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ASSISTED REPRODUCTION TECHNOLOGIES

Acceptable, hopeful, and useful: development and mixed-method evaluation of an educational tool about reproductive options for people with sickle cell disease or trait

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Abstract

Purpose People with sickle cell disease (SCD) or trait have many reproductive options, some of which decrease the chance of passing SCD to children, including in vitro fertilization with preimplantation genetic testing (IVF + PGT). Few are aware of these options, and educational materials are needed. This study aimed to develop an accessible, non-directive patient education material about reproductive options for those with SCD or trait via a process that incorporated stakeholders from the SCD community.

Methods Multidisciplinary stakeholders guided development and revision of a novel pamphlet. Researchers applied health literacy scales to measure pamphlet understandability. We interviewed nine patients with SCD and six multidisciplinary clinicians to evaluate the pamphlet. Interviews were recorded, transcribed, and coded by a five-member team who developed a codebook and proposed themes that were revised by all research team members. Feedback was incorporated into a revised pamphlet.

Results A two-page pamphlet describing reproductive options for people with SCD including IVF + PGT was acceptable to key stakeholders, including people with SCD. Material about this complex topic met health literacy standards, including being written at a 5th grade level. Patients reported feeling hopeful after reviewing the pamphlet, and participants considered the pamphlet useful, clear, and appropriate for distribution in clinics and online.

Conclusions Though awareness of reproductive options for those with SCD or trait is low, patients and providers find a novel pamphlet about this topic acceptable and useful. Educational materials about complex topics including IVF + PGT can be written at a level understandable to the average American.

Keywords Sickle cell · Patient education · Reproduction · Assisted reproduction · Preimplantation genetic testing

Introduction

Individuals with sickle cell disease (SCD) and sickle cell trait (SCT) are at risk of passing SCD, a morbid autosomal recessive disease, to their offspring [1]. Reproductive options for these individuals include genetic carrier

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screening with partner selection, spontaneous pregnancy with or without prenatal testing, in vitro fertilization with preimplantation genetic testing (IVF + PGT), IVF with use of unaffected donor egg or sperm, adoption, or forgoing having children. IVF + PGT is an over 20-year-old technology that reduces the chance of having a child with SCD by over 98% [2]. Recent studies identify that individuals with SCD and their parents have limited awareness, but high levels of interest in IVF + PGT [3–6]. Individuals with SCD or SCT use IVF + PGT less often than people with other conditions of similar prevalence, including cystic fibrosis [7].

There are individual-, provider-, and system-level barriers to providing comprehensive reproductive counseling that includes IVF + PGT for people with the chance of having a child with SCD [8]. Many individuals do not know their hemoglobinopathy trait status despite universal newborn screening in the USA [9], and unplanned pregnancy is common [10]. While primary care providers, hematologists, and obstetricians-gynecologists commonly encounter people who could pass SCD to their children, there is no established "work flow" to ensure those individuals receive proper testing and counseling. Furthermore, providers report discomfort explaining IVF + PGT to patients due to its technological complexity [11]. Providers might also neglect this topic because the high cost of IVF + PGT in the USA limits access for many patients. While some patients might attempt to educate themselves about reproductive options, written materials that describe the process of IVF + PGT are written at a college reading level [12], while the average American adult cannot read a book at the eighth-grade level [13].

Tools to navigate complex reproductive counseling that support non-judgmental, shared decision-making are needed for individuals with SCD and SCT and their providers. Reproductive choices are highly individualized decisions informed by historical and cultural contingencies. In the USA, where couples at risk for SCD are disproportionately Black, reproductive coercion of African American women [14] and advocacy for eugenic approaches to "eradicate SCD" [15, 16] may inform community perspectives and provider behavior. Reproductive choices may feel morally ambiguous and emotional, especially as they relate to preventing a genetic condition. Incorporating opinions of members of the affected community can help ensure judicious presentation of a sensitive topic and understand the needs and perspectives of the target audience.

The purpose of this study was to develop an accessible, non-directive patient education material about reproductive options for those at risk of having a child with SCD using a participatory process with stakeholders from the SCD community. We hypothesized that this pamphlet could be designed to meet national plain language standards [17, 18] and be acceptable and understandable to patients and healthcare providers.

Methods

The Johns Hopkins Institutional Review Board approved this study. Our three-step approach to pamphlet development, evaluation, and revision is described here (Fig. 1). These methods adhered to the Standards for Reporting Qualitative Research [19] (Supplemental material 1).

Pamphlet development

We reviewed existing educational materials about reproductive options for genetic conditions [20–22] and assisted reproductive technologies (ART) [12] to select the pamphlet content. We also met with a geneticist, genetic counselor, hematologist, reproductive endocrinologist, and two SCD-focused community health workers, one of whom has SCT and is the mother of a child with SCD, for input on content.

Two collaborators created the text, layout, and graphics using Canva [23]. Toolkits from the Centers for Disease Control and Prevention (CDC), Agency for Healthcare Research and Quality (AHRQ), and Center for Medicare and Medicaid Services [24–26], containing research-supported techniques to enhance patient understanding, guided the pamphlet's design.

