



## RESEARCH ARTICLE

**REVISED** Human-centred design of a new microneedle-based hormonal contraceptive delivery system [version 3; peer review: 1 approved, 2 approved with reservations]

Benedetta Gualeni <sup>1</sup>, Louise Hughes<sup>1</sup>, Isabelle Stauber <sup>2</sup>, Louise Ackers <sup>3,4</sup>, Angela Gorman<sup>5</sup>, Dorothy Gashuga<sup>4</sup>, Nettie Dzabala <sup>6</sup>, Frider Chimimba <sup>6</sup>, Ibrahim Chikowe<sup>6</sup>, Sion A. Coulman<sup>1</sup>, James C. Birchall <sup>1</sup>

<sup>1</sup>School of Pharmacy and Pharmaceutical Sciences, Cardiff University, Redwood Building, King Edward VII Avenue, Cardiff, CF10 3NB, UK

<sup>2</sup>Maddison Limited, Walnut Tree Yard, Lower Street, Fittleworth, RH20 1JE, UK

<sup>3</sup>School of Health and Society, University of Salford, Allerton Building, Salford, M6 6PU, UK

<sup>4</sup>Knowledge for Change, Plot 39 Saaka Road, Kagote, Fort Portal, P.O. Box 392, Uganda

<sup>5</sup>Life for African Mothers, Suite 18, Big Yellow Storage, Cardiff, CF10 5DL, UK

<sup>6</sup>College of Medicine, University of Malawi, Mahatma Gandhi Road, Blantyre, Malawi

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**Abstract**

**Background:** It is estimated that 225 million women worldwide have an unmet need for family planning, and more than half live in low- and middle-income countries. Increasing the choice of contraceptive methods available can reduce this unmet need. Microneedle drug delivery systems represent a new technology for minimally invasive self-administration of contraceptives. We explored stakeholders' views on different aspects of a proposed microneedle-based hormonal contraceptive delivery system. The feedback was used to iteratively develop this delivery system.

**Methods:** Focus group discussions and semi-structured interviews were conducted with potential stakeholders (women and trans males of childbearing age, their partners, and health professionals and organisations that provide family planning advice and contraception services) in Uganda, The Gambia, Malawi, and the UK, exploring concept acceptability and gathering feedback on different aspects of design and usability of the proposed delivery system.

**Results:** Participants viewed the concept of a new, microneedle-based contraceptive favourably. In Uganda, participants were presented with 7 different prototype applicators and identified desirable features of a preferred delivery device; their input reducing the number of prototypes that were subsequently evaluated by stakeholders in The

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1. **Maggie Kilbourne-Brook**, PATH, Seattle, USA
2. **Rebecca L. Callahan** , FHI 360, Durham, USA
3. **Aluisio J.D. Barros** , Universidade Federal de Pelotas, Pelotas, Brazil

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Gambia and the UK. Participants in these countries helped to identify and/or confirm the most desirable characteristics of the applicator, resulting in design consolidation into a refined concept applicator. The final, optimised applicator prototype was validated during user research in Malawi. This human-centred design approach was also used to iteratively develop an information leaflet for the device.

During these user studies, other preferred aspects of a contraceptive delivery system were also evaluated, such as anatomical site of application, duration of action, and return to fertility.

**Conclusions:** A new microneedle-based contraceptive delivery system was iteratively developed using a human-centred design approach and was favourably received by potential stakeholders. The product is now being refined for testing in pre-clinical studies.

### Keywords

Human-centred design (HCD), Microneedles (MNs), Hormonal contraceptive, User studies, Family Planning, Low- and middle-income countries (LMICs), Medical device development.

**Corresponding author:** Louise Hughes ([HughesML@cardiff.ac.uk](mailto:HughesML@cardiff.ac.uk))

**Author roles:** **Gualeni B:** Formal Analysis, Investigation, Writing – Original Draft Preparation, Writing – Review & Editing; **Hughes L:** Conceptualization, Data Curation, Formal Analysis, Investigation, Methodology, Writing – Original Draft Preparation, Writing – Review & Editing; **Stauber I:** Investigation, Methodology, Resources, Visualization, Writing – Original Draft Preparation, Writing – Review & Editing; **Ackers L:** Resources, Supervision, Writing – Review & Editing; **Gorman A:** Resources, Writing – Review & Editing; **Gashuga D:** Investigation, Resources, Writing – Review & Editing; **Dzabala N:** Investigation, Resources, Supervision, Writing – Review & Editing; **Chimimba F:** Investigation; **Chikowe I:** Investigation; **Coulman SA:** Conceptualization, Funding Acquisition, Supervision, Writing – Review & Editing; **Birchall JC:** Conceptualization, Funding Acquisition, Investigation, Project Administration, Resources, Supervision, Writing – Review & Editing

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**REVISED Amendments from Version 2**

In response to the comments from the reviewers, we have added some clarifications in the manuscript.

In particular, we have briefly highlighted the broader context of this research, clarified why the 6-months duration was chosen and how we selected the countries for our user studies.

A brief description of the meaning of “dummy prototype applicator” was given and clarification regarding what was shown to which participants and when was added.

A paragraph explaining that IP issues prevent us from showing detailed images of the prototypes used was added.

**Any further responses from the reviewers can be found at the end of the article**

## Introduction

The United Nations (UN) Sustainable Development Goals for 2030 recognise the importance of Family Planning (FP) as a key component of global good health and wellbeing (Goal 3.7)<sup>1</sup>. In addition to providing decision-making autonomy on whether, when and how many children to have, numerous studies have demonstrated that increasing access to FP can reduce maternal and infant mortality, decrease unsafe abortions, increase educational prospects, and reduce poverty<sup>2–10</sup>.

Despite a worldwide increase in contraception use, it is estimated that currently 225 million women worldwide have an unmet need for FP (to limit or space births). More than half of the women with this unmet need live in low- and middle-income countries (LMICs), including countries in Sub-Saharan Africa (SSA)<sup>11</sup>. A wide range of factors influence contraceptive use including, but not limited to, socio-cultural norms, socio-economic status, education and occupational status, proximity to FP clinics, knowledge and understanding of methods, availability of educational tools, fear of side effects, gender power imbalances, provider’s skill and personal bias, and ability to discuss FP with partners, friends, and healthcare providers<sup>12–16</sup>. Enhanced education and improved access to FP is paramount to satisfy the unmet FP needs of individuals in LMICs<sup>17,18</sup>. Increasing the number and variety of methods of contraception available to potential end-users has also been proposed as a strategy to help reduce the unmet need for FP in these countries<sup>12,19</sup>. A new minimally invasive microneedle-based hormonal contraceptive delivery system that requires minimal training and is easy-to-use is therefore potentially an attractive proposition<sup>20</sup>.

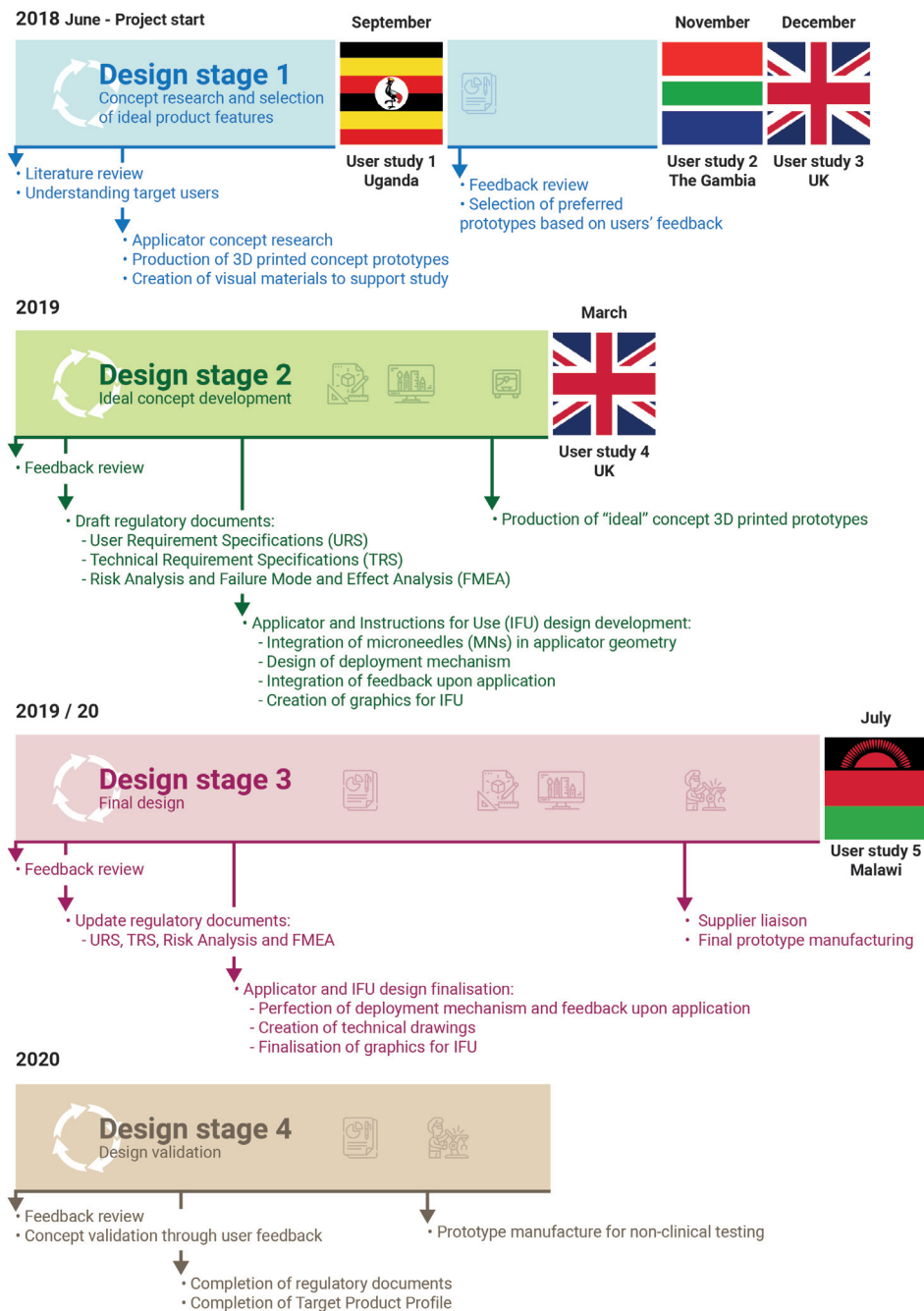
Microneedles (MNs) are medical devices containing microscopic needle shaped projections that can be applied to the skin to deliver a wide range of therapeutics in a minimally invasive, painless, and safe manner<sup>21–24</sup>. Biodegradable polymer MNs are able to facilitate controlled release of the therapeutic cargo<sup>25</sup> and therefore could be exploited for the release of hormonal contraceptives over extended periods of time ( $\geq 1$  month)<sup>26–29</sup>.

In this study, an innovative MN-based, progestin-only hormonal contraceptive delivery system with the potential for self-administration was explored with prospective stakeholders. A human-centred design (HCD) approach was used to directly inform specific design features of the system and develop prototype products. HCD, which originated in the computer science and artificial intelligence fields<sup>30</sup>, is increasingly being used to design novel solutions for complex problems in global health<sup>31</sup>, including reproductive health<sup>32–34</sup>. This highly multidisciplinary method incorporates the voice of end users throughout all stages of iterative product development. In this study, end users and stakeholders were recruited and engaged to inform the aesthetics and usability of a proposed new MN-based delivery system, and to iteratively develop a user-friendly instruction leaflet. During the study, participants were also encouraged to share their thoughts on the proposed mode of administration, mode of access, duration of contraceptive effect, and time to return to fertility after discontinuation of the contraceptive. Feedback facilitated the development of a user-informed delivery system with desirable features and iterative optimisation of prototypes, resulting in a validated optimised product that is currently being tested in pre-clinical studies.

## Methods

### Concept development

The concept of a new MN-based progestin-only hormonal contraceptive delivered by an applicator was developed by the team after reviewing the available literature and discussing the expectations of stakeholders regarding novel contraception solutions with experts in the field of FP in LMICs. The initial concept was to develop a long-acting, reversible, MN-based, progestin-only hormonal contraceptive, that is delivered by an applicator, can be self-administered (or administered with minimal training), is stable at high temperatures and high humidity, and can be mass produced at low cost. An assortment of potential products, with different features (Design Stage 1, Figure 1) were therefore developed. These initial product designs were informed by the published literature, the opinions of stakeholders with experience of developing and/or using FP in LMICs and the multidisciplinary research team, which includes product designers, engineers, pharmaceutical scientists and polymer scientists. Injectable contraceptive products provide 12 weeks (3 months) of contraception and implants provide more than 12 months of contraception to the user. The proposal was therefore to develop a product with an alternative duration of action that would provide users with another contraceptive choice. Based on current technology, a 6-month duration of action is at the technical limit of what can be achieved using a relatively small microneedle array patch, considering drug loading limitations and the preferred size of patch indicated by potential users. A HCD approach (Figure 2) was used to integrate the views of potential end users and other key stakeholders at all stages of product development. This process however does not guarantee that the final product will be commercially viable or approved in a particular territory, with other issues such as manufacturability, scalability, regulatory issues, cost of goods, market access and distribution also playing

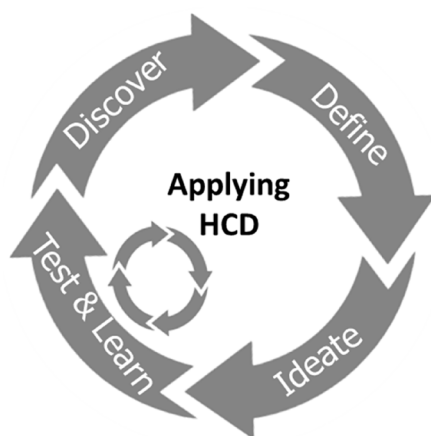


**Figure 1. Project timeline.** Following the HCD approach schematised in Figure 2, the project started with concept research based around the published literature on the unmet need for contraception in LMICs. Multiple prototypes covering a wide range of desirable features for a contraceptive product were produced and evaluated by potential stakeholders in LMICs. Participant feedback helped refine the product according to stakeholders' preferences and consolidate the final product design. This was then validated through a final users' evaluation prior to pre-clinical testing.

important roles. These issues are also being scrutinised in product development, but are not reported here as they are outside of the scope of this article.

