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Attitude and acceptability of IVF add-ons to improve reproductive outcomes: a focus group qualitative study

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ABSTRACT

STUDY QUESTION: What factors are important for patients when evaluating the efficacy, safety, cost, and acceptability of IVF add-ons?

SUMMARY ANSWER: Although efficacy is the most important factor for patients, interim markers of success can also be important.

WHAT IS KNOWN ALREADY: IVF add-ons are increasingly offered alongside assisted conception despite limited evidence of their efficacy, safety, or value for money. Capturing patient perspectives on their acceptability and outcome priorities is essential to guide ethical clinical practice and inform future research.

STUDY DESIGN, SIZE, DURATION: Three online focus groups were conducted with 12 people who had used assisted reproductive technologies and were not currently in treatment. The focus groups were conducted in small groups of three to five people with each focus group lasting ~2 h.

PARTICIPANTS/MATERIALS, SETTING, METHODS: Participants were recruited through fertility charities and patient advocacy groups. All 12 participants were women and lived in the UK. All were currently in a relationship, and most had prior experience of using IVF add-ons. Online focus groups were conducted to discuss views on the efficacy, safety, and acceptability of IVF add-ons, and to identify preferred outcomes.

MAIN RESULTS AND THE ROLE OF CHANCE: Nearly all participants defined the most important outcome of using an add-on to be achieving a live birth. However, they recognized that a live birth could feel a distant endpoint within the IVF treatment and therefore valued interim milestones as indicators of success. The main theme found in relation to understanding the risks involved was the need for patients to balance risk with desperation to have a baby. In terms of cost, two themes emerged, the need to balance cost with needing money for future treatments and the differing views on what is an acceptable cost. When receiving information about add-ons, participants reflected on the importance of finding reputable sources while also having to navigate conflicting information. Overall, the effectiveness of an add-on was valued over cost and safety, although cost and the risk of regret remained important considerations in decision-making. Most participants would not regret using add-ons, although some said they may regret not having used them.

LIMITATIONS, REASONS FOR CAUTION: All participants were women, and most were White. Findings may not be applicable to other populations.

WIDER IMPLICATIONS OF THE FINDINGS: Capturing participants' views on efficacy, safety, cost, and acceptability is essential not only to guide future research priorities but also to inform ethical clinical practice and policy. By incorporating patient perspectives, future trials can ensure that outcomes reflect what matters most to those undergoing treatment, thereby improving the relevance and impact of research in reproductive medicine.

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Introduction

Assisted reproductive technologies (ARTs) have transformed infertility care over the past four decades, offering hope to millions of couples worldwide. Globally, more than 2.5 million IVF cycles are performed annually, reflecting both the increasing prevalence of infertility and the growing accessibility of ART services (Baker *et al.*, 2025). Advances such as ICSI and the use of exogenous hormones have improved conception rates, with current estimates suggesting that ∼30% of ART cycles result in pregnancy (Liu *et al.*, 2025).

Alongside the expansion of IVF, there has been a rapid rise in the use of supplementary interventions, commonly referred to as 'IVF add-ons' (Serdarogullari *et al.*, 2025). Many add-ons are offered at significant additional cost, despite limited evidence of their safety, clinical effectiveness, or cost-effectiveness (Feng *et al.*, 2024). Regulatory bodies have attempted to provide guidance, but the poor quality and inconsistency of available evidence have hindered robust recommendations (ESHRE Add-Ons Working Group *et al.*, 2023).

The widespread use of IVF add-ons has raised concerns about commercial exploitation and the overselling of unproven interventions to vulnerable patients. In the UK, regulators and advocacy groups have highlighted profiteering practices, where patients desperate to conceive may be offered costly treatments without adequate evidence of benefit (Rutherford, 2017; Cirkovic *et al.*, 2023). The conflicting evidence, or lack thereof, has lead patients to frequently rely on anecdotal evidence or informal online sources when making decisions about their use of add-ons (Armstrong *et al.*, 2023). An Australian survey of 1590 patients found that 82% of patients had used add-ons which often led to additional costs, and a third experienced moderate to severe regret about doing so (Lensen *et al.*, 2021). There are wide variations in the use of add-ons internationally, and this can depend on the extent to which public services fund IVF cycles. For example, there is a low uptake of add-ons in France, Belgium, and The Netherlands where public funding is generous. Conversely, the UK has one of the highest rates of add-on use (Serdarogullari *et al.*, 2025).

