, there may have been too many design options for the participants to choose from during the interviews. In general, too many choices can overwhelm patients and impair their abilities in decision-making. ³⁹

Probably, saturation was not reached in this study. As DEEPs are new dosage forms, not yet in use, this is a very explorative study. It would be hard to know when content saturation was reached as we can only hypothesize about what factors would be important to consider, for example when selecting participants. However, we included a heterogeneous sample to get as many perspectives as possible. Repeat interviews made it possible for participants to reflect on their answers in the first interview, and to get used to the idea of DEEPs. In addition, the sampling was made in steps to make it possible to include perspectives not covered by the first interviews. The transferability of the results is dependent on the populations in any other context. For example, Denmark is a country with rather high digital literacy.

5. Conclusions

The study showed that most patients were open-minded towards DEEPs. Especially the orodispersible dosage form, the possibility for individualized doses, and multiple design choices were considered as helpful factors that could benefit their daily medicine intake. The preferences, perceptions, and acceptability towards the appearance of DEEPs depended on personal preferences, convenience, and aesthetics. Acceptability of digital healthcare in connection to DEEPs was closely related to the patients' health and digital literacy. For patients to engage in it, the digital solutions should be adaptable and user-friendly, and not an excessive addition to their current healthcare. Overall, this study suggests that the opportunities of DEEPs and digital healthcare could contribute to better treatment outcomes by increasing patient adherence and safety in the future.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

References

- Carrasco-Ramiro F, Peiró-Pastor R, Aguado B. Human genomics projects and precision medicine. Gene Ther 2017;24:551–561. https://doi.org/10.1038/gt.2017.77.
- The Personalized Medicine Coalition (PMC). Personalized Medicine at FDA A Progress & Outlook Report. https://www.personalizedmedicinecoalition.org/Userfiles/PMC-Corporate/file/PM_at_FDA_A_Progress_and_Outlook_Report.pdf; 2018.Accessed Sept 23, 2021
- Raijada D, Wac K, Greisen E, Rantanen J, Genina N. Integration of personalized drug delivery systems into digital health. Adv Drug Deliv Rev 2021;176, 113857. https://doi. org/10.1016/J.ADDR.2021.113857.
- Fastø MM, Genina N, Kaae S, Kälvemark Sporrong S. Perceptions, preferences and acceptability of patient designed 3D printed medicine by polypharmacy patients: a pilot study. Int J Clin Pharm 2019;41:1290–1298. https://doi.org/10.1007/s11096-019-00892-6
- Eleftheriadis GK, Fatouros DG. Haptic evaluation of 3D-printed braille-encoded intraoral films. Eur J Pharm Sci 2021;157, 105605. https://doi.org/10.1016/J.EJPS.2020. 105605

- MacKenzie-Smith L, Marchi P, Thorne H, Timeus S, Young R, Le Calvé P. Patient preference and physician perceptions of patient preference for oral pharmaceutical formulations: results from a real-life survey. Inflamm Intest Dis 2018;3:43–51. https://doi.org/10.1159/000493346
- Seoane-Viaño I, Trenfield SJ, Basit AW, Goyanes A. Translating 3D printed pharmaceuticals: from hype to real-world clinical applications. Adv Drug Deliv Rev 2021;174:553

 575. https://doi.org/10.1016/j.addr.2021.05.003.
- Norman J, Madurawe RD, Moore CMV, Khan MA, Khairuzzaman A. A new chapter in pharmaceutical manufacturing: 3D-printed drug products. Adv Drug Deliv Rev 2017;108:39–50. https://doi.org/10.1016/j.addr.2016.03.001.
- Jamróz W, Szafraniec J, Kurek M, Jachowicz R. 3D printing in pharmaceutical and medical applications – recent achievements and challenges. Pharm Res 2018;35.
- Zheng Z, Lv J, Yang W, et al. Preparation and application of subdivided tablets using 3D printing for precise hospital dispensing. Eur J Pharm Sci 2020;149, 105293. https://doi.org/10.1016/j.eips.2020.105293.
- Öblom H, Sjöholm E, Rautamo M, Sandler N. Towards printed pediatric medicines in hospital pharmacies: comparison of 2D and 3D-printed orodispersible warfarin films with conventional oral powders in unit dose sachets. Pharmaceutics 2019;11:334. https://doi.org/10.3390/pharmaceutics11070334.
- Beer N, Hegger I, Kaae S, et al. Scenarios for 3D printing of personalized medicines a case study. Explor Res Clin Soc Pharm 2021:4. 100073.
- 13. Di Prima M, Coburn J, Hwang D, Kelly J, Khairuzzaman A, Ricles L. Additively manufactured medical products the FDA perspective. 3D Print Med 2015;2(1).
- Chao M, Öblom H, Cornett C, et al. Data-enriched edible pharmaceuticals (DEEP) with bespoke design, dose and drug release. Pharmaceutics 2021;13:1866.
- Öblom H, Cornett C, Bøtker J, et al. Data-enriched edible pharmaceuticals (DEEP) of medical cannabis by inkjet printing. Int J Pharm 2020;589, 119866. https://doi.org/ 10.1016/j.jipharm.2020.119866.
- Edinger M, Bar-Shalom D, Sandler N, Rantanen J, Genina N. QR encoded smart oral dosage forms by inkjet printing. Int J Pharm 2018;536:138–145. https://doi.org/10.1016/j.iipharm.2017.11.052.
- Leem JW, Kim MS, Choi SH, et al. Edible unclonable functions. Nat Commun 2020;11: 1-11. https://doi.org/10.1038/s41467-019-14066-5.
- Patel A, Jacobsen L, Jhaveri R, Bradford KK. Effectiveness of pediatric pill swallowing interventions: a systematic review. Pediatrics 2015;135:883–889.
- Liu F, Ranmal S, Batchelor HK, et al. Patient-centred pharmaceutical design to improve acceptability of medicines: similarities and differences in paediatric and geriatric populations. Drugs 2014;74:1871–1889.
- Hansson Scherman M, Löwhagen O. Drug compliance and identity: reasons for noncompliance. Experiences of medication from persons with asthma/allergy. Patient Educ Couns 2004;54:3–9. https://doi.org/10.1016/S0738-3991(03)00199-X.
- Klugman C, Dunn L, Schwartz J, Cohen I. The ethics of smart pills and self-acting devices: autonomy, truth-telling, and trust at the dawn of digital medicine. Am J Bioeth 2018;18: 38–47. https://doi.org/10.1080/15265161.2018.1498933.
- 22. Zelezny-Green R, Vosloo S, Conole G. Digital inclusion for low-skilled and low-literate people: a landscape review available online. https://unesdoc.unesco.org/in/documentViewer.xhtml?v=2.1.196&id=p::usmarcdef_0000261791&file=/in/rest/annotationSVC/DownloadWatermarkedAttachment/attach_import_0db84645-e500-

