ORIGINAL REPORT

Patient Perspectives, Unmet Needs and Dilemmas in Reproductive Decision-making for Genodermatoses: A Qualitative Interview Study

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Impact on quality of life due to inherited skin diseases (also known as genodermatoses) may lead to reproductive dilemmas for affected couples or individuals considering parenthood. Currently, little is known about reproductive decision-making (RDM) for those affected by or at-risk of genodermatoses. Couples/individuals' perspectives with genodermatoses were qualitatively explored by focusing on (*i*) the impact of these diseases on the desire to have children, (*ii*) the knowledge of different reproductive options and personal considerations and, (*iii*) experiences with reproductive counselling. Semi-structured interviews were conducted with participants aged ≥16 years, diagnosed with a genodermatosis, and an active, (un)fulfilled or future desire to have children and analysed using a reflexive thematic content approach. Thirty participants were interviewed until saturation. Two main themes and 9 subthemes were identified. Participants preferred wanting to avoid passing on their genodermatosis to offspring, thereby complicating RDM. This preference was influenced by negative experiences with the disease, resulting in fear and uncertainty about severe manifestations in offspring. Positives and shortcomings in clinical practice were expressed, particularly the lack of reproductive counselling as a standard part of care. This study highlights the substantial impact of genodermatoses in RDM and the importance of routine reproductive counselling for those affected by or at-risk of genodermatoses.

Key words: skin diseases, genetic; qualitative research; reproductive behavior; genetic counseling; prenatal diagnosis; preimplantation diagnosis.

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SIGNIFICANCE

This interview study explored the unspoken reproductive dilemmas for those affected by or at-risk of inherited skin diseases. Having an inherited skin disease can influence and complicate reproductive decisions. Many couples/individuals wanted to avoid transmission to offspring and some even decided to refrain from having children. Affected couples/individuals were often not fully informed by healthcare professionals about the available reproductive options. Current clinical practice had positives and shortcomings, particularly the lack of offering reproductive counselling. Our findings can help healthcare professionals, including dermatologists and clinical geneticists, to provide better information and support for affected couples/individuals facing these decisions.

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Having children is one of the most important, demanding and personal life decisions. "Reproductive decision-making" (RDM) refers to any decision about fertility or reproduction, such as conceiving children, assisted reproduction or voluntary childlessness (1–3). Patients with genetic disorders and their partners are often found to experience difficulties regarding their RDM, generally due to the risk of affected offspring (4).

Several reproductive options are available to couples/individuals with a severe genetic disorder aspiring to have children. Options that result in offspring genetically related to both parents, include natural conception without genetic testing, prenatal diagnostics (PND) or preimplantation genetic testing (PGT). During pregnancy, PND enables the detection of a familial genetic variant from amniotic fluid or chorion villi, thereby offering the possibility of termination of

pregnancy (TOP) of an affected fetus. PGT, on the other hand, enables the selective transfer of an unaffected embryo into the uterus via *in vitro* fertilization, preventing the birth of offspring affected with a familial pathogenic variant. Regulations differ per country as to how and for which indications PGT is performed. In the Netherlands, all new indications are assessed by a national assessment committee. Other reproductive options include adoption, foster parenting, the use of donor gametes or refraining from having offspring.

Inherited skin diseases, also known as genodermatoses, often require symptomatic treatment, care and/or monitoring, and impact patients' biological, psychological and social quality of life (QoL) (5–8). The risk of transmitting genodermatoses to future offspring depends on the mode of inheritance. Predicting the exact phenotypic manifestation is challenging due to inter- and intrafamilial variability (9).

Given the life-long impact on QoL, it is plausible to assume that patients with genodermatoses may face challenges when considering parenthood. Currently, studies on RDM in the field of genodermatology are scarce (10, 11) and do not focus on exploring the perspectives of affected couples/individuals (12). This sensitive subject may represent a blind spot in dermatological care, as both patients and dermatologists may be hesitant to discuss it.