Capturing patient views on efficacy, safety, cost, and acceptability is essential, not only to guide future research priorities but also to inform ethical clinical practice and policy. The aim of the present study was to understand patients' views, acceptability, concerns, and barriers to using IVF add-ons when undergoing ART using a focus group design. The work formed part of a larger project aimed to design a clinical trial which will evaluate the efficacy of IVF add-ons.

Materials and methods

Design

We conducted serial qualitative focus groups as part of the AFFINITY research programme using a prospective registered protocol (OSF 10.17605/OSF.IO/UYAZ2).

Participants

Participants were recruited through fertility charities and patient advocacy groups. Purposeful sampling was used to ensure representation across UK regions, age groups, gender, ethnicity, sexual orientation, and previous IVF experience. Participants were informed about the study through mailing lists, social media, and charity networks. The inclusion criteria included participants with previous lived experience of ARTs and IVF add-ons, ability to provide consent, and ability to join the planned focus group over video conference. We excluded participants currently undergoing ART treatment.

Twelve participants took part in this study, and their characteristics can be seen in Table 1. The majority of participants were aged between 36 and 45 years. Most (10) were White, and were in a heterosexual couple relationship (10), 2 were in same-sex relationships. The majority (10) had experienced private care with 6 having experienced NHS care. Most (9) of the participants had children as a result of assisted reproduction, but not all have had children (3).

Table 1. Participant characteristics.

	N	%
Gender		
Female	12	100
Age at time of study (years)		
31–35	1	8.3
36–40	5	41.7
41–45	4	33.3
>45	2	16.7
Ethnicity		
Caucasian	10	83.3
Asian/Asian British	1	8.3
Mixed/multiple ethnic groups	1	8.3
Black/Black British/Caribbean or African	0	0
Other	0	0
Relationship status		
In partnership—heterosexual	10	83.3
In partnership—same sex	2	16.7
Single	0	0
Undisclosed	0	0
Geographical location		
Greater London	3	25.0
Yorkshire and Humber	3	25.0
North East England	2	16.7
North West England	1	8.3
East Midlands	1	8.3
Wales	1	8.3
East of England	1	8.3
Location of care		
National health service only	2	16.7
Private only	6	50.0
Both	4	33.3

Method

Online focus groups lasting 2 h were conducted via video call in October 2025. Each focus group comprised three to five participants and were conducted by two researchers (K.K. and L.N.). The focus group discussions were recorded, transcribed verbatim, and anonymized. Transcripts were checked for accuracy against the original audio recording. Quotations in the results section are presented exactly, ellipsis have been used when words have been omitted, and repeated words and pause fillers ('er', 'um') have been removed.

The focus group began by explaining the project aims and research questions. At the start of each focus group, the researcher explained that IVF add-ons are an additional treatment suggested to help improve the chance of becoming successfully pregnant and of having a baby. We further defined IVF add-ons as per the AFFINITY Research Team's definition, as having an effect on 'one of the key elements of an ART cycle (ovarian stimulation and egg harvesting, gamete and embryo selection, fertilization and embryo culture, embryo transfer and implantation)' (Wattar, 2026, p. 2). We also explained they are often at extra cost and with variable or uncertain evidence regarding efficacy and safety. We asked participants to discuss add-ons as a broad category rather than evaluate a specific intervention (Supplementary Data File S1: Explanation of what an IVF Add-on is and questions asked).

Open-ended questions about participants' views on efficacy, safety, cost, and acceptability of add-ons were asked in turn. The questions were pre-screened and discussed within the research group to reduce the risk of leading questions and were designed to facilitate discussion. Questions included 'What do you think people will consider a measure of success of an add-on?', 'How much would you think people will expect the add-on to improve the chances of success?', and 'How much do you think that people will expect an add-on should cost?' Questions were also asked to ascertain whether perceptions of acceptable costs would differ based on success rates, whether patients may regret their use of an add-on and what factors (cost, effectiveness, safety, or other) would be most important when selecting an add-on. Questions were deliberately phrased to ask for thoughts about how people will respond in general rather than directly ask for personal experiences. We purposely did not phrase any question with 'you', as we felt it could put the participant in the position to share their personal feelings to a group of people they had never met before. Despite the general phrasing of questions, participants could discuss their own experience if they wished, which all of them did (Supplementary Data File S2: Questions).