A detailed timeline of the performed activities is provided in Figure 1.

A total of 31 focus group discussions (FGDs) and 15 semi-structured interviews (SSIs) were conducted with participants in Uganda (September 2018 – Stage 1), The Gambia (November 2018 – Stage 1), The UK (December 2018 – Stage 1; March 2019 – Stage 2), and Malawi (July 2020 – Stage 3) to explore participants' feedback and preferences regarding



**Figure 2. Diagram illustrating the different steps of a Human Centred Design study.** After defining the area of innovation, the target end users and the context of use are considered to ideate possible solutions for the unmet need that is being addressed. The proposed solutions are tested by potential end users and their feedback is incorporated into a refined design. Multiple iterations of this process lead to the development of the final product.

different aspects of the applicator design and appearance of the instruction leaflet. Uganda, The Gambia, and Malawi were selected amongst FP2020 countries due to existing academic or charitable links. Studies in the UK were conducted to explore the views on a new long-acting contraceptive in an industrialised country. During FGDs/SSIs, participants views were also explored regarding the proposed anatomical sites of application, scenarios for contraceptive provision, duration of action, acceptable time to return to fertility after discontinuation, and any other identified benefits and/or concerns; these are described in more detail in the subsequent text.

### Study design

A pragmatic, qualitative approach was developed due to the exploratory nature of the research aims. SSIs and FGDs were used, with the choice of method dictated by local needs, participant preference, and ability to arrange homogeneous groups. Where no preference was expressed by the participants and there were no logistical issues, FGDs were the preferred method due to the dynamic nature of discussion amongst participants leading to increased opportunity to understand their views<sup>35</sup>.

Illustrated scenarios and prototype delivery systems were used during FGDs and SSIs. This allowed participants to visualise the concept, interact with the prototypes and express their preferences. Pre-interview questionnaires were also used to obtain demographic information and to understand participants' views and experiences of contraception.

### Ethical considerations

Ethical approvals for the studies were sought and obtained from Cardiff University School of Pharmacy and Pharmaceutical Sciences Research Ethics Committee (UK) (SREC references: 1718–29 and 1920–17), University of Salford Research Ethics Committee (UK) (HSR1617-129), Mountains of the Moon

University Research Ethics Panel (Uganda) (MMU/DPGSR/061218), the Gambia Government/MRCG Joint Ethics Committee (R018030) and the College of Medicine Research Ethics Committee (Malawi) (COMREC reference: P.01/19/2580).

Participants provided written informed consent prior to data collection; a detailed information sheet was provided, and potential participants were able to ask questions before deciding whether to participate. Due to the potentially sensitive nature of the topic, participants were reminded of the confidentiality of discussions at the beginning of the exercise. SSIs and FGDs were held in locations convenient to the participants, and where they could not be overheard by others. All interview transcripts were anonymised. Recordings and transcripts were retained on a password protected folder only accessible to the research team and all paperwork (consent forms and screening questionnaires) held in a locked filing cabinet.

### Development of research materials

A demographic questionnaire was developed to obtain brief background information about the participants. This was based on published research detailing those factors which might influence views and preferences of FP, including age, religion, family status, education and occupational status, previous and current experience with contraception<sup>12–17</sup>, and allowed the research team to ensure a range of participants with different background characteristics were included in the SSIs/FGDs.

A topic guide for the FGDs/SSIs was designed to explore the participants' general views around current contraceptive options, to provide context, before moving on to discuss the proposed new method in more detail. This second part of the topic guide included broad questions about the concept, following a brief introductory explanation, and the participants were then shown a range of prototype delivery systems and associated instructions. Questions and prompts related to the participant's preferences around the aesthetics, functionality, and usability of these prototypes, as well as suggestions for improvements. Questions were based on published research literature, discussions within the team, and specific technical features that required prospective stakeholder input. Advice from the Population Council (an international, non-profit, non-governmental organisation specialising in reproductive health), local SSA researchers, local SSA District Health Officers and contacts who undertake charity, research and health work in the countries concerned was crucial for developing the topic guide described above, in order to assure its local socio-cultural acceptability. In addition, two pilot FGDs (one with potential users, and one with potential providers) were used to test the topic guide; no changes were required. Feedback from the Bill & Melinda Gates Foundation (who provided funding for this research) also informed development of materials. All materials used in the study can be found as extended data<sup>36</sup>.

Illustrated scenarios and prototype 3D delivery systems were produced by Maddison Ltd. (a specialist product design consultancy), offering a range of options regarding potential use environment and design features. These enabled participants to imagine using the product, handle prototype models, and

give more specific feedback about design, functionality, and usability. At this stage we are not able to share any images of the prototypes, as publishing them will constitute a prior art disclosure that will inhibit our ability to protect the novel mechanism used within the applicator.

Different versions of user instructions were also prepared, ranging from very detailed text instructions to simplified coloured visual images, and feedback on the clarity and messaging in these resources was sought during FGDs and SSIs.

### Sampling and recruitment

Feedback from four distinct groups was sought: potential users of the proposed contraceptive solution (Uganda, The Gambia, Malawi, United Kingdom), men whose partners are potential future users of such a product (Uganda, The Gambia), health professionals who are potential suppliers of the proposed device (Uganda, The Gambia, Malawi, United Kingdom), and organisations that provide FP advice and contraception in SSA (Uganda, The Gambia) (Figure 3). There were no sample size calculations, rather data collection continued until all opportunities had been exhausted within the limits of the data collection period, e.g. the duration of the field visit (Uganda, The Gambia, UK). In Malawi a target of 30 users and 30 providers was identified as being realistic to provide sufficient feedback within the research timescales, based on experience in earlier phases. Each group is considered in turn below.

Eligible potential users (n=88) were classed as women or trans males of childbearing age (nominally aged 18–45), regardless of prior or current contraceptive use or non-use. Recruitment was predominantly through convenience and purposive sampling. Local gatekeepers used their knowledge to purposively sample and recruit (face-to-face or via telephone) via different contacts and settings to facilitate a diverse demographic (age, education, living arrangements, marital status, family status, use of contraception, religion) that would encompass different views and preferences<sup>12–16,37</sup>. In addition, posters were placed in community venues to allow individuals to self-select (UK only).

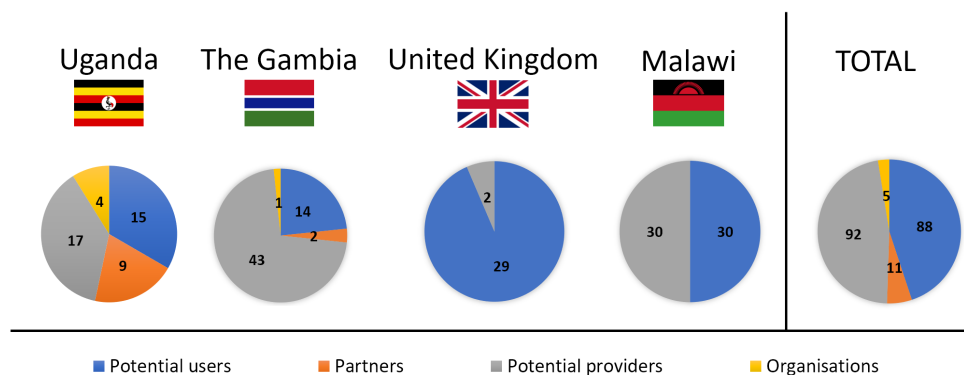
Partners of potential users (n=11) were loosely defined as men whose partners may consider using contraception. They were convenience-sampled opportunistically using local links, and invited to participate, since prior research has shown that in some settings male partners’ views can play a significant role in the use (or non-use) of contraception<sup>38–40</sup>.

Potential providers (n=92) were defined as health professionals of any type, whose role involves the provision of contraceptive advice and / or methods. They were recruited through clinics, workplaces, and local contacts, using purposive sampling to identify providers with a range of roles (medics, nurses, midwives, interns, and healthcare students) and experience in different work environments (rural or urban). Other characteristics (age, religion, personal experience with contraception) were also identified where possible, to check for the further diversity of the sample.

Organisational stakeholders (n=5) were identified by team members and local links using convenience sampling. These were defined as individuals working for non-governmental organisations, which play a role in the provision of contraception in the relevant countries. Typically, an introduction was made initially by a local contact and then the interview set up directly by the researchers. Interviews with these key informants focused on their views on the proposed delivery system in terms of acceptability within the country.

### Data collection process

A questionnaire (as described above) was used with all groups, except organisational stakeholders, to identify relevant background/demographic data. This was provided alongside the participant information sheet and requested to be returned, completed, to the researchers before or during the interview or FGD if they consented to participate. A semi-structured topic guide (as discussed above) was used to guide the SSIs/FGDs performed at Design Stage 1, 2, and 3 which were audio-recorded, with consent. Where consent was not given for audio-recording, detailed written notes of the conversation were taken with the consent of the participant.



**Figure 3. Participants in the study grouped by country.** Four different groups were included in focus group discussions and semi-structured interviews: potential users (blue), partners of potential users (orange), potential providers (grey) and organisations that provide family planning (yellow).

Interviews and FGDs in the UK, The Gambia and Uganda were undertaken by members of the research team or their students with experience and/or training in data collection methods (n=6, JB, BG, LH, IS plus 2 MPharm students). (FGDs/SSIs conducted in English, or through pragmatic use of a local, neutral translator). Local, trained, researchers collected the data in Malawi (FGDs conducted in Chichewa, translated for data analysis, and back-translated to ensure the accuracy of transcription). Typically, FGDs involved two researchers and SSIs one researcher, with the exception of SSIs with organisations. Female researchers were used to collect data from potential users in case any participants would find it difficult or inhibitory to talk to a male researcher about the topic. Conversely, where possible male researchers collected data from partners. Researchers presented themselves as neutral members of the wider project team, with a focus on obtaining open and honest views on the new device to feed back to colleagues in the technical team. Participants were therefore encouraged to say what they genuinely thought about the idea without fear of offending anybody.

The choice of whether data was collected via SSI or FGD depended on logistics and participant preference. Focus groups were ideally intended to have between 4–6 participants but a pragmatic approach was taken to ensure convenience for participants (e.g. pre-formed groups slightly larger than this were accepted). While groups involved only one type of stakeholder to ensure a degree of homogeneity, allocation to specific FGDs within each category was based predominantly on logistics. Each participant took part in just one SSI/FGD (I.e. the same individuals did not contribute to more than one SSI/FGD or stage of research). Locations were chosen based on convenience to the participants and their ability for the data collection to be carried out without being overhead or interrupted, for example a meeting room in a workplace or private space in a local community venue. Typically, interviews were anticipated to take 30 minutes and FGDs around 60–90 minutes. Although the time-limits on the field trips meant it was not necessarily possible to reach data saturation, the research team reflected on the experience and findings after each data collection point to ensure data was obtained on all of the key aspects as identified in the topic guide.

As noted above, SSIs/FGDs were audio-recorded with consent, and brief field notes were made where appropriate to supplement the recordings. During FGDs and SSIs with potential users, providers and organisations, dummy prototype MN applicators were used to obtain feedback on handling/ergonomics and aesthetics. This portion of the FGDs/SSIs was video recorded, with consent, to enable visual feedback on the handling of the delivery systems, with filming focused on the participants' hands and not faces. The dummy prototypes used in the studies consisted the fully functional applicators without the presence of MNs. This allowed participants to experience the mechanism of deployment, usability, duration of application and feedback from the applicator.

All of the participants were first shown the visual renderings, to familiarise them with the basic concept. After the

concept was explained using these illustrations, participants were encouraged to ask general questions regarding the concept (side effects, duration, return to fertility, etc). After this discussion (usually lasting 15–20 minutes) all participants were shown the dummy prototypes (without MNs) with examples of associated instruction leaflets. All participants then had the opportunity to handle and deploy the prototypes multiple times (on themselves and/or on other participants). After handling the prototypes for about 10 minutes, participants were asked to provide specific feedback on the applicators (ease of use, size, mechanism, aesthetics, etc) for the rest of the discussion (10–15 minutes).