This qualitative study aimed to gain an in-depth understanding of the RDM-process among couples/individuals with different types of genodermatoses. We focused on the impact of genodermatoses on the desire to have children, the knowledge and considerations of different reproductive options, and the patient's experiences with reproductive counselling.

MATERIALS AND METHODS

Study design

A descriptive study was carried out with a phenomenological position. The study adhered to the Declaration of Helsinki, Standards for Reporting Qualitative Research (SRQR) (Table SI), and Consolidated Criteria for Reporting Qualitative Research (COREQ) (Table SII) (13, 14). Ethical approval was obtained (METC 2023–0193).

Participant recruitment

To represent genodermatoses with primary cutaneous manifestations and broad clinical spectrum ranging from mild to lethal, we included epidermal differentiation disorders (EDDs) (15–17), epidermolysis bullosa (EB) (18), ectodermal dysplasia (ED) (19) and dermato-oncogenic syndromes (DOS) (20, 21). Purposive sampling was used to attempt diversity in participant demographics in terms of age, education level, genodermatosis and its impact. Participants were recruited face-to-face and by mail through Dutch patient associations and specialized medical centres (Maastricht UMC+, Leiden UMC and UMC Groningen). Inclusion criteria were couples or individuals, either carriers of or affected by a genodermatosis with a molecular diagnosis or fulfilment of diagnostic criteria, and having an active, (un)fulfilled or future desire to have children. Participants had to be proficient in Dutch or English and aged≥16 years, as this is the Dutch legal age for scientific consent (22). Written informed consent was obtained from each participant.

Data collection

Data were collected from January to November 2024. Semi-structured interviews were conducted by two qualitative researchers, (F.v.V.) and (O.B.), either face-to-face (n=2) or via video call (n=28). They had no personal or direct professional relationship with the interviewees and were trained in interviewing and the characteristics of genodermatoses. The interview guide and its design are demonstrated in Table SIII. Prior to the interview, participants received an informational leaflet on reproductive options (Appendix S1), to ensure a basic understanding, and completed a digital questionnaire on personal characteristics (Appendix S2). Interviews had a median duration of 50.5 min (range 26–82), were audio-recorded and transcribed verbatim. An iterative approach was applied to achieve data saturation, which was suggested after 28 interviews. This indicated that no longer new information, themes or codes emerged, as existing data patterns became consistent and repeated. Two additional interviews were conducted for confirmation.

Data analysis and reflexivity

Interview data were analysed using an inductive and reflexive thematic content approach. The process involved initial coding, clustering codes into themes and performing comparative analysis of the codes and (sub)categories (more details, Appendix S3). Clustering into representable themes was done together with the research team, conforming to the principle of investigator triangulation. ATLAS.ti version 25.0 (Scientific Software Development GmbH) was used for qualitative data analysis. Summaries of the transcripts were sent to the participants to ensure correct interpretation of the interviews, in accordance with the principle of member checking. Quantitative data from the questionnaires were imported to IBM SPSS Statistics 27 (IBM Corp, Armonk, NY, USA), the participants demographics were described using descriptive statistics.

RESULTS

Participant characteristics

We interviewed 30 participants, *n*=11 with (non)syndromic or palmoplantar EDDs, i.e., ichthyoses, pachyonychia congenita (PC) and Hailey-Hailey disease, *n*=6 with epidermolysis bullosa, *n*=5 with ectodermal dysplasia and *n*=8 with basal cell nevus syndrome (BCNS) or germline *CDKN2A*-pathogenic variant (PV) (**Table I**). Five interviews were conducted with both the affected individual and their partner present, the remaining with only the affected individual. Participants' median age was 33.0 years [range 17–63], and 80.0% (*n*=24/30) were female. Five (16.7%) participants had an active desire to have children, 17 (56.7%) a past desire (fulfilled or unfulfilled) and 8 (26.7%) a future desire. Three (10.0%) participants had experience with PGT and three with PND (10.0%). Two major and 9 subthemes were identified and linked illustrative quotes are presented in Table II and **Table III**.