A multidisciplinary SCD research group reviewed the initial draft. This group included hematologists, SCD research staff, trainees, and public health professionals. The pamphlet was revised with this group's feedback prior to formal evaluation.

Pamphlet evaluation

Health literacy scales

Graders assessed the pamphlet's adherence to health literacy standards using three tools. The Flesch-Kincaid measures the reading grade level required to understand a text [27]. The Flesch-Kincaid score was generated automatically in Microsoft Word. The Patient Education Material Assessment Test (PEMAT), developed by AHRQ [25, 28], and the Clear Communication Index (Index), developed by the CDC [24], are validated scales that assess understandability of written materials. Both tools are previously described [12]. Two graders who did not design the pamphlet evaluated the pamphlet with these health literacy standards.

Interviews

We recruited adults with SCD from the Johns Hopkins Sickle Cell Center for Adults' outpatient panel and a list of patients from a previous study who agreed to be contacted

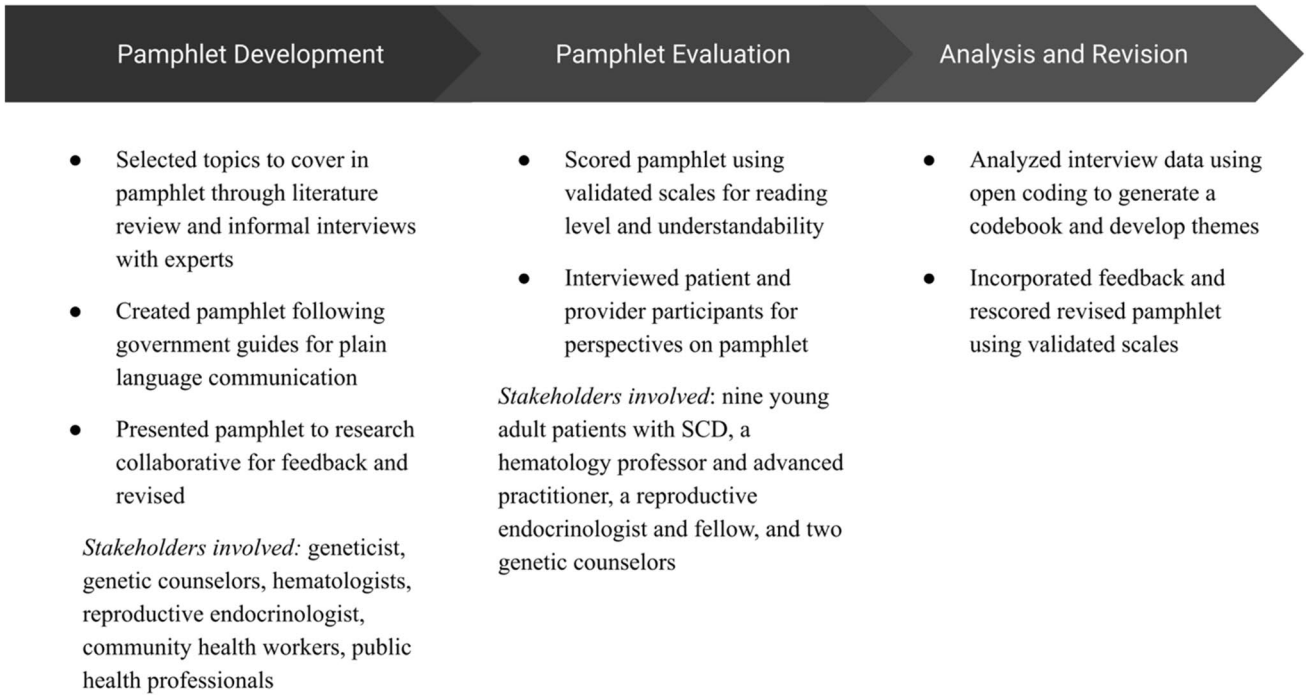


Fig. 1 Methodology for collaborative development of patient education material

for future research. Inclusion criteria included 21–35 years old, English-speaking, and comfortable reading a two-page pamphlet. We designed a purposeful sampling technique [29] to target individuals with a range of education levels. We recruited one man and one woman who (a) completed high school or less, (b) had some college experience, and (c) completed college or more, and one additional man and woman with any level of education.

We recruited provider participants using a purposeful sample targeting one hematologist; one advanced practice provider from the Sickle Cell Center; two reproductive endocrinology-infertility fellows or faculty; and two genetic counselors in the obstetrics and gynecology department. A medical student emailed these divisions inviting participation from eligible faculty or staff.