### Data analysis

Audio-recordings were transcribed, translated when necessary, anonymised, and thematically analysed. Data collection and analysis were iterative, with results from one stage feeding into the product design and enabling more focussed and detailed information to be collected in the next stage, as presented in [Figure 1](#).

Coding and analysis were undertaken by three members of the research team with independent coding of the same data, followed by discussions, as an internal assurance check. At each stage, coding was carried out manually by reviewing and annotating transcripts line by line; decontextualization and recontextualization to group codes and development of themes was facilitated using MSWord®. A theoretical framework was not used: data were predominantly analysed inductively, with themes being derived from the data collected, although constant comparison was used to deductively review earlier SSIs/FGDs where a new theme arose from a later SSI or FGD. Deductive content analysis was used for the factual background information provided at the start of the SSI/FGD (e.g. providers' roles and responsibilities).

Logistically it was not possible to provide the transcripts or findings to the participants for comment, although all participants were provided with contact details for the research team should they wish to know more (none got in touch).

## Results

### Participants

As presented in [Figure 1](#), Stage 1 user studies were conducted in Uganda (User study 1), The Gambia (User study 2), and the United Kingdom (User study 3); Stage 2 user studies were conducted in the United Kingdom (User Study 4); Stage 3 user studies were conducted in Malawi (User study 5). An overview of the participants who took part in the user studies is presented in [Figure 3](#). In User study 1, 15 potential users, 9 partners of potential users, 17 potential providers and 4 organisational stakeholders were confirmed as eligible and took part in the study. In User study 2, 14 potential users, 2 partners of potential users, 43 potential providers and 1 organisational stakeholder were confirmed as eligible and interviewed in SSIs/FGDs. In User study 3, 23 eligible potential users participated in the study. In User study 4, 6 potential users and 2 potential providers were confirmed as eligible and gave feedback on the concept refined during Stage 2. Finally, in User study 5, 30 potential users

and 30 potential providers evaluated the final prototype designed during Stage 3.

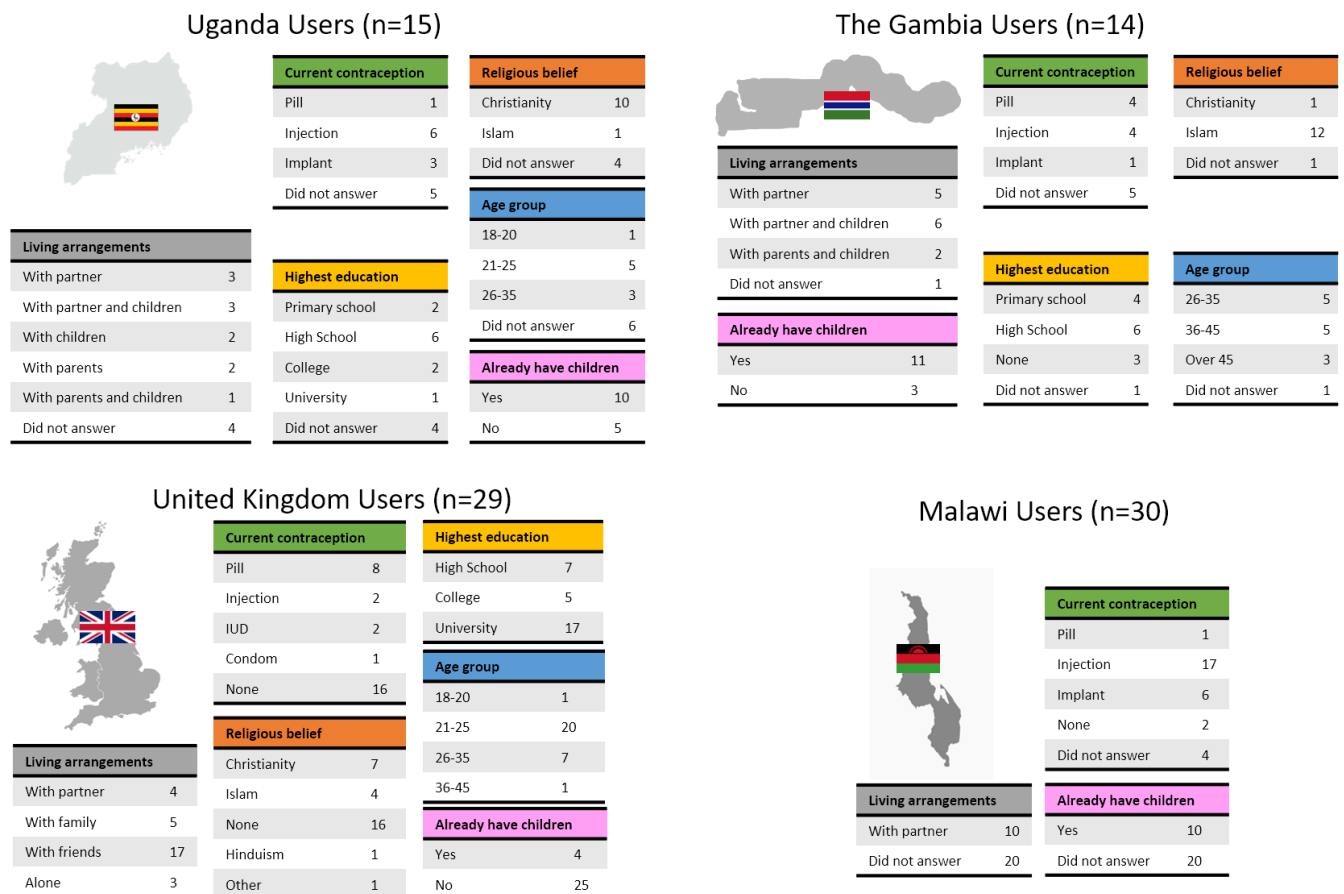
Potential users were selected to cover a range of ages, educations, religious beliefs, family status and experience with contraception (Figure 4). Male and female potential providers holding clinical and non-clinical roles took part in the study (Figure 5).

### Iterative applicator design

Concept research at Design Stage 1 (Figure 1) led to the creation of a series of prototype delivery systems, which explored different aspects of ergonomics, overall product dimensions, actuation force, feedback on application and potential for self-application. These prototypes, and other visual materials created to support the formative studies, were used to get feedback directly from stakeholders in different countries, as detailed in the section above. The feedback received at each stage helped iterate and refine the design concept to create a final end-user informed prototype. This iterative HCD process is detailed below, and follows the diagram presented in Figure 2 and the timeline presented in Figure 1.

Participants in Uganda (User study 1) were presented with 7 prototype delivery systems and identified positive (ease of use, ease of self-administration, presence of a feedback confirming correct application, small size, easy to understand functionality) and negative (large size, not easy to self-apply, too complicated, scary aesthetic) features of the different prototypes. After handling and discussing the prototypes, participants helped identify four preferred devices out of the seven concepts, with one prototype in particular being preferred by 23 out of 32 potential users and providers because of its intuitive mechanism of action and the ability to be applied it easily with one hand. Overall, the feedback received in User study 1 helped determine the essential features of a successful user experience. The prevailing characteristics of the applicator being as small a size as possible, having a “friendly” aesthetic, and an intuitive actuation mechanism resulted in design refinement and a reduction in the number of prototypes used in subsequent field visits.

Participants in The Gambia and the UK (User studies 2 and 3) were presented with the 4 preferred applicator prototypes (determined in User study 1), to facilitate more focussed and



**Figure 4. Demographic data of end users grouped by country.** To receive comprehensive and diverse feedback, potential users of different age, education, religion, and at different stages of family planning were included in the study.



Uganda Providers (n=17)			
Role		Gender	
Clinical	15	Male	0
Non-clinical	1	Female	17
Data not available	1	Data not available	-

United Kingdom Providers (n=2)			
Role		Gender	
Clinical	2	Male	0
Non-clinical	0	Female	2
Data not available	-	Data not available	-

The Gambia Providers (n=43)			
Role		Gender	
Clinical	15	Male	4
Non-clinical	9	Female	29
Data not available	19	Data not available	10

Malawi Providers (n=30)			
Role		Gender	
Clinical	25	Data not available	
Non-clinical	2		
Data not available	3		

**Figure 5. Demographic data of providers grouped by country.** Potential providers with a range of roles took part in this study. Tables are based on the available data only, as not all participants completed the questionnaire.

richer feedback. The four prototypes provided participants with a narrowed selection of feedback mechanisms upon application, different small geometries, and a range of actuation methods. Potential users and providers in User studies 2 and 3 preferred the same prototype design as participants in User study 1. The favoured design was perceived as easy and quick to use; one potential provider in The Gambia noted: *“I can do it for somebody, and I can do it for myself”*. In The Gambia, when others observed fellow participants using this particular prototype, appreciative comments, loud cheers and even applause were noted. Specific features of other prototype designs were also recognised as desirable by Gambian and British participants, including smaller size, presence of a feedback mechanism providing visual confirmation of correct administration, and the need for a greater actuation force to provide confidence that an application has been performed correctly. The desirable features identified during User studies 1, 2 and 3 were combined to provide a refined concept for the delivery system. This was subsequently manufactured and presented to potential users in the UK (user study 4). The presence of both visual and audio feedback in this refined applicator design was appreciated by British participants, but they felt that the visual and audio feedback cues could be amplified, giving them more confidence that an application was performed correctly. Participants noted that the force required to actuate the prototype was too low, potentially risking unintended activation, and suggested a greater force for actuation of the device. The transport/disposal cap included in this optimised prototype was considered too easy to remove and therefore not childproof. Feedback from User study 4, together with lessons learned during the previous user studies, directly informed the development of a final optimised prototype device.

In the final optimised iteration, loud audio and clear visual feedback mechanisms were incorporated to indicate effective actuation of the delivery system. The force necessary to deploy the device was doubled, to prevent accidental activation, and

the transport/disposal cap was improved to increase childproofing and prevent accidental exposure after disposal. The device dimensions were finalised to accommodate the number of MNs that would be necessary to provide 6 months' dose of contraception. The internal mechanism, allowing simple actuation and deployment, was engineered and integrated in the design while always considering the end-user preferences for a small, easy to use delivery system; this did not affect the ergonomics of the previously validated prototype and was informed by the data gathered during the user research and feedback received throughout this study. The optimised final prototype delivery system was tested in Malawi (User study 5) where potential users and providers validated the size of the device and commented positively about its aesthetics. Most providers in User study 5 felt the device could be packaged in a comparable way to other medical products. Transparent packaging, to allow users to view the device, or an image of the device on the packaging were suggested to instil trust in potential users. The presence of visual and audio feedback confirming a successful application was considered important by both potential users and providers, particularly given the painless nature of the application.

During the different stages of development, participants were also asked, with the help of visual renderings, if they would prefer the device to have an obvious 'medical product' appearance, or an aesthetic totally removed from the clinical environment. Some potential users felt that a colourful device that shared a similar appearance to a make-up accessory would be easy to conceal if taken home, but most potential users and providers expressed a preference for a medical-looking device, with a medical aesthetic (i.e. clean, neutral colours) deemed to help instil trust in the product. The final prototype reflected this; it was designed with clean lines and it is white apart from the visual feedback indicator. An option to apply a custom label to the top of the applicator was also integrated into the design. This provides a simple way of adapting the appearance of the product to a wide range of users and settings.

### Iterative development of the instruction leaflet

Providing clear and reassuring instructions is key to a product's success, even though it is an aspect of usability which is often overlooked. Therefore, significant effort was put into developing an instruction leaflet that could be easily understood by all potential users, irrespective of their background. Concept research led to the design of three versions of the instruction leaflet, which were presented to participants in User studies 1, 2 and 3. One version looked more clinical, with precise imagery and detailed text describing the application process. The second version contained simple, cartoon-like illustrations of the application process, with numbered steps as the sole text. The third version was pictorial-only, with detailed illustrations outlining the application steps with colour used to provide emphasis and explain the application process.

Participants felt that the more detailed text instructions were very clear but maybe more suited to health professionals, while the visual-only instructions were perceived to be more suited to women that did not like reading or were illiterate. As one provider in Uganda explained: *"For women, this one [colour coded images] can work. But for us, this one [detailed writing]"*. Generally, participants considered a combination of words and images as the best option, being suitable for all users, no matter their level of education.

A new instruction leaflet was produced in response to this feedback. In this iteration, emphasis was given to the step-by-step visual instructions using a combination of detailed illustrations and use of colour to highlight key elements of the application process. Each illustrated step was also detailed with text, to allow users to correctly apply the product by reading the text and/or looking at the imagery. This improved instruction leaflet was subsequently presented to participants in Malawi (User study 5), who considered it appropriate. However, both providers and users suggested that the instructions need to be available in multiple languages as appropriate to the location (e.g., English and Chichewa for Malawi).

### Anatomical site of application

Participants feedback was sought on the proposed anatomical sites of device application, with the help of visual renderings (Figure 6). The concept was developed for application to 'fleshy' areas of the body, such as the thigh or the side of the hip, and so a limited number of options were offered.