Prevention of a genodermatosis in offspring

Personal and family impact on QoL. Most participants reported that the genodermatosis substantially affected their reproductive decisions, with a pronounced preference for avoiding transmission to future children. Consequently, many participants opted for genetic testing (e.g., PGT or PND) of their offspring during or prior to pregnancy, rather than conceiving naturally. Some even refrained from having children altogether, often due to the risk of affected offspring and were unaware of their reproductive options.

Their decision-making was influenced by physical, psychological and social challenges associated with genodermatoses. These challenges included limitations in daily functioning, the current lack of effective/curative treatments, mental health issues and social exclusion. These perspectives were not only based on personal experiences, but also on those of affected family members. Moreover, some participants expressed a desire to avoid passing on their reproductive dilemmas. Some participants (i.e., *KRT16*-pEDD-PC and *CDKN2A*-PV) opted for natural conception as they were able to maintain a sufficient QoL and were satisfied with medical care and follow-up.

Unpredictability regarding more severe manifestations. Anxiety, guilt and uncertainty were mentioned as emotions regarding the phenotypic variability among genodermatoses, and the fear of transmitting a more severe disease-variant to offspring. These emotions were triggered by, e.g., seeing severely affected peers within patient associations.

Hereditary awareness and intergenerational influence. Participants' relationships with their parents also influenced decision-making. Most participants' parents were unaware of the inheritance risk and availability of reproductive options at the time. In contrast, when parents had been aware of this inheritance risk, some participants expressed feelings of anger or frustration that no steps had been taken to prevent transmission. This, in turn, often strengthened their own motivation to avoid passing genodermatosis on to their children.

Some participants were raised with the belief that they should not have offspring because of their genodermatosis, and therefore deliberately chose to refrain from having children. Some were unaware of the inheritance risk, due to carrier status or mosaicism. When this risk became known after their first affected child, they wanted to either actively prevent transmission in the future (e.g., with PGT) or refrain from having other children.

Couple dynamics and prospective role as parents. RDM was typically a couples-process, though females often had a leading role, as they carried pregnancies and underwent reproductive treatments. Single participants felt that partner selection was complicated by the importance of finding a person open to options such as PGT or PND. Some of the affected individuals expressed concerns that their partner would need to take on the primary caregiving role and found it undesirable.

Key motivation for preventing transmission of their disease was the desire to become a parent rather than a caregiver, i.e., not wanting and being able to provide full-time skincare. Nevertheless, many participants acknowledged that affected parents can care best for affected offspring as experts by experience.

Difficulties achieving pregnancy. Besides genetic transmission concerns, other barriers to pregnancy were reported such as dyspareunia, high risk of miscarriage (e.g., affected boys in X-linked incontinentia pigmenti), or ovarian fibromas in BCNS. The issue of medication teratogenicity, such as acitretin used in the EDD group, was also raised. Some females struggled with the idea of having a treatment break from oral retinoids, as it may cause a flare-up, and eventually did not pursue or achieve pregnancy.

Knowledge on and experience with reproductive options and counselling

Lack of knowledge and decisional conflict. More than half of the participants were aware of their reproductive options, largely through self-sought information. Most highly educated participants reported that they were able to find reliable information themselves, lower educated participants did not mention this. Almost half of the participants were only partially or never informed on their options such as PGT by their healthcare professional (HCP). More than half of the participants who received counselling from a clinical geneticist