Participants provided verbal consent. Two trained medical students conducted interviews virtually. Patient participants were interviewed by phone, and provider participants through a video conferencing platform. All participants received a PDF of the pamphlet prior to the interview and had unlimited time at the start of the interview to review the material. The interviewers asked open-ended questions from one of three semi-structured interview guides: one each for patients, hematologists, and genetic counselors and reproductive endocrinologists. Multidisciplinary consultants with experience in qualitative research refined the guides prior to their use (Supplemental material 2). The guides included questions about whether any aspects of the pamphlet were confusing, features that improved or hindered understanding, emotional reactions, and recommendations for future use. After five interviews were completed, we added questions to address issues that emerged: how to discuss cost of IVF + PGT and the appropriateness of phrases including "spontaneous pregnancy," "embryo," and "mother/father."

All patient participants were compensated with $30 gift cards. The interview period lasted from June 2020 to March 2021. Interviews were recorded, deidentified, and transcribed by a secure transcription service [30].

Interview analysis

For the health literacy scales, arithmetic means of the two graders' scores for the pamphlet were reported with inter-rater percent agreement.

The five-member coding team analyzed interviews using grounded theory, a qualitative content analysis framework [31]. The code team, two of whom had previous qualitative research experience, was trained by reviewing and discussing qualitative methods described in published literature [31, 32]. No coding team member was a provider or patient stakeholder, though all team members were medical students at the same institution. All members of the code team read and coded the first two expert and patient interviews. The team developed a consensus preliminary codebook with code trees, definitions, and examples.

Two coders independently reviewed and coded each transcript using the preliminary codebook and proposed new codes as necessary. Coding dyads met together to discuss codes and reached consensus on each transcript. The full coding team met periodically to debate new codes and refine preliminary codes. We determined whether saturation of themes was reached with the first round of purposeful sampling by assessing whether any new higher-level codes were added when coding the last transcript. Coding dyads recoded transcripts using the final codebook. The coding team met to finalize classification of codes into trees. From these trees, key themes were proposed and refined by research team members until consensus was achieved.

Pamphlet revision

We revised the pamphlet to comply with the standards in the health literacy scales, as described below. We incorporated interviewee feedback except where opinions contradicted each other or where the suggestion was determined to be outside the pamphlet's scope. The final pamphlet was rescored using the Flesch-Kincaid, PEMAT, and Index.

Results

Pamphlet design

The initial pamphlet was a double-sided, full-color introduction to reproductive options for people with SCD or SCT. The initial pamphlet addressed hemoglobin electrophoresis testing, family planning options, details of IVF + PGT, the multidisciplinary experts involved in reproductive care, and a list of steps to support patients' decision-making.

Pamphlet evaluation

The Joint Commission recommends writing materials at a 5th grade reading level [18]. The Flesch-Kincaid score for the initial pamphlet was 7th grade. The AHRQ recommends PEMAT scores greater than 70% [28]. The initial pamphlet met a mean of 84% of PEMAT standards (82% agreement). The CDC recommends Index scores greater than 90% [24]. The initial pamphlet met a mean of 78% of Index standards (94% agreement). The initial pamphlet did not meet the following standards: it did not "almost always" use the active voice (PEMAT item 5), explain what is not known about the topic (Index item 11), or sufficiently address both risks and benefits (Index items 18 and 19). We addressed these shortcomings during final revisions, as detailed below.

Researchers contacted 22 eligible patients for interviews and 13 consented to participate. We excluded three men with a high school education due to missed interviews, and one woman with a high school education disenrolled due to hospitalization. We mistakenly recruited and interviewed an additional woman with some college education after meeting the "some college" quota. Analysis of her interview was underway when the error was identified. We decided to include the data from her interview. Our analyses aimed to represent the breadth of patient perspectives, and themes were not selected based on the frequency with which the idea was expressed, so we were not concerned that adding an additional patient with some college education would bias the results. We completed all other purposeful sampling categories, so there were nine total patient participants. Twenty-four providers received division-wide emails inviting participation. Eight providers volunteered, and six were enrolled to meet sampling quotas. We filled each sampling category by enrolling participants in the order in which they volunteered.

The patients were 21–29 years old. Two patients were college graduates, two had a high school education, and five had completed some college coursework. Most had hemoglobin SS disease (56%), while others had SC (33%) and $S\beta^+$ thalassemia (11%). Of the six clinicians, all were female,; four were non-Hispanic White, one was Black, one was South Asian, and one was Hispanic White. They included two attending physicians, a reproductive endocrinologist and a hematologist; one fellow in reproductive endocrinology; one advanced practice provider from the Sickle Cell Center; and two genetic counselors. Interview length was 10 to 45 min.

Interview analysis

We identified seven key themes about attitudes towards the pamphlet and its distribution. Table 1 provides themes with exemplar quotes.

Theme 1. Clear, concise overview of a complicated topic: Patient and providers thought the pamphlet was straight-forward and understandable; several described the pamphlet as "self-explanatory." Features that aided in understanding included a glossary of terms, graphics depicting the steps of the IVF + PGT process, and a bulleted summary.