The thigh (if self-applied) and the upper arm (if applied by a provider) were identified as the preferred anatomical sites for administration by most participants at all stages of product development. As one provider in Uganda explained: *"On the thigh if it [is] self-administered. But if it can be administered by a nurse, it can be the arm."* These sites were perceived as easy to access, easy to conceal with clothing after administration (Potential user, The Gambia: *"If people don't see it, then it's where I'm going for"*), less painful (Potential user, UK: *"I don't think I would like it on the side of the hip coz I think that would hurt more"*), and familiar due to the fact that they have experience with other medicines that are applied to these body sites.

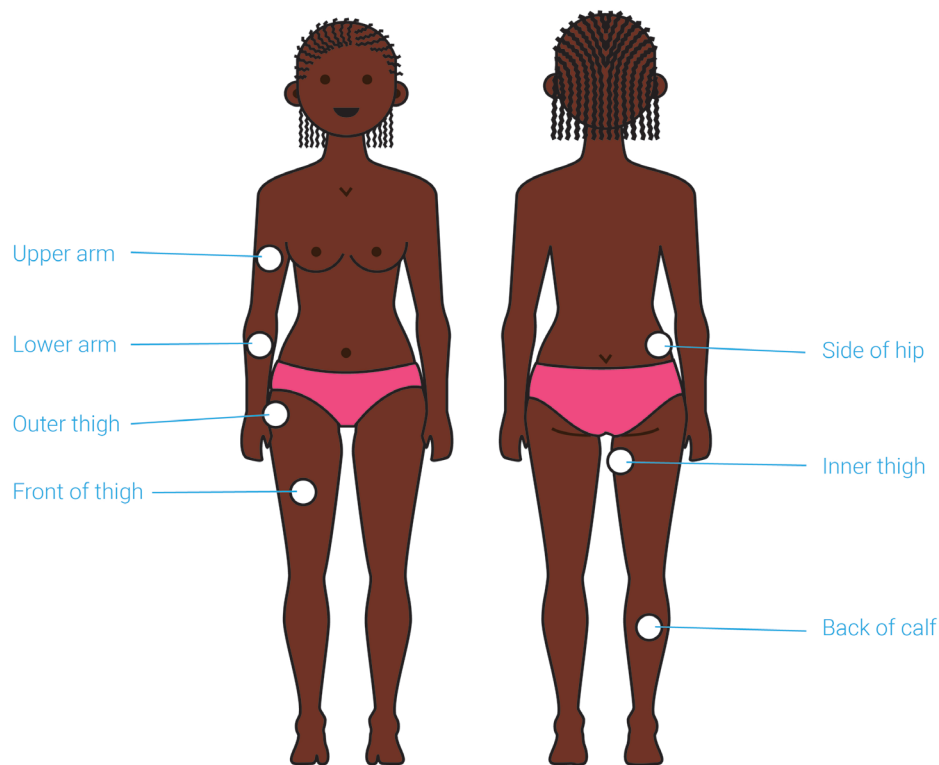
### Scenario for contraceptive provision

Three different scenarios to access the contraceptive solution were presented to participants (Figure 7). The majority of potential users in The Gambia and Malawi felt the device should be distributed by hospitals and clinics and administered by a health professional (scenario A) to ensure appropriate application of the device and privacy (Potential user, The Gambia: *"Example, if you have a husband, he travels outside The Gambia and you are taking this device, what will your neighbours say? The husband is not here and she's taking contraceptive"*). Potential users in Uganda expressed an interest in obtaining the device through hospitals and clinics prior to self-administration at home, but this was caveated with the requirement for practical demonstration by a healthcare provider upon first use (scenario B). Potential users in the UK preferred access to a stock of the new product via health clinics or pharmacies for subsequent self-application at home (scenario C) (Potential user, UK: *"It's [a] hassle making appointments and stuff if you could just have a stock that you have at home that you apply every 6 months"*, Potential user, UK: *"I'd want to be shown how to do it first and then if it doesn't actually seem that difficult to do then I'd be happy to do it on my own then after that... Even if they had like a dummy one so without the actual ingredient in it to show you how to do it because it is a new technique and then give me the thing"*).

Potential providers and organisations in Uganda and The Gambia expressed a preference for administration of the contraceptive by health professionals (scenario A). There were multiple reasons for this including correct application (Provider, The Gambia: *"If they take it, some women, they cannot apply properly"*), appropriate storage (Provider, Uganda: *"Some mothers have homes which cannot keep that safely"*) and disposal of the device, maintaining regular healthcare appointments (for review and accurate completion of medical records), and concerns over women distributing unused devices to others. Potential providers in Malawi felt the potential to self-administer was very attractive for women and most felt that women would be capable of self-administration, albeit with training or experience (scenario B); only 2 out of 30 providers said women would not be able to self-administer. There was however some disagreement about whether women would want to self-administer, a view that would be dependent on the woman and/or her partner. Several advantages to self-administration were noted by providers in Malawi, in particular the need for fewer trips to hospital and the resulting decrease in workload for the clinics. However, as in Uganda and The Gambia, some concerns were raised about incomplete medical records, incorrect and unsafe administration of the contraceptive, inappropriate storage and disposal, and the opportunity for misuse and abuse.

### Duration of action

When the concept of a long-acting contraceptive delivered by biodegradable MNs was explained to participants, a 6-month duration of action was used as an exemplar (Figure 7 and Figure 8). When asked to comment about this duration, potential users, providers, and organisations generally found this



**Figure 6. An illustration presented to participants to capture their views on the preferred anatomical site of application.** The suitable anatomical sites for application are highlighted on this illustration. Participants were asked to identify their preferred site and explain their choice. This exercise helped identify the upper arm and front thigh as the preferred anatomical site for application of the proposed contraceptive delivery system.

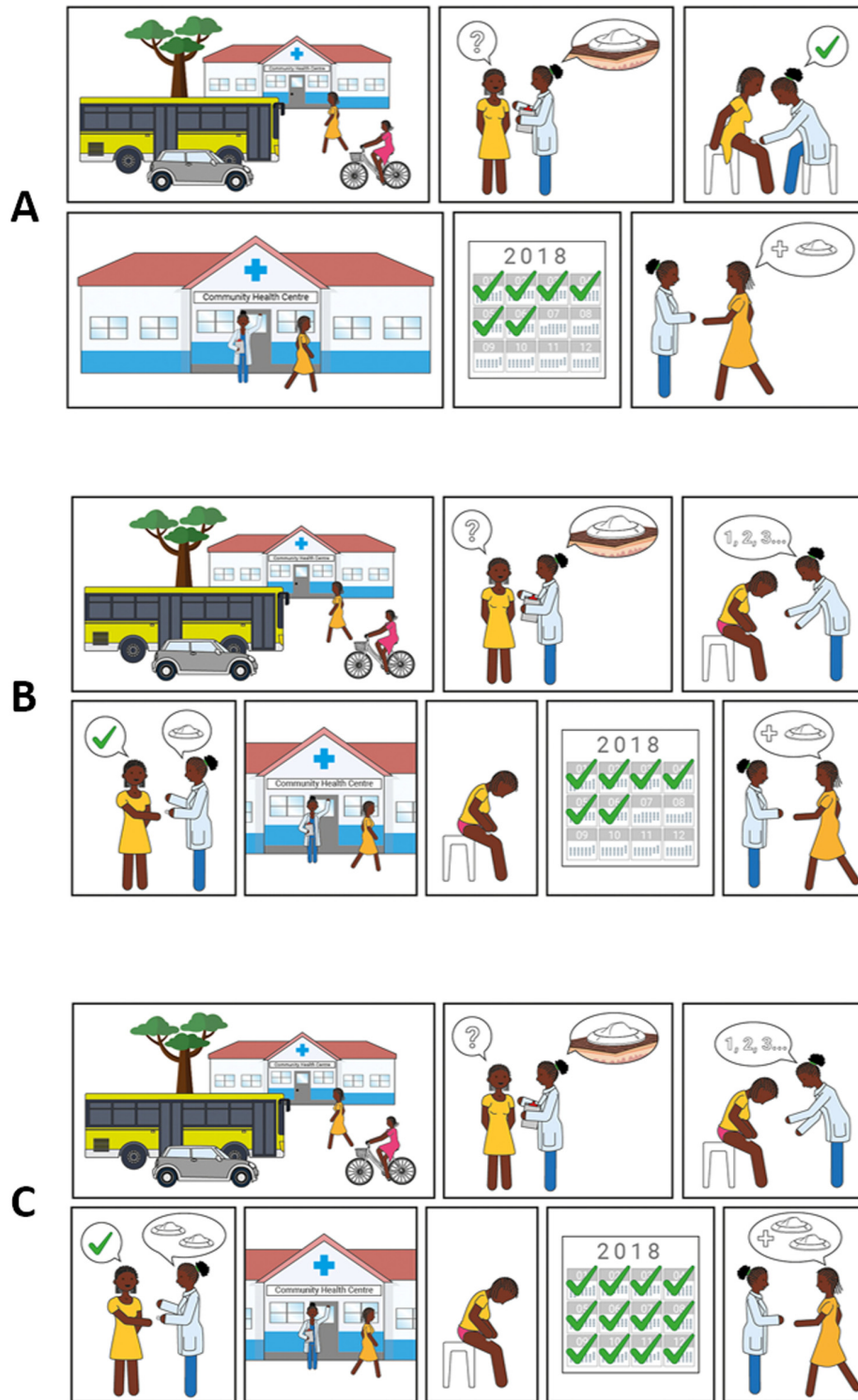
duration attractive, predominantly because it would prevent repeated visits to the clinics (Provider, The Gambia: “*Coming to the health facility every month will be a burden, but if they have something like six months and upwards, it will be better*”). It was also noted by many stakeholders that a method of contraception with a 6-month duration is not currently available on the market, and this would provide potential users with more choice (Potential users, UK: “*It’s quite nice because it’s...*”*in-between other things that are already available*”). Some participants in Uganda, The Gambia, and the UK highlighted the value of a shorter acting ‘trial’ option to determine efficacy, acceptability, and tolerability before committing to a longer duration of action, particularly as this method of contraception, unlike an implant, cannot be reversed once administered (Potential user, Uganda: “*If you would say, ‘First have a smaller interval’ then they see how they can go*”, Potential user, UK: “*I’d wanna trial the trial period before I committed to 6 months of having something because like side effects and stuff is such a big thing with contraception*”). However, it was also noted that having different versions of the product with different durations may cause confusion. Potential users in Malawi commented that, most importantly, the duration that is specified on the user instructions must be guaranteed.

The inability to terminate (i.e. remove) the contraceptive effect once administered caused some concerns with potential providers in Malawi, as they felt potential users may not understand this. Many providers considered this to be acceptable if carefully explained to potential users, while some considered this to be problematic. The majority of potential users in Malawi did not identify this as an issue.

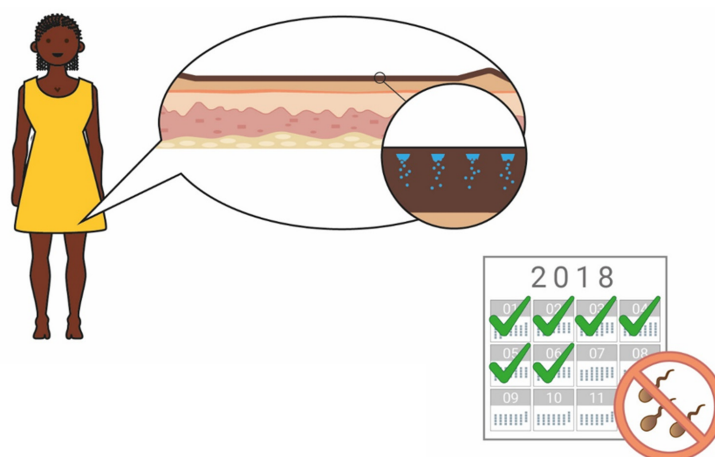
#### Return to fertility

The return to fertility following the use of the proposed MN-based hormonal contraceptive delivery system explored in this study would not be immediate after the 6-month protective period. We explored participants’ views on this matter and asked them what interval of time would be acceptable to return to fertility.

Participants identified the time to return to fertility as very important (Provider, The Gambia: “*Even if you are not using any contraceptives and even if physically normal state... it may, may take you months before they get pregnant. However, if a woman takes contraceptive, the woman is two, three months they are not pregnant, they think it’s still the contraception*”). However, there was no consensus amongst participants on the most acceptable time for a return to fertility, with answers



**Figure 7. Illustrations used to present different access scenarios to participants.** Scenario **A**) Access is always via a health centre, where a health care professional applies the contraceptive. Scenario **B**) Access is via a health centre, where a healthcare professional trains the user on how to apply the contraceptive correctly; self-applications are then performed when desired. Users must return to the health centre to receive subsequent contraceptives when needed. Scenario **C**) Access is via a health centre, where a healthcare professional trains the user on how to apply the contraceptive correctly and gives them 2 devices. Users do not need to return to the health centre for a second application when the contraceptive effect of the first application lapses.



**Figure 8. An illustration used to explain the concept to participants.** The concept of a 6-month duration, reversible contraceptive based on biodegradable microneedles was explained to participants with the help of this illustration.

ranging from immediately to up to one year. It was noted that the answer might depend on the individual user and their circumstances, but a large proportion of women would prefer a relatively rapid return to fertility, in the range of 0–3 months.