Table I. Patient demographics

	Epidermal differentiation disorders (*N*=11)	Epidermolysis bullosa (*N*=6)	Ectodermal dysplasias (*N*=5)	Dermato-oncogenic syndromes (*N*=8)
Age, years	40 (20–63)	31 (17–63)	33 (24–63)	32 (26–49)
Male, n/N	1/11	4/6	0/5	1/8
Nationality, n/N				
Belgian	2/11	0/6	0/5	0/8
Dutch	9/11	6/6	5/5	8/8
Ethnicity, n/N				
White	11/11	5/6	5/5	8/8
Asian	0/11	1/6	0/5	0/8
Civil status, n/N				
Married/registered partnership	8/11	1/6	2/5	4/8
Co-habiting	3/11	0/6	2/5	2/8
Single	0/11	4/6	1/5	2/8
Not registered	0/11	1/6	0/5	0/8
Completed education level, n/N				
Primary education	2/11	2/6	0/5	0/8
Secondary vocational education	2/11	2/6	1/5	1/8
Bachelor's degree university/ applied sciences	4/11	2/6	2/5	4/8
Master's degree university/ applied sciences	2/11	0/6	2/5	3/8
PhD or postdoctoral researcher	1/11	0/6	0/5	0/8
Religion, n/N				
Roman catholic	2/11	0/6	1/5	1/8
Baptist	1/11	0/6	0/5	0/8
Protestant	0/11	0/6	0/5	1/8
Buddhism	0/11	0/6	1/5	0/8
None	8/11	6/6	3/5	6/8
Skin disease, n/N				
	ATP2C1-nEDD (1/11)	EB simplex dominant (3/6); *KRT5* (2/3), *KRT14* (1/3)	ADULT syndrome (1/5); *TP63*	BCNS (5/8); *PTCH1* (4/5), low-grade mosaic *PTCH1* (1/5)
	KRT10-nEDD-epidermolytic (2/11)	Dystrophic EB dominant (1/6); *COL7A1*	AEC; Hay-Wells syndrome (2/5); *TP63*	Hereditary melanoma due to *CDKN2A*-PV (3/8); confirmed (2/3), at-risk* (1/3)
	KRT16-pEDD-PC (2/11)	Dystrophic EB recessive (1/6); *COL7A1*	HED X-linked (1/5); *EDA*	
	NIPAL4-nEDD (1/11)	Junctional EB recessive (1/6); *COL17A1*	X-linked IP (1/5); *IKBKG*	
	SPINK5-sEDD (1/11)			
	STS-sEDD (1/11)			
	TGM1-nEDD (3/11)			
Start of symptoms, n/N				
From birth/preschool (0–4 y)	9/11	6/6	4/5	2/8
Primary school period (4–12 y)	0/11	0/6	0/5	0/8
Teenage period (12–18 y)	1/11	0/6	1/5	3/8
Adulthood (>18 y)	0/11	0/6	0/5	3/8
No symptoms carrier status	1/11	0/6	0/5	0/8
Dermatologist visit (at least once in last 12 months), n/N	4/11	2/6	0/5	8/8
Medication skin complaints, n/N	8/11	4/6	1/5	2/8
Symptoms, n/N				
Itch	5/11	4/6	0/5	0/8
Desquamation	6/11	1/6	1/5	0/8
Hyperkeratosis	2/11	0/6	0/5	0/8
Dry skin	7/11	2/6	3/5	0/8
Pain or burning sensation	4/11	4/6	0/5	0/8
Cosmetic disturbance	5/11	3/6	3/5	3/8
Blisters, pustules, or wounds	3/11	6/6	3/5	1/8
Alopecia	1/11	0/6	2/5	0/8
Teeth or nail complaints	0/11	0/6	2/5	0/8
Inability to sweat	0/11	0/6	1/5	0/8
History of skin cancer	1/11	0/6	0/5	6/8
Impact score**	8.0 (5.0–9.0)	7.5 (4.3–10.0)	2.0 (1.5–5.0)	4.5 (1.3–6.0)
Desire to have children, n/N				
Active, unfulfilled	2/11	1/6	1/5	1/8
Past, fulfilled	6/11	0/6	2/5	5/8
Past, unfulfilled	1/11	2/6	1/5	0/8
Future	2/11	3/6	1/5	2/8
Pregnancy method, n/N	Subgroup n=6	Subgroup n=0	Subgroup n=2	Subgroup n=5
PGT	1/6	0/0	1/2	1/5
PND	2/6	0/0	0/2	1/5
Natural	3/6	0/0	1/2	4/5
Children count, n/N				
0	5/11	6/6	3/5	3/8
1	2/11	0/6	1/5	1/8
2	3/11	0/6	1/5	3/8
3	1/11	0/6	0/5	1/8