Theme 2. Useful to patients and providers: Patients were asked if they would recommend this pamphlet to a friend or family member with SCD or SCT. All stated that they would recommend it ($n = 9$, 100%). Several named specific individuals for whom it would be useful. Many patients ($n = 6$, 67%) spontaneously stated that the pamphlet would be useful for their own future family planning. Providers imagined incorporating the pamphlet into their workflows before visits as an introduction to the topic, during visits to structure conversa-

Table 1 Themes with exemplar interview excerpts show patient and provider acceptance of pamphlet

Theme	Patient interview excerpts	Provider interview excerpts
Pamphlet strengths		
1. Clear, concise overview of a complicated topic	"But to me, the pamphlet was very easy to read. Pretty easy to digest" — Patient, 28 M	"This is obviously a super complex topic, and I think it does a good job of kind of breaking it down and introducing a 10,000 foot overview of how IVF can help prevent people who are at risk for sickle cell disease passing it on to a child" — Reproductive Endocrinologist
2. Useful to patients and providers	"It was just perfect for me because this was something that me and my wife had talked about before, and we weren't sure about the details of the process…And now I can ask more from my doctor and all that sort of stuff" — Patient, 26 M	"Any time that you have a patient handout that lists the steps of PGT is so helpful because it's something that, in preconception counseling, you really need to walk through it with them one step at a time and make sure that you are giving them material to go home with and really ruminate on" — Genetic counselor
3. Appropriate for distribution online and in clinic	"I use social media; I feel like it's a great outlet. More people can get educated and then they can hook up with a doctor to talk about this process together" — Patient, 28 M	"If I had a patient who was thinking about having a child and I'm counseling them on it, I would say, 'Here take this home. Read about it. And then come back to me'" — Hematologist
4. Universally acceptable to participants and hopeful for patients	"I felt a little bit lighter knowing that I still have options if I wanted to have a child. I'm 26 now, so it's something that I do think about. So I feel like I know a little bit more just with this pamphlet alone" — Patient, 26F "Honestly, I was excited about it, because I had really come to the conclusion that I had to adopt…that adoption is my only choice unless they find a cure… And I keep thinking, 'This sucks.'…But the pamphlet gives me kind of hope that it doesn't have to go that route if I don't want it to…So yeah, it helped quite a bit" — Patient, 24F	Interviewer: "Is there anything that would make you less likely to share this with patients? Participant: "No. It is good information. This is going to make them more knowledgeable. If they know about this, it's going to give them more insight" — Advanced practice provider, Sickle Cell Center
Suggestions for improvement		
5. Lacking information about uncertainties and risks, including potential cost	"I know that it says you can do a treatment where… they could try to pick the embryo that doesn't carry the genes during the IVF treatment. But is that for sure? Is that 100%?" — Patient, 22F "And there's no explanation of how much it would cost…I think that's my biggest thing" — Patient 26F	"But plenty of people, IVF and PGT is really not an option for them. We can tell them all we want, 'Oh you have options. You have options.' And they really don't if it's going to cost them 20 K out of pocket" — Genetic counselor
6. Disagreement about gendered language and inclusivity	"I understand that you feel some type of way about mother/father, but in reality, the father has sperm; the mother has eggs and ovaries, end of story. A guy can't have ovaries and eggs. It's just a medical fact…I feel like trying to use female or male, it kind of makes it too generic" — Patient, 24F	"This pamphlet is very, very not sensitive to issues of gender identity, and I would not want to give this pamphlet to a trans patient. There are lots and lots of instances throughout the pamphlet where it talks about the mother and the father" — Genetic counselor "As someone who is not particularly religious, I think my reaction was like, well I don't necessarily need a spiritual advisor. …It just seemed a little bit narrow" — Reproductive Endocrinologist
7. Not sufficiently explicit that IVF + PGT can prevent SCD	"I guess a question I would have is if you could do PGT without doing in vitro or if you could do one without the other, if it's a process that you have to do together" — Patient 26F	"Where it says, 'in vitro fertilization with preimplantation genetic testing is one option to have a child,' I think…it's not clear that the reason why you're doing this is to decrease your chance of having a child with sickle cell disease. I know it says it there; it's just not emphasized enough for it to be clear that this is what this is for" — Genetic counselor

Themes were articulated and defined by research team members based on collaborative code book. Representative quotes were selected with the goal of representing the key points encompassed by each theme, where appropriate, patient, and provider perspectives were included

tion, or after visits as a summary. The genetic counselors identified the stepwise description of IVF + PGT in the pamphlet as filling an unmet need: "I appreciate that [IVF + PGT] is the part that is discussed in detail because when a patient comes in to a genetic counseling visit, patients often have questions about the IVF process, but I'm not the IVF expert."

Theme 3. Appropriate for distribution online and in clinic: Patients recommended disseminating the pamphlet through a website, social media, online SCD support groups, or at local clinics. Providers envisioned distributing the pamphlet during clinic visits. Other suggestions included emailing the pamphlet to a clinic's patient list and circulating the material through SCD organizations.