Ethical approval was obtained from the UCL Institute for Women's Health Local Research Ethics Committee prior to starting data collection (UCL REC 1742).

Analysis plan

Qualitative thematic analysis (Braun and Clarke, 2006) of the focus group transcripts was conducted by the first author (K.K.) and was facilitated by the qualitative computer software package NVivo. Transcripts of the focus groups were carefully read and coded inductively and themes were developed. The codes and themes were then checked by a second coder (V.J.) and any discrepancies were discussed. The main themes within each of the different areas (e.g. efficacy, safety, cost, and acceptability of add-ons) are presented alongside illustrative quotations.

Consensus meeting

Participants were invited back for a consensus meeting after data analysis to confirm the findings were accurate and representative of their views.

Results

Successful IVF add-ons

Two themes emerged in understanding what participants viewed as a successful add-on. The first theme 'success in every step' related to the different milestones that make up a fertility treatment and the second theme 'differing definitions of success' highlighted the individual differences in seeing an IVF add-on as being successful.

Success in every step

Patients defined a good outcome as 'having a baby', specifically a baby who is well with no abnormalities. However, they recognized that live birth as an outcome can be a distant measure of success and felt that reaching interim milestones can also be considered a good outcome. These milestones could include the number of eggs collected, the number of embryos created, a positive pregnancy test, an early pregnancy scan showing a heartbeat as well as positive outcomes during subsequent pregnancy scans. For example,

> *'I think for me a measure of success is whether it results in a change in outcome and I don't think that always necessarily needs to mean a pregnancy'*

Many participants felt that if using an add-on allowed them to progress further in an IVF treatment than previous cycles, or if it taught them something new about the reason for their infertility and how best to treat it, this would also be considered success.

Definitions of success

Some participants reflected on how '*a successful outcome could mean different things for different people*' and this may depend on factors such as their age, how many previous IVF cycles they have had, any current health conditions and if patients already had a child. However, they also cautioned against using any other interim outcome marker of success, as sometimes these milestones are not met due to other reasons separate to add-on use. For example:

> *'… if you can find a way to, yes, have more embryos that fertilise successfully but then that's only one thing because you can have as many embryos as you want, if for some reason the environment that they get, you know, transferred into, like the womb environment maybe is not receptive, for whatever other reason … '*

Participants expressed their views that an add-on should almost certainly have a positive effect on most people (80–100%) who use it. The expected increase in success rate varied greatly between participants, from 'any improvement', 0.5% to over 50%. The majority of participants had low expectations of an add-on being successful and

they felt that as long as there was some improvement, they would consider it successful. One participant said:

> *'I don't think that you can expect it to be that high, because if it was, everybody would be doing it and IVF wouldn't be so … you know difficult in the first place'.*

Another participant commented

> *'IVF is so different and so personalised and individual to each couple, each person … and there are so many even variables and different factors at play between their own cycles, that for lots of add-ons, that success rate is, you may as well stick your finger in the air'.*

Some participants mentioned that if the add-on enabled an abnormal pregnancy that was destined to fail to continue for longer than it should, this could cause physical and emotional distress to the person involved. They felt that their expectations from an add-on would change depending on how many failed cycles they had experienced previously, the anticipated increase in success rate would reduce over time, but their 'hope' for that IVF cycle would increase.

Balancing risk with desperation

The main theme to emerge from understanding the level of risk patients would be willing to undertake when using an IVF add-on was navigating the balance between taking risks and feelings of desperation in wanting a baby. Participants described having a generally high tolerance for risk when using add-ons. However, willingness to take risks was seen to shift over time; as the number of unsuccessful cycles increased, they became more open to considering higher-risk add-ons. One participant said, '*I would have thrown anything at it if somebody said… go skydiving after having your embryo transfer, and it'll work for you. I would have done it.*' Despite this greater willingness to take risks, participants were clear that they would not accept anything that might compromise their own health, negatively affect future treatment cycles, increase the risk of cancer, or pose any potential harm to a future child. One participant stated how their willingness to use higher risk treatments was far less when having their second child as they were less 'desperate', again reflecting how previous experiences may influence the future uptake of add-ons.