#### Identified benefits and concerns

The concept of a new MN-based progestin-only hormonal contraceptive was generally viewed positively by all participants. Some of the advantages identified by participants included the pain-less, blood-less, user-friendly and time-saving nature of the application (User, Malawi: *“This device is not frightening because the needles are small and hard to see unlike the other injections whereby the syringe is big and it’s frightening when you see it”*; Provider, The Gambia: *“I believe that they would prefer to take this one... it’s easy, it’s friendly, it’s user-friendly. ... And at the same time, they’re having no pain. Most of these women, they are scared of this pain”*; Provider, Malawi: *“It is user friendly. Even a school drop-out can manage to use it”*), the intermediate duration of action, the potential for greater compliance compared to other methods, the potential for self-administration, the discreet nature of this solution (Provider, Uganda: *“Some husbands don’t consent to family planning. So if this wasn’t able to be seen, then it’s okay”*), the reduced risk of needle-stick injury and cross infection (Provider, The Gambia: *“As a nurse, one of the other benefits is you’ve got a reduced risk of sharps injury”*), and the biodegradable nature of the system, i.e. no need for surgical removal.

Overall, the proposed method was recognised as a means to offer women more choice and was viewed positively and many potential users expressed an interest in trialling the new method when it becomes available. (Users, The Gambia: *“So many will go in for it!”*, *“If this one is available the other methods will not be used!”*, *“When will you get this? I want it.”*). Potential users that were unhappy with their current method of contraception were particularly enthusiastic. Potential

providers noted that painless application and the potential for self-administration are particularly attractive features that could be empowering for women and they would recommend such a method to potential users, although more detailed information would be required when the product becomes available (Provider, Malawi: *“People will opt for it because it is pain-free as well as the duration... even if it is me, I can opt for it”*).

The majority of the concerns that were raised by participants related to possible side effects (especially bleeding abnormalities) that are common with all hormonal contraceptives (User, The Gambia: *“Does it not have side effects? Cos I’d like that, no side effects.”*). The novelty of this approach was also identified as a potential source of apprehension, with thorough testing being recognised as essential to engender trust in the product and confidence in its use. Providers said that word of mouth is a common factor in making contraceptive choices in SSA and it would take time to build this trust with potential users (Provider, Malawi: *“This new development will be hard to intercept for the first time but with time those who will take it will help in disseminating the information to other people in their communities, especially in their various groups...slowly people will be familiar with it”*) and women commented on the importance of experience in engendering trust (User, Malawi: *“Once six months elapses without conception, I will know that it is good”*). There was also some concern over potentially being the first users of the new product (Provider, Malawi: *“You’ve said that the method has not yet been implemented anywhere in the world and you are doing a research which means if it is to be implemented, it will also start here in Africa - so people would be afraid”*).

Generally, providers believed that the concerns of potential users may be addressed through education and awareness, and suggested training packs and visuals would be important to help explain the new concept to women. The irreversible nature of

the contraceptive effect for the duration of action was identified as a potential issue, and providers felt that this feature would need to be clearly communicated to users prior to administration. Potential users were more concerned about the fate of the dissolved material in the body, the potential detectability by others (User, Malawi: *"It should not leave a mark because even now my child keeps on asking me questions about the mark I have on my arm"*) and the cost of this new method.

In Malawi only, even though lack of pain was recognised as a benefit in most cases, some providers and users were concerned about the painless nature of the method, noting that women may want to feel pain to provide reassurance that an application was successful and that it would be effective (Provider, Malawi: *"Here in Malawi most people believe that the medicine is very effective and powerful when they feel pain and bleed after they are injected....so if it is painless they will think that the medicine is not very effective"*, Users, Malawi: *"We should feel pain a bit as an assurance that the medicine has entered the body"*, *"It could be that this method won't have such effect as other injections that make us take painkillers after being injected"*).

The name of the product was also identified as a potential barrier as the term 'needles' is associated with a metal product and this may provoke negative connotations with respect to deposition in the body (Providers, Uganda: *"Of course, if you mention the needle that is going to remain in your body"*, *"They get scared"*). Some participants also raised a concern related to the storage and transport conditions of the product, more specifically the inability of a potential user to effectively store a product at home if it requires refrigeration and concern that a device could be inadvertently deployed in transit or storage.

Several additional questions were raised by providers, including the time taken to establish contraceptive effect following administration, the method of disposal, and suitability of the product for under 18s, breastfeeding mothers or women being treated for HIV infections.

## Discussion

In this study, the HCD approach used to develop a new MN-based progestin-only hormonal contraceptive delivery system targeted at women who have an unmet need for contraception is described. We anticipate that the involvement of the intended end users and other stakeholders during all phases of product development has facilitated the design of a product that is more likely to be accepted and adopted in LMICs.

This study is consistent with other comparable studies<sup>12,19</sup>, indicating that new methods of contraception are welcomed in LMICs to increase the range of available options. A method that requires minimal training would be more accessible and with this in mind our research team have developed a user-informed device that is simple to use and can potentially be self-administered.

Throughout all stages of product development, participants feedback was used to identify the most desirable features

of the MN delivery system, and to iteratively improve these characteristics according to users' preferences. Initially, participants were shown many prototypes with different sizes, modes of action and feedback mechanisms. The preferred features at this stage were: small size, ease of use, unalarming appearance, and clear feedback on application. A refined concept prototype was developed according to users' preferences, and participants identified features of this prototype that needed improvement. In particular, participants viewed the presence of a visual and audio feedback mechanism as a very positive feature but suggested that the visual cue and sound could be amplified to increase confidence that the application was performed correctly. Participants also expressed a preference for the force required to actuate the device to be increased, to avoid unintentional activation, and for the transport/disposal cap to be made more difficult to remove and therefore more childproof. This feedback was integrated into the final prototype, which was validated in a final round of user testing.

Participants' views were also sought on additional aspects of the suggested MN-based progestin-only hormonal contraceptive, such as anatomical site of application, mode of access, contraceptive duration, and time to return to fertility. The results emphasised that the preferred site of application for such a device could depend on who was performing the application: women would prefer to self-administer the MN-based contraceptive to their own thighs but would prefer the upper arm as a site of administration if the device was applied by a health care professional, as they wouldn't be comfortable showing their legs, in particular to male health care providers. In both cases, the ability to cover the treated site with clothing immediately after application was deemed crucial by participants, since discretion can be a key factor in choosing a contraceptive method in LMICs<sup>20,41</sup>. This was considered when refining the product design, ensuring that this delivery system is suited to application at either of these two body sites (including being deployed by one hand) and is as discreet as possible.

Regarding access to this new method, some women in LMICs highlighted how going to the clinic for contraception is a good opportunity to discuss their sexual health with a professional, while others would prefer to be given the device to apply in the comfort of their home, in their own time. Some women thought that storing/using the contraceptive at home could be an issue if they wanted to conceal it from partners/family members, while for women whose partners are involved in contraceptive decision making this would not be an issue. Whilst recognising the advantages of self-administration, many of the health care professionals in the LMICs preferred the application to happen in a clinical setting, to maintain accurate records and check on the women's health during the appointment. Both health care providers and organisational stakeholders in LMICs were also worried about women sharing or selling the contraceptive if they were provided one to take home. Women and providers in the UK were less concerned about access to the device, suggesting it should be available in health clinics and pharmacies for home application. The proposed delivery system has the flexibility to be applied by a health care professional or self-administered and could be

accessed in different ways in different countries, to reflect different socio-cultural norms. The final optimised device also has the flexibility to have an unassuming, medical look or a more colourful, unrevealing appearance.

Interestingly, users' opinions on duration of action and return to fertility were mixed and mostly dictated by the women's personal experiences and needs. Women with no or fewer children found the proposed 6 months duration attractive as a mean to delay their first pregnancy or space their children according to their preferences; a return to fertility in the range of 0–3 months was considered acceptable in these circumstances. Women with many children expressed an interest in even longer durations, as a mean to stop having children; return to fertility was not a big concern for these women. Users who previously experienced problems with long-acting methods mostly preferred a shorter duration with a quick return to fertility. While the proposed duration for this new MN-based contraceptive is 6 months, the manufacturing method provides flexibility, allowing for a range of durations of action. In each case the return to fertility would need to be assessed during pre-clinical and clinical testing.

Users identified many possible advantages of the new proposed MN-based contraceptive delivery system, including benefits related to the minimally invasive nature of MNs (pain-free, blood-free, discreet), the intuitive operation of the applicator (quick, easy, user-friendly, requiring minimal or no training), and the proposed 6 months duration (fewer visit to the hospital, fills a duration gap in the market between injectables and implants).

Users expressed a range of concerns related predominantly to side effects. This is consistent with other studies on new proposed contraceptive devices<sup>20,42</sup>. Participants frequently inquired about the side effects of the device, and repeatedly mentioned bleeding changes, weight changes, and the fear of permanent infertility as particular worries regarding any contraceptive product. Whilst the proposed device has not yet entered the clinical stage of development and we are not in a position to confirm side effects, given the requirement for ovulation inhibiting blood levels of contraceptive we anticipate a comparable hormonal side effect profile to LNG subcutaneous implants<sup>43</sup>. Another concern that was repeatedly raised was the name of the new technology. Users did not like the word 'needles' due to an association with pain. Careful naming and branding of the technology, alongside education, information, and discussions with healthcare professionals, will be critical to create trust in the new product.

In conclusion, the concept of a new MN-based hormonal contraceptive delivery system was generally viewed positively in the visited LMICs, but some potential user concerns were identified. This product was iteratively developed using a HCD

approach, meaning that potential stakeholders identified features of their ideal product and influenced the final design of the delivery system. This prototype is now being evaluated in pre-clinical testing. Having followed this approach, validation of the final product through a summative study, which will in time be required for the certification of the MN contraceptive delivery system, should be rendered a more straightforward exercise. The team is integrating the valuable feedback received by participants in this study in the final design of this novel minimally invasive hormonal contraceptive delivery system, that will be taken forward for pre-clinical testing.

## Data availability

### Underlying data

Full qualitative transcripts are not available for ethical reasons because even after removing directly identifiable information such as names and addresses, participant identity may be difficult to fully conceal, and research locations may remain potentially identifiable, presenting a risk of deductive disclosure. However, codebooks and relevant excerpts of transcripts are available from the authors on reasonable request. Requests should be sent to the corresponding author at [HughesML@cardiff.ac.uk](mailto:HughesML@cardiff.ac.uk) or to [BirchallJC@cardiff.ac.uk](mailto:BirchallJC@cardiff.ac.uk). Requests will be granted to researchers for the purposes of comparative analysis, upon approval from relevant ethics committees.

### Extended data

Figshare: Supplemental material manuscript for "Human-centred design of a new microneedle-based hormonal contraceptive delivery system". <https://doi.org/10.6084/m9.figshare.14697393><sup>36</sup>.

This project contains the following extended data:

- Supplemental material manuscript 13233.pdf (participant information sheets, consent forms, questionnaires, and FGD/SSI topic guides used)

Data are available under the terms of the [Creative Commons Attribution 4.0 International license](https://creativecommons.org/licenses/by/4.0/) (CC-BY 4.0).

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## Open Peer Review

Current Peer Review Status: ? ✓ ?

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### Version 3

Reviewer Report 19 April 2022

<https://doi.org/10.21956/gatesopenres.14731.r31912>

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**Aluisio J.D. Barros**

International Center for Equity in Health, Universidade Federal de Pelotas, Pelotas, Brazil

#### General comments:

The manuscript presents the process of perfecting the design and characteristics of a new microneedle contraceptive device. A human centered approach was used to design a multicountry qualitative study. The main objectives were to direct the design of the new device, the duration of its effect and guide the contents and layout of the user guide.

The methods used, even considering the qualitative design, were very flexible with many aspects defined by convenience, such as the type of interview (focus group or semi-structured interview), source of participants, numbers, selection of partners.

The results are described in very general terms, in a narrative fashion, with nearly no organization or tabulation of the aspects studied and respective preferences. Notably, no clue about what the device in study looks like is given to the reader. As a consequence, the reported preferences by participants sound a bit obvious like a choice of a smaller device that is easy to use or a user guide that is an illustrated step by step document.

#### Specific comments:

1. Abstract – To say that more than half of women with an unmet need for contraception live in LMIC is not informative. Nearly 85% of the world population live in LMIC. The same statement is repeated in the introduction.
2. The frequent use of acronyms makes the text difficult to follow. The authors go on accumulating abbreviations like MN, HCD, FGD, SSI. I suggest that only easily recognized acronyms are used (e.g. LMIC).
3. There is a detailed presentation of methods, but we are left with the impression that several important aspects such as sample size, selection of participants, type of interview were essentially based on convenience. I wonder what impact this may have had in the results.
4. The section “Iterative applicator design” is rather awkward to read, as the text goes on describing theoretical advantages sought – like obviously small size and ease of use – but

without the reader having a clue of what the device is, looks like or does. If the device cannot be presented due to commercial issues, I think it would be easier to just present a table with the main characteristics found relevant by the participants and how each version scored.