Theme 4. Universally acceptable to participants and hopeful for patients: Provider and patient participants did not express concerns about pamphlet topic or content or raise concerns about reproductive coercion or eugenics. Patients reported a sense of "empowerment" from learning about their reproductive options. One patient appreciated new knowledge about reducing the risk of SCD in children saying, "I don't know anybody who would actively want their child to have sickle cell disease." When asked about their emotional reactions after reading the pamphlet, patients reflected on the possibility of biological parenthood with reduced risk of passing SCD to children and expressed optimism and hope.

Theme 5. Lacking information about uncertainties and risks, including potential cost: Participants suggested inclusion of more information about the benefits, uncertainties, and risks of IVF + PGT. All participants requested more information about the cost of IVF + PGT. Patients and providers identified that procedural and financial risks and benefits need to be individualized. However, they recommended briefly mentioning common risks to guide conversations with providers. Patients wanted information about the uncertainties of IVF + PGT, such as diagnostic accuracy and chances of successful pregnancy. Others wanted more information about the experience of the IVF + PGT process, especially related to ovarian stimulation and oocyte harvest.

Theme 6. Disagreement about gendered language and inclusivity: Providers criticized a lack of inclusive language related to gender identity, family structure, and religious affiliation. The concern centered on the repeated use of "mother" and "father," which excluded transgender people and those with nontraditional family structures. The revised patient interview guide included a question about the use of gendered language. Among the seven patients interviewed after the revision, two recommended using less gendered terms, while five recommended keeping "mother" and "father." Some of these patients ($n = 3$) believed gender neutral language like "male" and "female" dehumanized the pamphlet.

Finally, all participants supported the inclusion of a spiritual advisor in the section outlining members of the care team. However, one patient and one provider worried that referencing a spiritual advisor as a resource when considering issues of embryo selection and disposal might be exclusionary for non-religious readers.

Theme 7. Not sufficiently explicit that IVF + PGT can prevent SCD: Providers worried that the purpose of IVF + PGT was not explained explicitly enough to ensure patient understanding. Patients suggested defining IVF + PGT earlier in the pamphlet. Another patient revealed, through their follow-up questioning, a lack of understanding about the function of PGT in the context of IVF, suggesting the pamphlet insufficiently explained this topic.

Revision and re-scoring

We revised the pamphlet based on the health literacy scales and stakeholders' interviews. We explicitly stated the purpose of IVF + PGT in the first half of the revised pamphlet and outlined the procedure's risks and benefits, including possible high costs. We included captions with the graphics illustrating the steps of IVF + PGT. We noted the accuracy rate of PGT testing and the possibility that a patient might not become pregnant. Although opinions were divided on the issue of inclusive language, we edited the pamphlet to be more broadly inclusive of gender identity, family structure, and religiosity. Language was simplified to minimize reading level. After we completed all steps, over 40 stakeholders (Fig. 2) had contributed to the development of the revised pamphlet (Fig. 3), which has a Flesch-Kincaid reading grade level of 5.7 and met 97% of PEMAT (percent agreement = 94%) and 91% of Index (percent agreement = 82%) standards.

Discussion

A pamphlet about reproductive options for people with SCD or SCT, including information about IVF + PGT as a method to reduce the risk of SCD in offspring, was unanimously acceptable to a sample of adults with SCD and clinicians. Participants identified the tool as useful, clear, concise, and understandable. The revised pamphlet meets national guidelines for plain language; this complex topic can be introduced at a fifth-grade reading level and meet both AHRQ and CDC understandability standards.

We hypothesized that some patients and providers would express concern related to ethical issues like marital control, selective abortion, or eugenics [14, 33, 34]. However, no patient or provider referenced these issues or found the pamphlet inappropriate or offensive. The results of this study add to the growing body of literature confirming that people with SCD find information about reproductive options including IVF + PGT acceptable [4–6]. This non-directive resource created with patient input can provide clinicians with a template for shared decision-making and serve as an introduction to patients, a discussion aid, or a visit summary to improve patient understanding.

We previously identified that existing written patient education materials about IVF + PGT exceed the reading level of average Americans [12]. Here, we demonstrate that creating educational materials about reproductive options including IVF + PGT that are accessible to average Americans is possible. Wide availability of understandable materials may expand patient awareness of reproductive options and facilitate conversations between patients and their care teams [3–6]. By meeting health literacy standards, this pamphlet includes those with low educational attainment, a group with disproportionately low utilization of ART [35], in the conversation about IVF + PGT. We are aware of one other patient education tool describing reproductive options for people with SCD or SCT [6]. This material targets parents of children with SCD and is written at a higher reading level. Both materials contribute to the closing of this resource gap.

Patient and provider participants recommended including information about the cost of and the chance of becoming pregnant through IVF + PGT, though both of these figures are variable and uncertain. In the USA, direct costs to patients of ART vary significantly by insurance [36]. There is sparse data regarding success rates of IVF + PGT in SCD [37], and no study analyzes success rates in a US sample. Participants were clear that this information is essential to set accurate expectations related to IVF + PGT, so we added text to briefly introduce financial and other harms while directing patients to experts for more individualized risk assessments.