(*Continued*)

Table I. Patient demographics (Continued)

	Epidermal differentiation disorders (*N*=11)	Epidermolysis bullosa (*N*=6)	Ectodermal dysplasias (*N*=5)	Dermato-oncogenic syndromes (*N*=8)
Affected children***, n/N	3/11	0/0	1/3	1/10
Reproductive counselling, n/N	7/11	4/6	3/5	5/8
Level of knowledge on reproductive options****, n/N				
Not informed	2/11	0/6	0/5	0/8
Partly informed	3/11	5/6	2/5	1/8
Fully informed	6/11	1/6	3/5	7/8

Variables were presented as counts (n/N) and medians (interquartile ranges).
*1 participant had no molecular diagnosis of *CDKN2A* but was at high risk due to positive criteria stated in Leachman SA, Carucci J, Kohlmann W, Banks KC, Asgari MM, Bergman W, et al. Selection criteria for genetic assessment of patients with familial melanoma. J Am Acad Dermatol 2009; 61: 677.e671-614. (e.g., positive family history, history of 4 histopathological melanomas under the age of 40).
**The impact score indicated the impact of the genodermatosis on participants' lives using a scale from 1 to 10, where 1 represented the least impact and 10 represented the greatest.
***These are children who have undergone genetic testing and have been found to be affected with genodermatoses or to be carriers.
****This represents the level of knowledge that participants had about reproductive options prior to the interview. 'Partly informed' means that they were aware of most, but not all options, such as PGT or PND.
ADULT:acro-dermato-ungual-lacrimal-tooth (syndrome); AEC:ankyloblepharon-ectodermal defects-cleft lip/palate (syndrome); BCNS:basal cell nevus syndrome; EB:Epidermolysis Bullosa; HED:Hypohidrotic, or anhidrotic, ectodermal dysplasia; IP:incontinentia pigmenti; nEDD:non-syndromic epidermal differentiation disorder(16); pEDD:palmoplantar epidermal differentiation disorder(17); PGT:preimplantation genetic testing; PND:prenatal diagnostics; PV:pathogenic variant; sEDD:syndromic epidermal differentiation disorder(15).

perceived it as a positive experience. Participants usually initiated reproductive counselling by proactively requesting referral to a clinical geneticist. Hardly, a HCP, such as dermatologist or general practitioner, discussed reproduction or initiated a referral. Most participants would prefer their HCPs to play an active role and provide decision support. However, some participants believed that they should initiate such conversations themselves, as it is a sensitive topic.

Few participants mentioned that their past reproductive decisions might have been different if they had been properly informed on the options. On the other hand, having options led to moral dilemmas for most participants, particularly regarding the extent to which one can consciously pass on an inherited disease when it might be preventable.

PGT: for some the only option? Because of the risk of having affected biological offspring, for most