Cost of IVF add-ons

Two themes reflected the thoughts of participants in relation to the cost of add-ons: (i) the need to balance cost with future treatments and (ii) recognizing that perceptions of what counts as an acceptable cost differ between individuals.

Balancing cost of IVF add-on with cost of needing future treatments

Overwhelmingly, participants expressed how much finances played into the decision-making of having IVF or using add-ons. Participants reported that if they were having treatment funded by a public body (National Health Service/NHS), it would likely be their first or second cycle and therefore they would be less likely to try an add-on. Many of the participants did not succeed during their NHS-funded treatment and then self-funded their subsequent treatment where add-ons were offered. They often felt it was a balance between spending as much as necessary to give the current cycle the best chance of success with having enough money left aside for another round of IVF if the current treatment was unsuccessful. Many participants felt that if they were paying for an add-on, it should increase their chances of success, even if marginally. Many mentioned that they had spent money they did not have, borrowing from family, taking out loans, or finding a new job to fund IVF. Factors that would increase their willingness to pay more for an add-on included if they were older and '*time was running out*', if the add-on proposed to fix a problem specific to them, if it was well evidenced from a reputable source, e.g. 'green-lighted' by the HFEA. The more 'desperate' they were, the more willing they were to pay more for it. Participants mentioned how differences in experiences between patients would likely affect the amount of money they would be willing to pay for add-ons. For example, one participant mentioned it was their last embryo, so they used three add-ons and paid the necessary cost. Another participant remarked that they already had a child so they would pay less for add-ons for a second child.

Differing views on what is an acceptable cost

Some participants reached a consensus within the group that the cost of an add-on should be less than 10% of an IVF round and that this would allow them to take account of using multiple add-ons per cycle. Some participants felt that the cost of an add-on was unacceptable if it was more than 50% of an IVF cycle. A minority of participants felt that add-ons should be free when having treatment on the NHS, especially if it was considered mutually beneficial between the clinician and patient. Others mentioned that clinics should offer add-ons for free if patients had experienced multiple rounds of unsuccessful treatment.

The perceptions of cost also differed between participants with some believing add-ons to cost less than expected while others felt they were unacceptably high '*I was shocked when I had a breakdown of costs, we had the sheet in front of us that said how much add-ons was and it was a big eye opener*.'

Thoughts on the evidence base for add-ons

Participants recognized the weak evidence base behind using add-ons and the conflicting advice they were often told by clinicians. '*I felt at least that there were differences in how they described (the add-on). You know, one person might be more optimistic about a particular add-on, where somebody else might be less optimistic about it*'.

One participant remarked that the lack of evidence behind add-ons is clearly acceptable to the public, as people still use them. The majority of the participants would be open to using add-ons, even if experimental, as long as they were not harmful. Some mentioned that their appetite for low evidence would change depending on how many failed cycles they had already undergone and would be open to trying add-ons with progressively weaker evidence over time. Participants in same-sex couples felt marginalized by the lack of research specific to their demographic, which they believed significantly hindered their ability to make informed decisions.

Sources of information

Participants used a variety of sources to guide their decision-making including: the HFEA website, to which many referred to as the traffic light website; Clinicians; Online forums; Social media; Support groups (mostly online); Counsellors; Research papers; and Friends. The main theme to emerge from this data was in relation to the importance of receiving reputable sources of information while navigating conflicting advice.

The main source of information was mentioned as coming from clinicians, followed by the HFEA website. Some reflected on their own personal experiences with clinicians who they felt were transparent about the uncertainties in outcomes when using add-ons. However, a few felt the information given by the clinician left them feeling conflicted as they were told '*that it may help, or it may not… but it's of course it's, it's your decision.*' There was also mention of conflicting advice between clinicians when they sought second or third opinions. Some mentioned worries about IVF clinics being a '*business*' and concerns over profiteering from add-ons.

The HFEA website was a trusted source of information for many participants. Not all had accessed it before considering add-ons in their treatment, but those who did, felt it was the most independent resource. However, some reflected that the information was not personalized, so they could not always apply the information to themselves. One participant noted that it has a '*negative connotation towards add-ons. Like oh, be careful, you know they just want to sell you something*'.

Words used to describe social media were 'overwhelming' and 'pushy', and some spent a long time looking for other people in a similar situation to see if they were successful with using specific treatments. Overall, the lack of reliable personalized non-conflicting information for the participants led them to feel 'frustrated'.