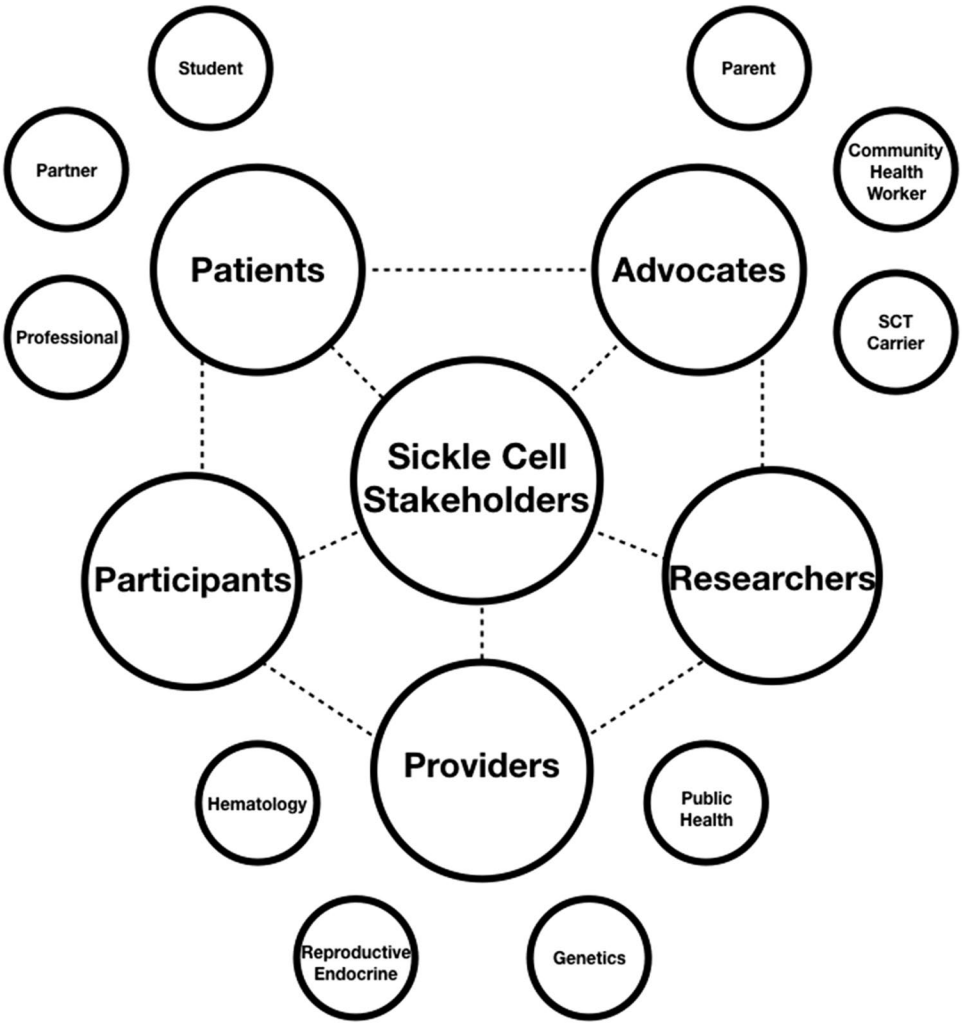


Fig. 2 More than 40 diverse SCD stakeholders involved in