Table II. Illustrative quotes from main theme 1

Theme 1: Prevention of a genodermatosis in offspring	
Subthemes	Illustrative quotes (patients/couples)
Personal and family impact on QoL	
Preference for avoiding transmission to future children	"When I started thinking about having children, I discovered that there was a 50 % chance of passing on my disease. Because of this chance, I never allowed myself to consider having children ever again." P15, AEC-syndrome
Physical, psychological, and social challenges	"I don't want a child to experience my syndrome. You can see how bad it is from the patient association group, and I have experienced it first-hand through bullying… and all those hospital visits. If I pass it on to a child, it will feel like it is my fault." P20, BCNS
Prevent dilemmas associated with RDM for future offspring	"My partner and I discussed what would happen if we decided to prevent the genodermatosis now. The hope would be that, in a later generation, this dilemma could be prevented." P23, incontinentia pigmenti
No impact on the desire to have children	"I think if it had been like 30 years ago, "you have a melanoma and it spreads quickly and we can't do anything about it", then I think I would have had a different view on my decision-making, then I would have gone for a PGT-trajectory. But now I am really satisfied with medical treatment and follow-up." P10, *CDKN2A*-PV
Unpredictability regarding more severe manifestations	
Emotions regarding phenotypic variability	"What makes it so difficult for us is that my syndrome is very broad. One patient has a lot of symptoms, and like me ... I have almost nothing. So, you cannot guess what you will be doing to your child." P21, BCNS
Hereditary awareness and intergenerational influence	
Decision-making of participants" own parents	"I have been angry at times with my parents for choosing to have a child anyway, even though they knew this could happen. I don't want my children to have my disease, so if I ever have children, I'll make sure they don't have my disease, otherwise I choose not having children at all." P14, *ATP2C1*-nEDD
Risks associated with inheritance	"For now, I think it's enough to deal with the fact that one of our children has BCNS. We really wanted a third child, but the risk of having another child with BCNS is too great... I'm much more aware of things that can go wrong." P9, BCNS (low-grade mosaic)
Couple dynamics and prospective role as parents	
Couple dynamics	"A child needs stability on the part of the parent, well I couldn't see myself guaranteeing that... At times being very badly wounded…, then everything would be on the shoulders of my partner, which I didn't want... all those aspects played a role in deciding not to have children." P35, JEB
"A parent, not a caregiver"	"If the baby is affected, my concerns are doubled: the baby's welfare, and the welfare of the baby's skin, as well as my own skin." P01, *KRT10*-nEDD
Difficulties achieving pregnancy	
Barriers to pregnancy	"Acitretin is great for my skin, almost addictive... If I had to stop taking acitretin to have children, it would have been a difficult decision for me, and not an obvious one." P06, *KRT10*-nEDD

AEC:ankyloblepharon-ectodermal defects-cleft lip/palate (syndrome); BCNS:basal cell nevus syndrome; JEB:Junctional Epidermolysis Bullosa; nEDD:non-syndromic epidermal differentiation disorder; PV:pathogenic variant; RDM:reproductive decision-making.

Table III. Illustrative quotes from main theme 2

Theme 2: Knowledge on and experience with reproductive options and counselling	
Subthemes	Illustrative quotes (patients/couples)
Lack of knowledge and decisional conflict	
Self-sought information	"My boyfriend said, "Oh well, there's no center of expertise for BCNS". But I read about it somewhere, so I thought it was strange. If you don't search thoroughly, you might not find the right information. I find this worrying." P09, BCNS (low-grade mosaic)
Not fully informed on reproductive options by HCPs	"We did not receive any information on the different reproductive options. We proactively had to ask the dermatologist to explain us the inheritance risk of ichthyosis and questions regarding desire to have children." P05, *SPINK5*-sEDD
Moral dilemmas when having options	"Thirty years ago, there were no options like PGT, so it's different now… I think it's a selfish choice: we want a child and then take the risk that he/she may become ill. Would you take that risk with your child? I think every parent would say "no"." P18, BCNS
PGT: for some the only option?	
Acceptable reproductive option for genodermatoses	"The only way for us to have almost a 100 % certainty of having a healthy child is through PGT. For me, it feels like it will either be a child conceived through PGT or no child at all." P20, BCNS
Physical and psychological burden	"The trajectory was very tough. It had quite an impact on my physical and mental health… But it was worth it." P01, *KRT10*-nEDD-epidermolytic
PND: emotional dilemma when considering termination of pregnancy (TOP)	
TOP traumatic dilemma	"The idea of prenatal diagnostics seems very difficult to me. If you can feel a baby kicking inside you, it feels cruel to end its life, even if you know, it might be better." P19, ADULT-syndrome
"Last" reproductive options: refrain from having offspring, adoption, foster care or donor gametes	
Preference for genetically related offspring	"I will only consider the options — donor gametes, adoption or foster care —when the other options don't work out for whatever reason... This is mainly because I would love to have a child of my own." P12, EBS