5. By the end of the section, audio and visual feedback mechanisms are mentioned and we are kept wondering what the size of this device is, or what it looks like. Not even an approximate size and format is presented in the text.
6. Having said that, I was curious to know about the likely situation of people not finding this device usable at all. How many of the women were not convinced by the proposed device?
7. Again, the development of the instructions is based on a presentation of preferences on general characteristics – text or illustration based – without presenting specific details. It is not surprising that users would prefer a clearly illustrated step by step guide.
8. I found the general preference of users for the device to be applied by a health worker in opposition to the user friendliness and ease of use stressed in the benefits and concerns section. Again, having no idea of what the device looks like or how it is used does not help.
9. Later in the section statements like “So many will go in for it!”, “If this one is available the other methods will not be used!” make me concerned about the lack of a comparison alternative method. People are very keen to agree and please the interviewers in focus groups. I myself had this kind of experience where participants were very positive about a device presented to them, and later, after getting one, they never used it.

**Is the work clearly and accurately presented and does it cite the current literature?**

Yes

**Is the study design appropriate and is the work technically sound?**

Yes

**Are sufficient details of methods and analysis provided to allow replication by others?**

No

**If applicable, is the statistical analysis and its interpretation appropriate?**

Not applicable

**Are all the source data underlying the results available to ensure full reproducibility?**

No

**Are the conclusions drawn adequately supported by the results?**

Partly

**Competing Interests:** No competing interests were disclosed.

**Reviewer Expertise:** Epidemiology, global health, RMNCH

**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 14 January 2022

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**Rebecca L. Callahan** 

FHI 360, Durham, NC, USA

I update my review status to “Approved”. However, I do encourage the authors to review the abstract and perhaps revise to include the key results of the design activities. As it currently reads, the abstract results describe more of the methodology rather than what emerged from the HCD process.

**Is the work clearly and accurately presented and does it cite the current literature?**

Partly

**Is the study design appropriate and is the work technically sound?**

Partly

**Are sufficient details of methods and analysis provided to allow replication by others?**

Partly

**If applicable, is the statistical analysis and its interpretation appropriate?**

Partly

**Are all the source data underlying the results available to ensure full reproducibility?**

Partly

**Are the conclusions drawn adequately supported by the results?**

Partly

**Competing Interests:** No competing interests were disclosed.

**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.**

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Version 2

Reviewer Report 23 August 2021

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**Rebecca L. Callahan** 

FHI 360, Durham, NC, USA

This article describes a novel approach for assessing and incorporating user preferences into the design of a new contraceptive delivery system. The authors' adaptation of human centered design for contraceptive R&D is innovative and provides a useful model for others working in new contraceptive product development. The inclusion of multiple study sites and types of participants – potential users, providers, and other stakeholders – strengthens the findings. While the authors cite other studies that have attempted to evaluate user preferences for new contraceptive technologies, they might consider reviewing the following paper, which also evaluated potential interest in and preferences for a microneedle (MN) patch for contraception: Callahan *et al.* (2021<sup>1</sup>).

While the paper presents an overview of the human centered design process used to iteratively devise the preferred MN contraceptive, it would help to describe in more detail some of the steps and the actual concepts developed during the process. Under “Concept development” the authors state that, “the concept of a new MN-based progestin-only hormonal contraceptive delivered by an applicator was developed by the team.” Can you provide a description of this concept? Maybe add an image? Also, who is “the team”? The authors? Adding images of the product iterations would help the reader better understand what study participants were reacting to and which product attributes changed over the course of the research.

- In the second paragraph of the Methods section the acronyms "FGDs" and "SSIs" should be defined (they are defined subsequently, but not at first use). The authors might also consider adding a table describing the number of FGDs and SSIs conducted in each country.
- The Study Design section could be strengthened. It would help to clarify the original data collection plan and what took place. Was it determined at the time of data collection which method would be used? What is meant by “pragmatic qualitative approach” and “dynamic nature of discussion”?
- Was ethical approval obtained in Uganda? It is not listed in the manuscript.
- Why not show images of the prototypes produced by Maddison Ltd? Also, were these prototypes based on ongoing MN product development research? If so, it would help to describe this.
- Under Sampling and Recruitment, who are “local gatekeepers”? How were they identified?
- The study generated many results. To more clearly relay what concepts/prototypes

participants were responding to in each phase of data collection and to better understand their reactions, it would help to show an image of the prototype and list the specific attributes of the product. Perhaps a figure illustrating the changes in the prototype over the course of the study resulting in the final product design. Images would help.

- What does “friendly” aesthetic mean?
- The term “applicator prototypes” is a little confusing since some MN products include an external applicator. Can you clarify what you mean?
- Though it becomes clear with further reading, it would help to define “actuation methods” up front. How is this different from “deployment”?
- In the second paragraph on page 9, you state that the device dimensions were finalized to accommodate the number of MNs that would be necessary to provide 6 months’ dose of contraception? How are these dimension known? This relates to my prior question about whether this study is associated with ongoing R&D efforts and, if so, how.
- Why not show an image of the “final optimized iteration”?
- What does “medical-looking” mean? Images would help.
- As described above, it would help to describe more the baseline requirements/underlying assumptions of the 6-month MNP (perhaps based on ongoing R&D work), show the initial prototype, and then show the iterations that were used in the subsequent studies.
- Can you explain what does it mean to “validate” the prototype?
- Some results seem to be presented in the discussion that do not appear in the results section.

## References

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**Is the work clearly and accurately presented and does it cite the current literature?**

Partly

**Is the study design appropriate and is the work technically sound?**

Yes

**Are sufficient details of methods and analysis provided to allow replication by others?**

Partly

**If applicable, is the statistical analysis and its interpretation appropriate?**

Not applicable

**Are all the source data underlying the results available to ensure full reproducibility?**

No source data required

**Are the conclusions drawn adequately supported by the results?**

Yes

**Competing Interests:** No competing interests were disclosed.

**Reviewer Expertise:** contraceptive research and development; global family planning; user preferences

**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.**

Author Response 25 Nov 2021

**Benedetta Gualeni**, Cardiff University, Redwood Building, King Edward VII Avenue, Cardiff, UK

We thank the reviewer for their positive comments relating to the important contribution that this article will make. We address specific comments in turn below.

Regarding the initial comment, the reviewer shared a recent paper that might be cited in the article. This is a very interesting article and we thank the reviewer for sharing it. The reviewer might not be aware that our manuscript was submitted to Gates Open Research on March 15<sup>th</sup> 2021, before the referenced article was published (available online from March 22<sup>nd</sup> 2021), and so we did not have knowledge of this body of work at the time of submission. Due to our submission date being before the publication of this article we presume that it is not appropriate to include reference to it, at this later stage.

Nevertheless, our work is in line with what is suggested in the referenced article, i.e. in developing our contraceptive MN-based product we are incorporating the perspective of potential end users to maximise its chance of being adopted in the future. Also, some of our findings via FGDs and SSIs are in line with the results from DCE described in the referenced paper. In particular, potential end users also highlighted to us the preference for minimal or no effect on their menstrual cycle while using the contraceptive; they were particularly interested in the contraceptive effect lasting 6 months and in a patch size as small as possible.

The effect of our product on the menstrual cycle will be evaluated in future clinical studies and we acknowledge that any possible effect on menstruation might deter some potential users to adopt this new solution. Nevertheless, adding a new method that has the potential to be self-administered might cater for the needs of some potential users whose needs are not currently met.

In response to the following comment, and also to comment 1 from the other reviewer we

have added the following paragraph to the manuscript:

“The initial concept was to develop a long-acting, reversible, MN-based, progestin-only hormonal contraceptive, that is delivered by an applicator, can be self-administered (or administered with minimal training), is stable at high temperatures and high humidity, and can be mass produced at low cost. An assortment of potential products, with different features (Design Stage 1, Figure 1) were therefore developed. These initial product designs were informed by the published literature, the opinions of stakeholders/‘experts’ with experience of developing and/or using FP in LMICs and the multidisciplinary research team, which includes product designers, engineers, pharmaceutical scientists and polymer scientists.”

As we have also mentioned in reply to point 13 from the other reviewer, we are unable to provide any further details at this stage due to a potential IP disclosure limiting our ability to further develop the product. Once IP is more secure a technical paper describing the development of the actual MN product will follow. We have added the following paragraph to the manuscript to clarify this issue:

“At this stage we are not able to share any images of the prototypes, as publishing them will constitute a prior art disclosure that will inhibit our ability to protect the novel mechanism used within the applicator.”

In response to the first bullet-point, thanks for spotting that FDGs and SSIs were not defined at first use. This has now been corrected in the manuscript. We have considered whether a table may be useful but do not think it necessary.

In response to the second bullet-point, the original data collection plan was to gather feedback from as many and as wide a range of potential users, partners, providers, and stakeholders as possible during the data collection period at each stage. FGDs were designed to be our method of choice for data collection as they allowed for more interaction and discussion but, at the time of recruiting, if participants showed a preference for SSIs we accommodated them. Also, if we would miss out on data waiting for sufficient numbers for a FGD to take place then we offered the opportunity for a SSI instead thereby capturing data that might otherwise be lost.

We ran this study in line with the original data collection plan but in a pragmatic manner (pragmatic qualitative approach) - in other words while trying where possible to stick to the original plan we were conscious that practical issues may impact on recruitment and data collection and so we were prepared to be flexible where needed - for example by offering SSIs instead of FGDs. We took the approach that rather than turn down data collection opportunities because, e.g., we had reached our desired numbers or had lots of people from a similar background, we would make the most of all opportunities given the limits of our logistics.

By “the dynamic nature of FGDs” we mean that discussion is more open and less directed than during an SSI, going beyond the topic guide. This interaction between participants really allows data collection to be more participant-driven than researcher-driven, with participants explaining, questioning and justifying their viewpoints to each other, and this enables a deeper understanding of the participants’ views and perspectives, often resulting



in unexpected findings being revealed.

In response to the third bullet-point, the ethical approval obtained for Uganda is the one listed as "Mountains of the Moon University Research Ethics Panel (MMU/DPGSR/061218)". To clarify this we added "Uganda" in brackets before the reference number.

In response to the fourth bullet-point, as already stated above, we are not able to share any images of the prototypes at the moment, as publishing them will constitute prior art that will interfere with securing IP for the novel mechanism used with the applicator. The applicators are currently being developed by our research team, and are innovative in terms of shape, manufacturing, deployment, mechanism of action and duration of action. They are absolutely based on our product development research.

In response to the fifth bullet-point, the gatekeepers were identified through our links with charitable organisations and academic collaborators and they are either listed as authors (when they also contributed to data collection) or acknowledged in the acknowledgment section (when their role was solely that of gatekeepers).

In response to the sixth bullet-point, even though we agree that showing different prototypes and how they were modified in response to participants and ultimately consolidated in a final design would be beneficial, unfortunately we cannot show any pictures due to IP reasons as stated above.

In response to the seventh bullet-point, participants perceived larger prototypes as "scary". Other published studies have also suggested that sharp corners might contribute to create wariness in a product. Also, certain colours might be perceived as frightening. A "friendly" aesthetic in our final design means a design with a small shape, rounded corners, and neutral colours to help reduce lack of trust into the device due to its physical appearance.

In response to the eighth bullet-point, participants in this study were not shown the final product, composed of MNs and an applicator to administer them to the skin. Only the proposed external applicator prototypes were shown to the participants. These consist of the fully functional applicators without any MNs (just a flat plastic surface where the MNs would be). This allowed participants to handle the applicator prototypes and inform on their preferred characteristics.

To clarify this issue we have added the following paragraph to the manuscript:

"The dummy prototypes used in the studies consisted the fully functional applicators without the presence of MNs. This allowed participants to experience the mechanism of deployment, usability, duration of application and feedback from the applicator."

In response to the ninth bullet-point, actuation refers to the mechanism by which the applicator is initially activated by the user, while deployment refers to completion of the application process.

In response to the tenth bullet-point, the present manuscript describes our effort to include users view in the development of a MN product in terms of usability, especially with the aim of self-administration in mind. In parallel to the user studies the team is undertaking

technical development of the MN product and we have calculated and manufactured the dimensions of MNs that will facilitate a 6 month dose of contraceptive. The studies described in this paper are both based upon, and informing, the R&D development.

In response to the eleventh bullet-point, we are unable to provide an image due to the aforementioned IP disclosure issues.

In response to the twelfth bullet-point, the “medical-looking” aesthetic we presented to the participants meant that the prototypes had neutral colours, without any patterns or colourful images on the casing. Participants themselves used this terminology to mean a more neutral design with colours more typical of a clinical setting or other clinical devices. We have added a clarification of the meaning of “medical-looking” in the manuscript: “(i.e. clean, neutral colours)”

In response to the thirteenth bullet-point, and also to comments from the other reviewer, we have added this sentence to the manuscript to clarify this point:

“Injectable contraceptive products provide 12 weeks (3 months) of contraception and implants provide >12 months of contraception to the user. The proposal was therefore to develop a product with an alternative duration of action that would provide users with another contraceptive choice. Based on current technology, a 6-month duration of action is at the technical limit of what can be achieved using a relatively small microneedle array patch, considering drug loading limitations and the preferred size of patch indicated by potential users”.

In response to the fourteenth bullet-point, to “validate” the prototype means to show the improved version of the prototype to users and confirm that the characteristics that received positive feedback in previous iterations are still liked by participants, while the features changed to reflect users’ preference receive positive comments.

In response to the fifteenth bullet-point, we reviewed the manuscript and could not find any specific examples of results presented in the discussion that did not appear in the result section. We remain available for further clarifications if the reviewer wishes to provide some specific examples.