- $4c57-85b5-e60e1fe60af2\%3F_\%3D261791eng.pdf\&locale = en\&multi = true\&ark = /ark:/48223/p; 2021.$
- Nymberg VM, Bolmsjö BB, Wolff M, Calling S, Gerward S, Sandberg M. 'Having to learn this so late in our lives...' Swedish elderly patients' beliefs, experiences, attitudes and expectations of e-health in primary health care. Scand J Prim Health Care 2019;37:41–52. https://doi.org/10.1080/02813432.2019.1570612.
- 24. Bryman A. Social Research Methods. 4. ed. New York: Oxford University Press. 2012.
- Currie M, Philip LJ, Roberts A. Attitudes towards the use and acceptance of eHealth technologies: a case study of older adults living with chronic pain and implications for rural healthcare. BMC Health Serv Res 2015;15:162.
- Braun V, Clarke V. Using thematic analysis in psychology. Qual Res Psychol 2006;3: 77-101. https://doi.org/10.1191/1478088706qp063oa.
- Bhugra D, Ventriglio A, Till A, Malhi G. Colour, culture and placebo response. Int J Soc Psychiatry 2015;61:615–617. https://doi.org/10.1177/0020764015591492.
- Januskaite P, Xu X, Ranmal S, et al. I spy with my little eye: a paediatric visual preferences survey of 3D printed tablets. Pharmaceutics 2020;12:1-16. https://doi.org/10.3390/PHARMACEUTICS12111100.
- Alyami H, Dahmash E, Alyami F, et al. Dosage form preference consultation study in children and young adults: paving the way for patient-centred and patient-informed dosage form development. Eur J Hosp Pharm Sci Pract 2017;24:332–337. https://doi.org/10.1136/EJHPHARM-2016-001023.
- Scarpa M, Stegemann S, Hsiao W, et al. Orodispersible films: towards drug delivery in special populations. Int J Pharm 2017;523:327–335. https://doi.org/10.1016/J. LJPHARM.2017.03.018.
- Takane A, Balignasay MD, Nigg C. Polypharmacy reviews among elderly populations project: assessing needs in patient-provider communication. Hawaii J Med Public Health 2013;72:15–22.
- Huygens M, Vermeulen J, Swinkels I, Friele R, van Schayck O, de Witte L. Expectations and needs of patients with a chronic disease toward self-management and eHealth for self-management purposes. BMC Health Serv Res 2016;16. https://doi.org/10.1186/ 512913-016-1484-5.
- Kaae S, Lind J, Genina N, Kälvemark Sporrong S. Unintended consequences for patients of future personalized pharmacoprinting. Int J Clin Pharm 2018;40. https://doi.org/10. 1007/s11096-018-0596-x.
- Zhang H, Hua D, Huang C, et al. Materials and technologies to combat counterfeiting of pharmaceuticals: current and future problem tackling. Adv Mater 2020;32:1905486.
- Lind J, Kälvemark Sporrong S, Kaae S, Rantanen J, Genina N. Social aspects in additive manufacturing of pharmaceutical products. Exp Opin Drug Deliv 2017;14:927–936. https://doi.org/10.1080/17425247.2017.1266336.
- Joyner M, Paneth N. Seven questions for personalized medicine. JAMA 2015;314: 999-1000. https://doi.org/10.1001/JAMA.2015.7725.
- Sim I. Mobile devices and health. N Engl J Med 2019;381:956–968. https://doi.org/10. 1056/NEJMRA1806949.
- Krendyukov A, Nasy D. Evolving communication with healthcare professionals in the pharmaceutical space: current trends and future perspectives. Pharmaceut Med 2020;34:247–256. https://doi.org/10.1007/S40290-020-00341-0.
- Zolkefli Y. Evaluating the concept of choice in healthcare. Malays J Med Sci 2017;24:92. https://doi.org/10.21315/MJMS2017.24.6.11.