pamphlet development

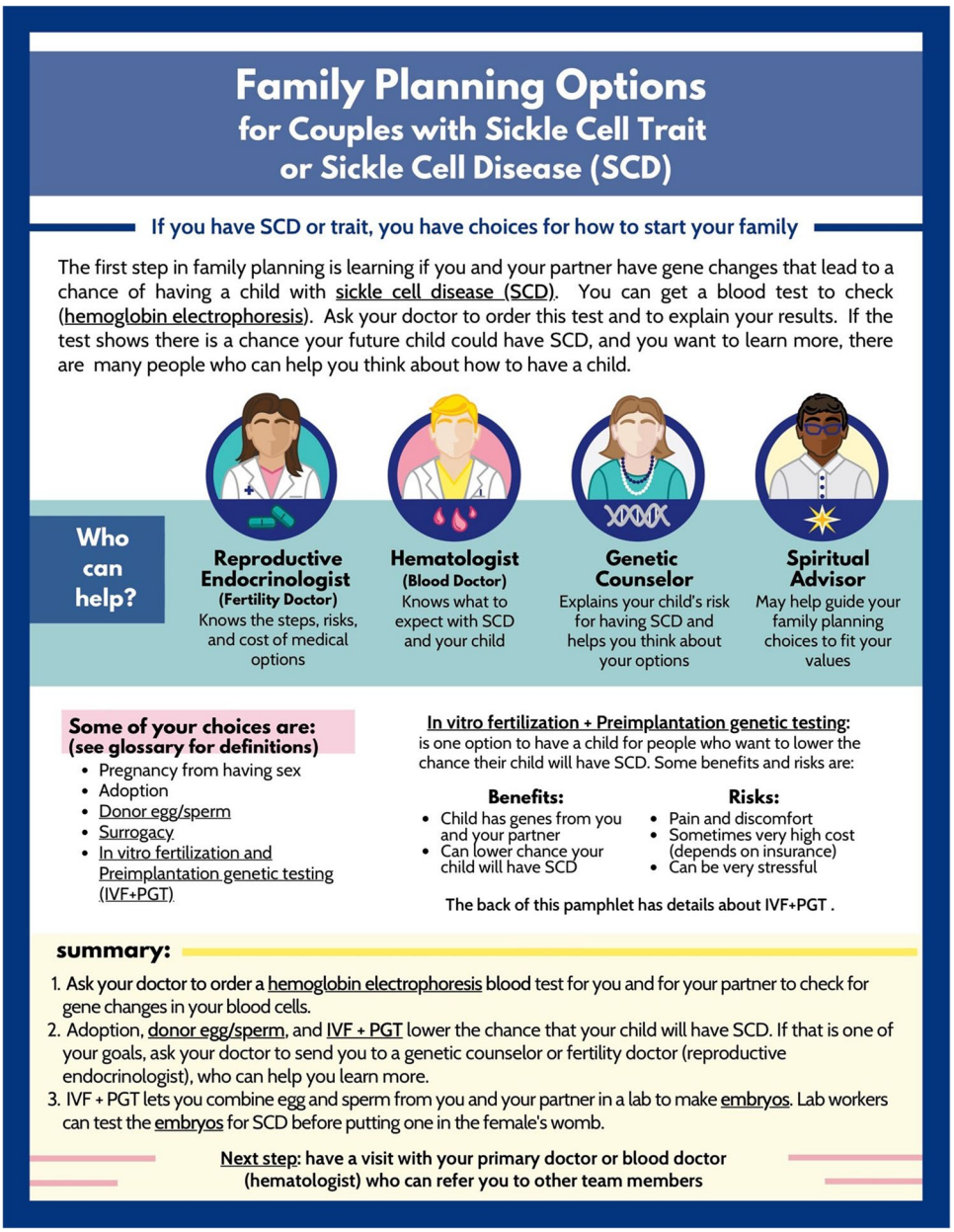
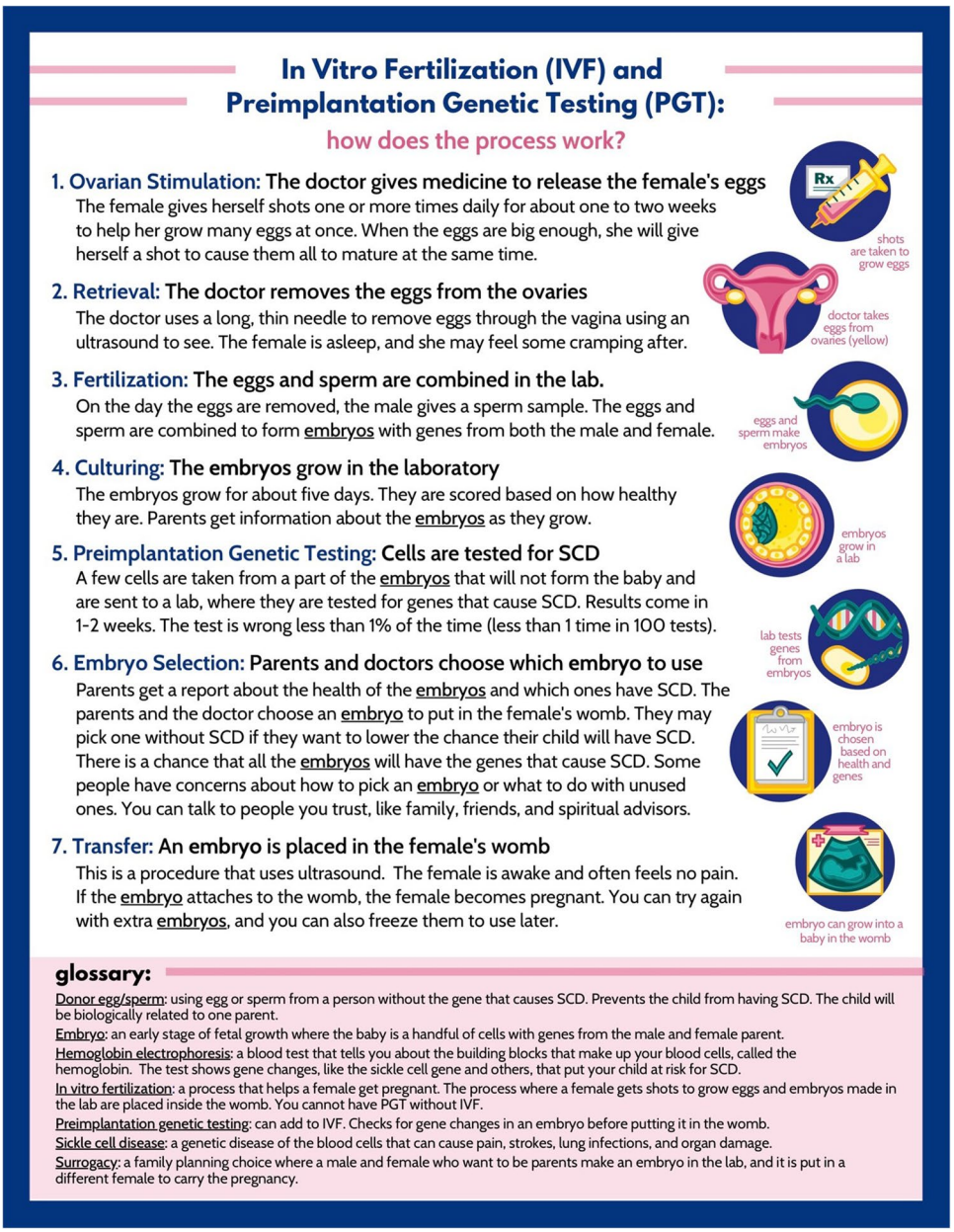