**Competing Interests:** No competing interests were disclosed.

Reviewer Report 11 August 2021

<https://doi.org/10.21956/gatesopenres.14599.r31060>

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**Maggie Kilbourne-Brook**

PATH, Seattle, WA, USA

This article details the process used to refine early-stage design development of a microneedle (MN) patch as a new drug delivery system for long-acting, progestin-only contraception for women.

Researchers assessed perceptions and preferences of users and stakeholders through iterative rounds of focus group discussions and interviews with participants in four countries. After exploring user/stakeholder perceptions from Uganda, The Gambia and the United Kingdom, prototypes were fabricated representing “ideal” product characteristics which were evaluated for acceptability and ease of use in Malawi. Potential users and providers were enthusiastic about the concept of a new type of product that would provide long-term protection (6 month duration), might be more convenient than other hormonal options, and has the potential for self-administration. User experience and perspectives helped refine the applicator design and the feedback mechanism, and informed preferences about packaging and instructions for use.

This article provides an important contribution to the growing body of work showing that user-centered development processes can be used when developing sexual and reproductive health products and provides an example about how user/stakeholder feedback can inform design decisions.

Below are some comments/questions/suggestions for the authors to consider which may strengthen comprehension of this article.

1. Page 3. Methods: Concept Development. Re: “The concept of a new MN-based progestin-only hormonal contraceptive delivered by an applicator was developed by the team (Design Stage 1, Figure 1) after reviewing the available literature and discussing the expectations of stakeholders regarding novel contraception solutions with experts in the field of FP in LMICs.”
  - Perhaps share a bit about what were these expectations that helped shape the initial design thinking about this contraceptive MN approach? Would be helpful to know the starting position for this concept so readers can see how this changed/evolved after user/stakeholder inputs. Did the concept of the MN patch change based on user input or simply the design features and characteristics?
  - The description of MN states they can deliver drug for therapeutic duration longer than 1 month, but in developers start with the assumption this would be a 6-month duration method. So, it might be helpful to clarify where that assumption comes from and why that is the target (especially since users from multiple countries talk about the desire for a MN patch with shorter duration to confirm it is appropriate for them).
2. The authors propose that adding a new method may help address unmet need for contraception. It is well-documented that adding a new option to the method mix can result in increased uptake of contraception overall, but simply adding another hormonal contraceptive delivery system does not seem to address key reasons identified by The Guttmacher Institute analyses as reasons for unmet need for contraception (see: Unmet Need for Contraception in Developing Countries: Examining Women’s Reasons for Not Using a Method <https://www.guttmacher.org/report/unmet-need-for-contraception-in-developing-countries>) such

as concern about side effects and infrequent sex. So, it might be helpful to more clearly understand where the developers think this product would fit in the contraceptive method mix; what is the gap they are aiming to fill and the value added by this new technology; and who are the potential users that a product like this might be most useful/attractive for.

3. Page 5 Figure 2. Diagram illustrating the different steps of a Human Centred Design study. "After defining the area of innovation, the target end users and the context of use are considered to ideate possible solutions for the unmet need that is being addressed. The proposed solutions are tested by potential end users and their feedback is incorporated into a refined design. Multiple iterations of this process lead to the development of the final product."

- While this statement is accurate, this description overlooks the potential importance of input from other stakeholders who influence whether a contraceptive product will be approved, come to market and become integrated into the healthcare system in specific countries. Collecting input from those other stakeholders may be outside the scope of this set of studies, but it should be acknowledged that developing an acceptable product that meets end-users needs and context of use is not sufficient to guarantee that the product will make it to commercialization and introduction/scale up.
- A key factor not much mentioned in this article relates to cost (manufacturing cost/cost of service delivery/cost to the consumer) relative to other currently available contraceptive products. Design considerations often have underlying cost implications. Cost will be an important consideration for a potential commercialization partner looking at the potential viability of this technology and also for donors, NGOs, procurement agencies, *et al.* involved in contraceptive supply. Perhaps the authors could state that cost considerations (design/manufacturing) were considered, but not reported at this time, or something like that?

#### Sampling and recruitment:

4. It might be helpful to add a statement about how/why these countries were selected as representative for user/stakeholder assessments. Given that 3 of the countries are in Africa, it seems the researchers are focusing on unmet need for FP in LMIC. If so, it would be helpful to also understand their rationale for including participants from UK, especially since the UK user groups (user studies 3 and 4) represent a large percent of the overall participants.

5. The authors identify unmet need for contraception globally as the rationale for developing the MN contraceptive patch. So, it might be helpful to better understand why they recruited such a high percentage of participants who already are using contraception (only 18 of 88 participants reported not currently using contraception; 14 participants did not respond to this question). Was this because persons using contraception were easier to identify and recruit? Or some other reason? Do the researchers feel they may have missed something by not more specifically including viewpoints of those not currently using contraception? Or those who were specifically dissatisfied with their current contraceptive method?

6. Page 6. It is surprising that the FGDs in Uganda and The Gambia were conducted in English by members of the research team rather than in local language (or at least to give the participants the option of which language to use) and with a local facilitator who is closer in culture/social location to the participants. Does the research team see this as a potential limitation of this study design? Or do they think this did not have any impact on their results and interpretation of

findings?

7. Page 7. Given that the assessments moved sequentially from country to country and that inputs from user studies 1,2,3 were validated by users in studies 4 and the final design in user study 5, it seems there was little opportunity to go back to previous participants and double check that the changes incorporated into the refined prototype design correctly addressed the needs identified and that the developers interpreted the preferences of participants from previous rounds of evaluation correctly. Is this accurate? Given that the profile of potential users in the UK (User Studies 3 and 4) differs from users in Uganda and The Gambia (studies 1 and 2), and we don't have a complete profile of users from Malawi (study 5), are the researchers confident that user needs have been adequately addressed in the final prototype...or is it possible that something has been lost in translation as they moved to these different user groups.

8. Page 7. "During FGDs and SSIs with potential users, providers and organisations, dummy prototype MN applicators were used to obtain feedback on handling/ergonomics and aesthetics." What do you mean by dummy prototype applicators? Were these functional prototypes (but without drug) that gave the look, feel, usability? Did the participant use the applicators in mock use? Is it possible to include an image of what these looked like?

9. Page 8. The demographic profiles in Fig 4 are not all equally complete. This makes it difficult to compare similarities/differences among user groups across countries.

- Perhaps add an explanation about why the profile for Malawi does not include age, education, or religion. Also do the researchers have any explanation/insight for why 2/3 of participants in Malawi did not respond to the questions about living situation and whether or not they have children? Without this information it is difficult to tell how similar or different the Malawi group is to the initial user groups in Uganda and The Gambia. This is important because Malawi is used to validate the final design.
- Also, only a small number of potential users (2) fall in the 18-20 age group, yet we know that unmet need for contraception is high among young women, especially young unmarried women. Do the researchers feel this may be a limitation of this study?
- The text says participants representing both urban and rural locations were recruited but we don't see this in Fig 4. What was the breakout of urban/rural participants? Is it possible to include this?

10. Page 8. Fig 5. Providers. Given that part of the intended value proposition of MN patch is self-administration, perhaps the authors can clarify why they included so many providers in these assessments (slightly more providers than potential users). In retrospect, do the researchers feel this was appropriate break down of participants?

11. In the text, the authors mention collecting input from male partners, but I don't see reference to any findings or male partner input in the text. Were the interviews not productive? Did the male partners have anything interesting to share that influenced design, or provided insights about potential acceptability, or support or concern for their partner potentially using a product like this?

12. Pages 8 and beyond. The researchers assessed perspectives and preferences of a range of potential users and stakeholders across multiple countries. Did the researchers find differences

between any of the user groups that were relevant or interesting? (perhaps based on age, education, contraceptive use, relationship status, or urban/rural location?) Were any comments particularly insightful/enlightening or surprising? Were there comments that pointed toward design trade-offs that needed to be made to fit within what was technically feasible or within the constraints of the project? If so, that would be interesting to bring forward. I feel like the voices of the users/stakeholders are a bit buried in the description of the process and the results - maybe perhaps that is because this is a summary of 5 user studies.

13. It would be helpful if the authors could include images or illustrations to show how the MN patch design and/or applicator evolved based on input from user/stakeholders. If that is not possible, perhaps add a statement indicating why images cannot be included at this time.

14. Overall, I found it difficult to follow which participants evaluated the MN concept via illustrations compared to those who handled and practiced using the MN prototypes and still am not sure if any of the participants used the prototypes in mock use. Is there a way to help make this more clear?

15. Page 9. "...the transport/disposal cap was improved to increase childproofing and prevent accidental exposure after disposal." This is a bit confusing. What is the risk of exposure during disposal since there are no needles and the drug has been delivered. Also, the text describes that the disposal cap was improved, but without any illustration or image, it is hard to understand what this means.

16. Page 9. "Each illustrated step was also detailed with text, to allow users to correctly apply the product by reading the text and/or looking at the imagery. This improved instruction leaflet was subsequently presented to participants in Malawi (User study 5), who considered it appropriate."

- What does "appropriate" mean here? Appropriate in style and format? Did the Malawi participants use the instructions to learn how to use the MN patch in mock use? Or did they just look at the IFU and comment on these? Were the images and text evaluated for comprehension? (FYI. There is a body of literature about creating instructional health materials for low literate audiences. Best practices include combining images and simple messages, so the authors findings in and of themselves are not surprising. Not sure you need to reference this, but here is a guide developed by PATH in 1996 that still contains helpful and relevant guidance as the authors move forward:  
[https://path.azureedge.net/media/documents/DC\\_Low\\_Literacy\\_Guide.pdf](https://path.azureedge.net/media/documents/DC_Low_Literacy_Guide.pdf)).

17. Page 14. Discussion: "A method that requires minimal training would be more accessible and with this in mind our research team have developed a user informed device that is simple to use and can potentially be self-administered."

- Since this is intended to be simple to use, it would be helpful to outline the steps or show the IFU, perhaps in the supplemental information?

**Is the work clearly and accurately presented and does it cite the current literature?**

Partly

**Is the study design appropriate and is the work technically sound?**

Yes

**Are sufficient details of methods and analysis provided to allow replication by others?**

Yes

**If applicable, is the statistical analysis and its interpretation appropriate?**

Not applicable

**Are all the source data underlying the results available to ensure full reproducibility?**

Yes

**Are the conclusions drawn adequately supported by the results?**

Yes

**Competing Interests:** No competing interests were disclosed.

**Reviewer Expertise:** I am a reproductive health professional with 35 years of experience at PATH. I've worked in the areas of contraceptive and reproductive health technologies, product development, regulatory approvals, contraceptive introduction, research, clinical trials, and HIV/AIDS.

**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.**

Author Response 25 Nov 2021

**Benedetta Gualeni**, Cardiff University, Redwood Building, King Edward VII Avenue, Cardiff, UK

We thank the reviewer for their positive comments relating to the important contribution that this article will make. We address specific comments in turn below.

1. We have reflected on the first bullet-point of this comment and to a similar comment from the other reviewer and have added the following narrative to the manuscript.

"The initial concept was to develop a long-acting, reversible, MN-based, progestin-only hormonal contraceptive, that is delivered by an applicator, can be self-administered (or administered with minimal training), is stable at high temperatures and high humidity, and can be mass produced at low cost. An assortment of potential products, with different features (Design Stage 1, Figure 1) were therefore developed. These initial product designs were informed by the published literature, the opinions of stakeholders with experience of developing and/or using FP in LMICs and the multidisciplinary research team, which includes product designers, engineers, pharmaceutical scientists and polymer scientists."

In response to the second question raised in the first point, elements of the concept were refined or reinforced following user input, e.g. the desired length of time for contraception, and specific features of different products, e.g. the size and the ergonomics, that were identified as attractive were used to inform product design.

We have reflected on the second bullet-point of this comment, and also on a similar comment from the other reviewer, and we have added the following narrative to the manuscript to better clarify this issue:

“Injectable contraceptive products provide 12 weeks (3 months) of contraception and implants provide >12 months of contraception to the user. The proposal was therefore to develop a product with an alternative duration of action that would provide users with another contraceptive choice. Based on current technology, a 6-month duration of action is at the technical limit of what can be achieved using a relatively small microneedle array patch, considering drug loading limitations and the preferred size of patch indicated by potential users”.

2. As stated in the addition we made to the manuscript following the previous comment, injectable contraceptive products provide 12 weeks (3 months) of contraception and implants provide >12 months of contraception to the user. The proposal was therefore to provide an alternative duration of action that would provide users with another contraceptive choice.

Another aim was to provide a method of contraception for users that was more discreet than current commercially available long-acting contraceptive implants.

This is a hormonal contraceptive though and we would envisage comparable side effects to other hormonal methods, although the lower dose in the proposed intradermal MN delivery system may produce fewer or less severe side effects. This could only be evaluated in clinical studies. Therefore the product may provide a choice for women who have experienced side effects from other forms of hormonal contraception.

Some users also described how their partners spend half the year working abroad and half the year at home. This type of product may appeal to these women.