What matters most between effectiveness, cost, and safety

Participants were asked what matters most to them between effectiveness, cost, and safety. Unanimously, they all considered effectiveness the most important factor. The value of cost and safety changed depending on factors such as how much money they had left to spend, how many cycles they had previously, cycle fatigue, and if it was their last cycle. However, if an add-on had low effectiveness but was safe and inexpensive, they would consider taking it. One participant mentioned that if the effectiveness was marginal and they had been through so many cycles, they would consider donor eggs over any further add-ons.

Feelings of regret

Most participants said they would not regret using add-ons, as '*you will always think that you're giving yourself the best possible chance*'. Indeed, many felt they were more likely to regret not using it. For example: '*I also have regret on the opposite end of it because I haven't used an add-on… um and I kind of regret not having that opportunity*'. A few participants regretted using add-ons for various reasons. One mentioned they used an add-on against medical advice, and that it did not work. Another participant found out they had a diagnosis of a disorder further along in their IVF treatment and had later realized that the add-on they used would not have worked because of their diagnosis.

A further participant was offered add-ons many years ago that no longer exist; she did not regret the financial impact of the add-on so much as the unnecessary physical stress she put her body through to use it.

Discussion

Our study highlights that patients' view of IVF add-ons were complex and nuanced. While the majority of participants recognized that a successful add-on would be one that helped them to have a healthy baby, reaching important interim milestones was also valued and it was recognized that the definition of success can vary between patients. The risks associated with using an add-on needed to be balanced alongside the benefits and the desperation that patients felt to have a baby. Participants highlighted the variation in what an acceptable cost for an IVF add-on would be, and how, in practice, patients balance these decisions with their knowledge of what may be successful and their own feelings of desperation. Patients often had to navigate conflicting information about different IVF add-ons, and some questioned whether the evidence base was applicable to the experiences of same-sex couples. All participants noted that the main criterion for deciding whether to use an add-on would be its effectiveness and many did not regret their decision to use them.

Implications for clinical practice

The findings of this study have important implications for clinical practice, particularly in relation to communication, shared decision-making, and the ethical provision of care. The prioritization of effectiveness over cost and safety observed among participants underscores the need for clinicians to support patients in making balanced and informed decisions, particularly in the context of emotional vulnerability and cumulative treatment burden. Consistent with previous research, patients undergoing IVF may overestimate the benefits of add-ons or accept interventions with limited supporting evidence, especially when faced with repeated treatment failure (Lensen *et al.*, 2021). Indeed, many clinics promote add-ons on their websites without disclaiming the scientific uncertainty of success, which can mislead patients into believing strong evidence of benefit (van de Wiel *et al.*, 2020). Clinicians therefore have a responsibility to provide clear, transparent, and consistent information regarding the effectiveness, safety, and uncertainty surrounding add-ons, while avoiding the inadvertent promotion of unproven interventions. This applies not only to the patient but also to the subsequent child (Harper *et al.*, 2017). The variability in patients' willingness to accept risk and financial cost, shaped by individual treatment histories and perceptions of urgency, highlights the importance of personalized counselling that is responsive to patient values and circumstances. Access to public body (NHS) funding for fertility treatment also interplays with their decision-making. Greater consistency in how add-ons are presented across clinics, alongside alignment with regulatory frameworks such as those proposed by the HFEA and ESHRE, may help reduce confusion and enhance trust (Harper *et al.*, 2017; ESHRE Add-Ons Working Group *et al.*, 2023). The integration of structured decision aids and evidence-based counselling approaches may further facilitate shared decision-making and mitigate the risk of patients feeling pressured to pursue add-ons of uncertain benefit (Elwyn *et al.*, 2012).