ADULT:acro-dermato-ungual-lacrimal-tooth (syndrome); BCNS:basal cell nevus syndrome; EBS:Epidermolysis Bullosa Simplex; nEDD:nonsyndromic epidermal differentiation disorder; sEDD:syndromic epidermal differentiation disorder.

participants PGT was perceived as an acceptable reproductive option. Despite some ethical concerns (i.e., disposal of affected embryos and Christian religious beliefs), most participants were willing to undergo a PGT trajectory. Some even felt it was their only option; if PGT was unsuccessful, they would refrain from having children.

There was limited awareness among participants that PGT was an option for their genodermatosis. Perceived disadvantages of PGT were the timeframe of the treatment, relatively low success rates, and the unromantic and clinical nature of conceiving. Participants who underwent a PGT trajectory experienced a physical and psychological burden due to hormonal stimulation, and felt somewhat mentally unprepared for unsuccessful cycles.

PND: emotional dilemma when considering termination of pregnancy (TOP). While some participants considered PND as an acceptable reproductive option for genodermatoses, most found the thought of TOP in the event of an affected fetus emotionally/morally challenging. These feelings were intensified by the mother's experience of feeling a baby growing inside her, and the belief that their own lives – despite their genodermatosis – were worth living. Consequently, most participants expressed greater ethical concerns about PND than PGT, and therefore preferred PGT.

"Last" reproductive options: refrain from having offspring, adoption, foster care or donor gametes. Most participants mentioned to refrain from having children if PGT and PND were unsuccessful, or due to moral objections. Adoption, foster parenting or donor gametes were a "last option" to have children. Main concerns regarding these options were not being genetically related to their offspring, high costs, strict rules of such procedures, the temporary nature of childcare, and the potential attachment issues between the child and the adoptive or foster parent.

DISCUSSION

This study revealed that having different genodermatoses can strongly impact couples/individuals' RDM, resulting for some in an unfulfilled desire to have children. Decision-making was influenced by personal/moral considerations, such as parental responsibility and child welfare. The inclination to prevent inheritance and navigate associated moral conflicts is frequently observed in genetic diseases, e.g., hereditary breast and ovarian cancer (23), Huntington's disease (24) and X-linked hypohydrotic ectodermal dysplasia (25). Similar to oncological hereditary syndromes (26), shortcomings in current clinical practice were expressed, particularly the lack of offering reproductive counselling as part of participants' medical care. Almost half of the participants were inadequately informed about all their reproductive options and some felt unable to make a well-informed choice. Those who received counselling from a clinical geneticist perceived it as a positive experience.

In our study, no differences in perceptions were found between participants with generalised genodermatoses (e.g., JEB and *SPINK5*-sEDD), and those with more localised forms (e.g. EBS and *KRT16*-pEDD-PC), as both groups wanted to actively prevent transmission of their genodermatosis to offspring. However, different perceptions of severity were observed within the same disease, as illustrated by two participants with *KRT16*-pEDD-PC. One reported that the disease did not influence her reproductive decisions, while for the

other PGT was the only way to have offspring. These findings suggest that for pEDD phenotypical variability is a contributing factor, and that the lived experience is highly subjective and often more nuanced than its clinical definition. This lived experience can inform how severe a genodermatosis is perceived, and therefore affect reproductive decisions (27).