Fig. 3 Family planning options for people with SCD or SCT

Our participants identified two avenues for pamphlet distribution: (1) directly to patients through social media, websites, or SCD organizations and (2) through providers alongside clinic visits. Direct distribution to patients could expand awareness of reproductive options in SCD, while distribution through providers creates space for follow-up questions and personalization. We will partner with the Sickle Cell Reproductive Health Education Directive, a collaborative patient-provider organization [38], to disseminate the pamphlet via both suggested pathways.

Reliance on self-report to affirm pamphlet comprehension has methodological limitations. Participants may be uncomfortable revealing their lack of understanding. This discomfort may especially be attributable to power dynamics between patient and interviewer [39] or discrepancy between education level and reading ability. Both concerns might lead patient participants to overstate their understanding of the material. Interviewers attempted to overcome this barrier by using prompts that normalized and invited this disclosure. In this sample, most patient participants completed some college coursework; however, education level tends to overestimate reading ability [40] and adults with SCD often have insidious neurocognitive injury [41, 42]. Some participants' reading ability may have been meaningfully beneath their education level. Together, these possibilities highlight that education material about reproductive options related to SCD, even one written at a fifth grade reading level, should be used in coordination with appropriate and comprehensive

Fig. 3 (continued)



clinical care and counseling for individuals with SCD and their families [8].

In addition, participants did not review the revised pamphlet, but our partnership with the Sickle Cell Reproductive Health Education Directive [38] will allow stakeholder input prior to dissemination. Our patient participants were all people with SCD less than 30 years old. While all people with SCD or SCT of reproductive age are the targeted audience for this pamphlet, young people are most likely to be making initial reproductive decisions, and people with SCD are at the highest risk for passing SCD to children and might experience particularly poignant emotions in response to conversations about reproductive options. Future studies should include patients from other geographic regions, parents of children with SCD, people with SCT, and primary care providers.

This mixed-method study engaged patient and provider stakeholders to rigorously develop and evaluate a pamphlet about reproductive options for individuals with SCD or SCT written at the fifth-grade reading level. Despite the potentially sensitive nature of the topic, the material was acceptable and useful to participants. This pamphlet may serve as a resource to share information and enable proactive, informed reproductive decisions.

Abbreviations AHRQ: Agency for Healthcare Research and Quality; ART: Assisted reproductive technology; CDC: Centers for Disease Control and Prevention; Index: CDC Clear Communication Index;

IVF: In vitro fertilization; PEMAT: Patient Education Material Assessment Tool; PGT: Preimplantation genetic testing; SCD: Sickle cell disease

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Author contribution MLE, SL, MSC, and LHP designed the research study and provided input for pamphlet content. MLE and IVL developed and revised the pamphlet. RJS, SMS, JAR, and JAS scored the pamphlet using health literacy scales. MLE and RJS conducted participant interviews. MLE, JAR, JAS, SMS, and RJS completed qualitative analysis of interviews. MLE, JWM, ERM, and LHP guided final data analysis and presentation. MLE and LHP wrote the manuscript, with significant editorial revision by JWM and ERM. All authors provided final input into the manuscript.

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Data availability Not applicable.

Code availability Not applicable.

Declarations

Ethics approval The study was approved by the Johns Hopkins School of Medicine Institutional Review Board.

Consent to participate Patients provided verbal consent to participate using an IRB-approved consent script.

Consent for publication Not applicable.

Conflict of interest MLE, IVL, JAR, JAS, SMS, JWM, MSC, and LHP have nothing to disclose. RJS discloses publication of an opinion article on privately owned fertility clinics in NBC News. ERM reports personal fees from CVS Caremark, Novartis, Novo Nordisk, and Forma Therapeutics and grants and personal fees from Global Blood Therapeutics, all outside of the submitted work. SL reports personal fees from Bluebird Bio and Novo Nordisk and other financial disclosures from Global Blood Therapeutics, Imara, Shire, Novartis, Pfizer, and Teva, all of which are outside the submitted work.

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