Participants regarded the HFEA website as an important and trusted source of information when making decisions about IVF

add-ons. Previous studies have found that nearly half of patients first learn about add-ons from clinics, and that their use is largely driven by clinicians (Lensen *et al.*, 2021; Cirkovic *et al.*, 2023). Participants in our study expressed frustration about receiving conflicting guidance from clinicians, underscoring the need for greater consistency and clearer communication across clinical teams. Although personalized advice was viewed as essential, this may, in practice, be challenging to deliver given the limited and often inconclusive evidence around the effectiveness of many add-ons. Despite widespread use, patient perspectives on the efficacy, safety, cost, and acceptability of IVF add-ons remain underrepresented in research. Existing studies and systematic reviews have largely focused on clinical outcomes, with little attention to patient preferences or lived experiences (Perrotta and Hamper, 2023). A recent Cochrane special issue reviewing 13 add-ons across 170 randomized controlled trials found no clear evidence of benefit for most interventions, with the certainty of evidence rated as low to very low (Lensen and Kostova, 2021). Similarly, the ESHRE guidelines issued 42 recommendations on 27 add-ons, but 95% were based on low-quality evidence or expert consensus (ESHRE Add-Ons Working Group *et al.*, 2023). This persistent knowledge gap underscores the importance of integrating patient voices into the evaluation of add-ons.

Future research need

The present findings also highlight several important priorities for future research. There remains a clear need for high-quality, adequately powered randomized controlled trials to evaluate the effectiveness, safety, and cost-effectiveness of commonly used IVF add-ons, particularly given the low certainty of evidence underpinning current clinical practice (Kamath *et al.*, 2019; Armstrong *et al.*, 2023). Future trials should prioritize outcomes that are meaningful to patients, including live birth as well as relevant interim milestones, reflecting the complex and staged nature of the fertility treatment. The integration of patient and public involvement (PPI) throughout the research process is essential to ensure that study design, outcome selection, and dissemination strategies align with patient priorities and improve the relevance and acceptability of research (Brett *et al.*, 2014). In addition, there is a need for more inclusive research that addresses the experiences of underrepresented groups, including same-sex couples, ethnically diverse populations, and men. Given the rapidly evolving landscape of ARTs, innovative methodological approaches such as adaptive and platform trial designs may offer efficient means of evaluating multiple add-ons within a single research framework (Bothwell *et al.*, 2018). Finally, further work is required to develop and evaluate effective strategies for communicating complex and uncertain evidence to patients, with the aim of supporting informed, value-consistent decision-making in clinical practice.

Strengths and limitations

The strengths of study stem from the use of a prospective protocol and serial qualitative focus group methodology to enable an in-depth exploration of patient perspectives, allowing participants to reflect on and build upon each other's experiences, thereby generating rich and nuanced data. By recruiting participants through fertility charities and advocacy groups, we engaged individuals with direct and varied experiences of IVF and add-ons, enhancing the relevance of our findings to real-world clinical contexts. We explored multiple dimensions of decision-making—including effectiveness, safety, cost, and acceptability—providing a comprehensive understanding of how patients evaluate add-ons in practice. We also strengthened the credibility and rigour of our findings through an iterative and collaborative approach to thematic analysis involving multiple researchers (Braun and Clarke, 2006). Collectively, these strengths support the trustworthiness of our data and its contribution to informing both clinical practice and future research.

The study has limitations which should be noted. The sample was self-selected and may not represent the broader experiences of patients undergoing treatment. Although an effort was made to recruit a diverse sample of patients, all were women, and most were White; two of the patients were in same-sex relationships. While the number of patients in this study was relatively small, thematic saturation was reached. This is consistent with qualitative research studies utilizing focus group methods (Carey and Asbury, 2016). An advantage of using focus groups is that they facilitate discussion between participants which can stimulate ideas, challenge assumptions, and spark deeper reflection (Kitzinger, 1995).

Conclusion

The findings from this study highlight an urgent need for a better evidence base on the effectiveness of IVF add-ons. Patients may prioritize efficacy above all else; however, they require honest discussion regarding the evidence base behind each add-on, as well as accurate and detailed guidance that can be tailored to their individual needs. This would improve their decision-making around the use of IVF add-ons.

Supplementary data

Supplementary data are available at *Human Reproduction* online.

Data availability

The data underlying this article cannot be shared publicly in order to protect the privacy of individuals that participated in the study.

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Authors' roles

All authors were involved in the conception and structure of the study. Participant recruitment was guided by K.K. and B.H.A.W., facilitated by K.B. and S.N., and coordinated by L.N. Ethical approval was obtained by K.K., B.H.A.W., and L.N. Focus group sessions were led by K.K. and recorded by L.N. Data were anonymized by L.N. Data analysis was performed by K.K. and V.J. The final manuscript was written by K.K., V.J., and B.H.A.W. All authors provided critical input to the manuscript and approved the current version.

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Disclosures

There are no conflicts of interest.

Appendix

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