When comparing participants with BCNS and those with *CDKN2A*-PV, we found that those with *CDKN2A*-PV were less affected by their genodermatosis in their RDM. This finding is consistent with results of a cross-sectional study, which reported that reproductive decisions were largely unaffected in *CDKN2A*-PV confirmed carriers and those at-risk (28). Patients with BCNS develop multiple basal cell carcinomas (BCCs) early in life, ≈90% are affected by age 35 (29). The recurrent nature of BCCs requires repeated (surgical) treatment, which can significantly impact patients' QoL (30). Furthermore, they may present with other clinical features, such as odontogenic keratocysts and risk of medulloblastoma (31, 32). Patients with *CDKN2A*-PV have an increased lifetime risk (up to 70%) of developing on average 2–3 melanoma, which typically develop around 40 years, and pancreatic cancer (up to 20%) (33–36). The burden of medical treatment is often limited to few diagnostic (re)excisions of suspicious nevi. Given the risk of melanoma metastasis and mortality, it is reasonable to expect that parents would desire to avoid transmitting their *CDKN2A* variant to offspring. By comparison, in carriers of *BRCA1/2* pathogenic variants, who face an increased lifetime risk of hereditary breast and ovarian cancer with onset between 30–50 years, PGT is a widely utilized option (37). Again, patients' lived experience is important: patients who only had one early-stage melanoma may not be constantly aware of their disease. This aligns with the participants' reasoning that they were satisfied with medical care and surveillance. Therefore, for patients with *CDKN2A*-PV, the risk of mortality may not be a profound factor when considering parenthood but rather their lived experience.

We found that the awareness of having multiple reproductive options may result in decisional conflict. This phenomenon was also observed in an interview study of *BRCA*-positive women's RDM (38). Another study explored the concept of choice overload, and how advancements in genetic and embryo testing can lead to an overwhelming number of reproductive options, thereby complicating RDM (39). To address this, HCPs can offer reproductive counselling by a trained clinical geneticist to streamline the available options. This can reduce cognitive strain associated with choice overload, supporting informed decision-making. Additionally, a so-called decision aid tool can simplify reproductive counselling information by providing tailored information and clarifying patients' values (40). In this study, for participants whose reproductive options were not (fully) discussed by HCPs, it is unclear whether this was due to a lack of available reproductive options for certain genodermatoses at the time, reluctance to discuss, or a lack of awareness among HCPs regarding these options. Currently, studies on the extent to which HCPs are aware of these options, and their reasoning for discussing them with patients affected by genodermatoses, are scarce.

Strengths and limitations

Our heterogenous study population, representing several genodermatoses and the iterative and reflexive approach allowed in-depth understanding of the impact of having a genodermatosis on RDM and considerations of different options. Consequently, this study offered a patient-centred context that was lacking in the limited literature available. Our methodological approach, and diverse expertise of our research team, enabled a comprehensive investigation with findings derived from interview data. Purposive sampling may have led to selection bias, by selecting those with positive or negative experiences and the preference to talk about it. We tried to minimize recall bias by screening patients on their recall prior to the interview. Our population was ethnically homogeneous and lacked diversity in terms of religion (e.g., no Islamic, Jewish or Hindu belief).

There is a need for professional decision support, such as routine referrals to trained clinical geneticists for reproductive counselling. Accessible information about the available reproductive options should be provided to couples/individuals with genodermatoses in an easy-to-understand digital format. Collaboration with patient associations could also help by providing informational tools, representing patient interests and facilitating contact between patients. Importantly, HCPs such as dermatologists, clinical geneticists and general practitioners, need to be aware of the lived experiences and reproductive dilemmas that affected couples/individuals may face, and refer them to specialized centres for appropriate care and well-informed support. Furthermore, decision aid tools and guidelines on this subject would be helpful.

Conclusion

In-depth exploration of couples/individuals' perspectives revealed that having a genodermatosis can substantially impact RDM. There was a preference to avoid passing on a genodermatosis to children, which was influenced by negative disease experiences, resulting in fear and uncertainty about severe manifestations in offspring. Reproductive counselling

should be included in healthcare guidelines of genodermatoses to guarantee well-informed decision-making.

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Data availability statement: The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

Ethics committee: This study has been reviewed and approved by the ethical review board of the Maastricht University Medical Centre+ (MUMC+), METC 2023-0193. Informed consent was obtained from all the participants to publish the findings from the interviews. ClinicalTrials.gov ID: NCT06330350.

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