The users that this product may be attractive to are therefore:

- women who don't have easy access to clinics (e.g. rural setting) and for whom frequent visits to the clinic are burdensome or impractical (interfering with work/daily activities). As noted in the cited report from the Guttmacher Institute, women from West and Central Africa do cite difficult access to a source of supply as a reason for non-use;
- women who would benefit from a longer duration contraceptive (IUDs or transdermal implants), but don't have access to facilities with trained medical staff;
- women who would prefer a more discreet method that could be self-administered;
- women who are returning to fertility after having had a child, who may want more children but would like a longer interval between pregnancies;
- women that are currently unhappy with their contraceptive options

3. These two points are very important, and indeed cost did influence some of our manufacturing decisions. We've added the following paragraph to the manuscript in response to this comment.

“This process however does not guarantee that the final product will be commercially viable or approved in a particular territory, with other issues such as manufacturability, scalability, regulatory issues, cost of goods, market access and distribution also playing important roles. These issues are also being scrutinised in product development, but are not reported



here as they are outside of the scope of this article.”

4. The countries for Stage 1 were carefully chosen to maximize the type of feedback gathered. We wanted to perform the studies in 2 countries in SSA, one in the West and one in the East, one with a Christian and one with a Muslim majority. The aim was to elicit a range of viewpoints considering different unmet needs and different usage of contraception as highlighted by FP202 ([Uganda | Family Planning 2020](#); [Gambia | Family Planning 2020](#)). The Gambia and Uganda were chosen due to existing academic or charitable links with the 2 countries and confirmed in discussions with the BMGF. With the research group based in the UK, it was considered valuable to gain insight from UK users as well, to explore the appetite for a new LARC in an industrialised country, as revenue from industrialised countries might create the opportunity to subsidize access in LMICs.

Finally, we considered the value of returning to either Uganda or The Gambia for the final, summative study, but we ultimately decided to perform this study in a different SSA country to widen the range of viewpoints further by bringing in a new population. This would allow opportunity for new perspectives, not previously identified, to be explored. Again, due to existing links in the country, the decision was taken to perform these studies in Malawi.

We have added a short paragraph in the manuscript to clarify this point.

“Uganda, The Gambia, and Malawi were selected amongst FP2020 countries due to existing academic or charitable links. Studies in the UK were conducted to explore the views on a new long-acting contraceptive in an industrialised country.”

5. This comment raises some important points worth clarifying. Accessing non-users to provide their views is always challenging, and in this study there were added logistical reasons which made this more difficult. During our limited duration field trips in Africa, logistically the easiest way to organise focus groups with providers and users was to visit FP clinics or hospitals and recruit participants there. A high percentage of the people attending FP clinics are already users of contraception, with only a few attending to enquire about the different options available as their first contraceptive, as a different contraceptive to what they have used in the past (and they haven't been happy with), or as a method to return to as they stop breastfeeding and return to fertility. Nevertheless some focus groups were organised outside of the clinical setting and included women with different backgrounds and different experience with use/non use of contraception, but recruitment of these individuals was more challenging, especially given the short period of time available, as women were a bit more wary to engage with us outside of the clinical setting. Ideally, with logistics being less of an issue we would have liked to speak with more individuals and we definitely feel that we are missing some viewpoints, especially from potential users of a young age and those living in a more rural setting. That said, the input from healthcare providers that regularly talk to these groups provided their views on these individuals' preferences, concerns and needs and this gave us confidence that this method might be popular with some of the women who are currently non users.

6. The health professionals involved in the study all spoke English well and were

comfortable conversing in English. For the potential users, some likewise had a very good mastery of the English language, and fellow participants in focus groups were helping each other if they had problems understanding some particular terms. In both countries a local contact was available to provide translation support during focus groups, with whom we held meeting explaining in detail the scientific background of the project beforehand. This was typically a local health professional.

Two FGDs in Uganda and two one-to-one interviews in the Gambia did take place predominantly in the local language, with the local facilitator providing translation support both in asking questions and reporting back answers. These were a bit more tricky to conduct, as the flow and rapport were disrupted. In addition, it wasn't possible for us to understand if the translator was being neutral or was unconsciously guiding the participant's responses, or changing the participant's words when translating back into English.

This was potentially a limitation of the study, and that's one of the reasons why we included Malawian researchers in the team for the summative study. These trained researchers had experience of qualitative data collection, knowledge about the project, could run focus groups in the local language, thus minimising the impact of bias resulting from language and translation issues.

Our findings from the studies in Malawi very closely mirror the ones from studies in The Gambia and Uganda, giving us confidence that the language barrier didn't have a major effect in early studies.

7. The reviewer is correct in pointing out that there was no opportunity to go back to previous participants to confirm the changes made were reflective of their feedback. Even returning to the same country for further studies wouldn't have guaranteed the presence of previous participants in the new study. Therefore it is possible that some of the users' needs haven't been accurately addressed during further iterations. It is worth noting that the main applicator features that were changed were:

- The addition of auditory and visual feedbacks to confirm correct deployment of the applicator. This was requested in some form in almost all of the FGDs and users in Malawi universally liked these, even if they hadn't seen a previous version without feedback. We are considering running another study in the UK presenting participants with 2 versions of the applicator: one with and one without auditory and visual feedback to gather their opinion.
- The stiffening of the transport/disposal cap, to make the applicator childproof. Even though we were not able to go back to participants to ask their opinion about this feature, we are convinced that the cap now serves also for this purpose. It's worth noting that a final packaging solution that will be developed prior to commercialisation might make a transport/disposal childproof cap redundant, so this feature will be re-evaluated in the future, keeping in mind that users will welcome some sort of childproofing feature.
- The increase in the application force to prevent accidental deployment. Even though the users didn't specify a particular force desired to actuate the applicator, we increased this force so that the applicator will be very difficult to deployed accidentally, but still easy to actuate with one hand during application.
- Efforts have been made to maintain the applicator as small as possible, as per user preferences. Even though users haven't specified a desired size, since the publication

of this study a lot of efforts have gone into reducing the size of the MN product to allow for a smaller applicator size.

We are therefore relatively confident that the main, general points raised during our studies in different country have been addressed. We keep in mind though that prior to commercialisation some other changes might need to be made to overcome some technical issues, and users feedback will be requested again at later stages.

8. The dummy prototypes consisted of the fully functional applicators without MNs (just a flat plastic surface where the MNs would be). This allowed participants to experience the mechanism of action, usability, duration of application, feedback from the applicator, etc without having any MNs pierce their skin. Participants were shown how to use the applicator and then performed multiple mock application on themselves and on fellow participants to familiarise themselves with the prototypes. Participants were then shown some drug free MNs under a magnifying glass to help them understand the small size and shape of these devices.

We have added the following paragraph to the manuscript to clarify this issue:

“The dummy prototypes used in the studies consisted the fully functional applicators without the presence of MNs. This allowed participants to experience the mechanism of deployment, usability, duration of application and feedback from the applicator.”

Unfortunately, we are not able to share any images of the prototypes at the moment, as publishing them will constitute prior art that will interfere with securing IP for the novel mechanism used with the applicator (see response to point 13 for more details), but we strongly feel that it is in the best interests of the project, the development of the product and the community of researchers working in this space to publish these results now, even if we cannot show the actual prototype employed. This allows others to benefit from the user studies and does not restrict the potential development and commercialisation of the MN product.

9. Regarding the first bullet-point, we agree that it would be an advantage to have the complete demographic information and that we are particularly lacking in demographic data within the Malawi cohort. Participants were asked to complete a short demographic survey (provided as supplemental material with the paper) but ethically they had the right to leave some questions blank if they were not comfortable sharing that information and this accounts for some gaps in the data. It would not be ethical to not use this data, even if the demographic data were not complete. Whilst we may have placed more emphasis on the importance of collecting information on these demographic questions (while respecting participants' rights) it was not practical or possible to retrospectively collect this data. It is important however to use the data obtained, rather than discount data from an important group of participants, even without the demographic context. Any future user studies with finalised product design will ensure that the demographic data is more complete.

Regarding the second bullet-point, we do feel that this is a potential limitation. As stated above (answer to point 5) it was difficult for us in this study to reach young unmarried women, whose views on the proposed product would have been extremely valuable. Input

from healthcare providers that regularly talk to these groups gave us confidence that this method might be popular with this group of potential users. It should also be noted that completing this study during the COVID-19 pandemic made it more difficult to ensure that all of the potential users were targeted.

Regarding the third bullet-point, the text says that potential providers with experience in different work environments (rural or urban) were recruited. Some potential providers who took part in the study reported that they travel regularly to rural locations to provide contraceptives and advice, and are therefore very mindful of the needs of potential users in those settings, which they expressed during our discussions.

All of the potential users that participated in the study were from an urban environment as, due to logistical factors including the short duration of the field trip, it was not feasible to travel to rural locations to recruit participants, even though we would have liked to. In the text when we refer to recruiting potential users from different living environments we meant, as shown in figure 4, people having different living arrangement, i.e. living with partner only, partner and children, living with children only, living with parents only, or living with parents and children. We acknowledge the terminology used might create confusion, so in the methods section of the paper we have changed the text from "living environment" to "living arrangements", to keep it consistent with the terminology used in Fig. 4.

10. This is a very interesting question. Ideally we wanted a balance between providers and users. The reality was that providers were very excited to talk to us and feed into this study, and everybody wanted to be included in the discussion. As such we ended up with more people wanting to participate than we planned for and we felt it would have been counterproductive to turn some of them away just because we had reached our intended number of participants.

Conversely, potential users were a bit more cautious and not everybody agreed to be involved in the discussion due to the sensitive nature of the subject. Even though we reached our target number of participants in this group, we found it very challenging to recruit more potential users to match the high number of participants in the providers group. It is important also to note that whilst self-administration will require the user to apply the product, this could be under the guidance of a provider and the providers also have a good understanding of what may be preferred by the user, based on their experience with multiple users.

11. Thanks to the reviewer for asking this question, which allow us to briefly share the findings from interviewing this group of participants. The interviews with male partners were very interesting, but not especially useful from a design perspective which is the focus of this paper. The few male partners that agreed to talk to us were already supportive of their partners using contraceptives and would welcome a product with fewer side effects and longer duration. They all stressed the importance of spacing children more, in order to give them better education and better prospect for the future, and some of them enquired if a long acting contraceptive for men was also being developed. They had little interest in trying to handle the applicators, hence their lack of input on the design, but they welcomed the concept of a long acting, minimally invasive contraceptive.

12. One of the most significant differences we found between countries was that users in Malawi seemed to be wary of the painless nature of the applicator, suggesting that they “need to feel pain to know it has worked”, while participants in other countries did not express this view.

Providers generally had more questions and concerns than participants, and we think this reflects their experience with multiple women with different needs as well as their medical training and scientific backgrounds.

We found particularly surprising and uplifting that partners of potential users, especially belonging to the younger generations, seemed to be very involved in the FP discussion and welcoming of different methods coming through, also hoping for new male contraceptives to be available in the near future.

Regarding design trade-offs, the main issue is size. There is a technical limit to how small the patch can be while still delivering 6-months contraception, and the users consistently reported that a small size was preferable, even though they never specified precise dimensions. We are confident that in our product development we are reaching an acceptable patch size, but this will need to be validated in further user studies. Another design issue that wasn't seen as concern by participants but which we think is important is disposal. Where it was discussed, it was usually just a comment in relation to using usual methods of disposal (e.g. incineration). Neither users nor providers expressed any major concerns about *safe* disposal although, for us, one of the challenges of this project is to design a product that can be safely disposed of at home after use, and work on this matter is still in progress.

13. As previously mentioned, images cannot be shared at this time due to IP issues. Hopefully we will be able to share them in a future publication focused more on the technical development than the design and usability element.

In reference to this comment and also comments made by the other reviewer, we have added the following statement to the manuscript:

“At this stage we are not able to share any images of the prototypes, as publishing them will constitute a prior art disclosure that will inhibit our ability to protect the novel mechanism used within the applicator.”

14. We apologise if this information was not clearly conveyed and have modified the manuscript accordingly:

“All of the participants were first shown the visual renderings, to familiarise them with the basic concept. After the concept was explained using these illustrations, participants were encouraged to ask general questions regarding the concept (side effects, duration, return to fertility, etc). After this discussion (usually lasting 15-20 minutes) all participants were shown the dummy prototypes (without MNs) with examples of associated instruction leaflets. All participants then had the opportunity to handle and deploy the prototypes multiple times (on themselves and/or on other participants). After handling the prototypes for about 10 minutes, participants were asked to provide specific feedback on the applicators (ease of use, size, mechanism, aesthetics, etc) for the rest of the discussion (10-15 minutes).”

15. We apologise that this was not explained clearly. It is possible that a proportion of drug remains in the device after the application, hence the comment on accidental exposure. For IP reasons, as previously explained, we cannot share images of the cap. The improvement made to this cap means that more dexterity and force is required to remove it from the applicator, comparable to child resistant screw-on lids for oral medications, making it more secure.

16. Thanks for sharing this content. The participants in Malawi were given the mock applicator with instructions and learnt how to perform an application by just following the instructions. They deemed the instruction as “appropriate” as in “suitable for their purpose”, i.e. they were able to learn how to use the applicator by reading the instruction, but they felt that text in the local language would have helped.

17. Unfortunately we cannot show the IFU without revealing some sensitive IP, so we cannot share it at the moment.

**Competing Interests:** No competing interests were disclosed.