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ARTICLE

Understanding sickle cell carrier status identified through newborn screening: a qualitative study

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The expansion of newborn screening (NBS) is increasing the generation of incidental results, notably carrier results. Although carrier status is generally understood to be clinically benign, concerns persist that parents may misunderstand its meaning, with deleterious effects on children and their families. Expansion of the NBS panel in Ontario, Canada in 2006 to include sickle cell disorders drew attention to the policy challenge of incidental carrier results. We conducted a study of consumer and provider attitudes to inform policy on disclosure. In this paper, we report the results of (i) qualitative interviews with health-care providers, advocates and parents of carrier infants and (ii) focus groups with new parents and individuals active with the sickle cell community. Lay and provider participants generally believed that carrier results were clinically insignificant. However, some uncertainty persisted among lay consumers in the form of conjecture or doubt. In addition, consumers and advocates who were most informed about the disease articulated insistent yet dissonant claims of clinical significance. Meanwhile, providers referenced research knowledge to offer an equivocal assessment of the possibility and significance of clinically symptomatic carrier status. We conclude that many interpretations of carrier status are in circulation, failing to fit neatly into the categories of 'clinically significant' or 'benign.' This creates challenges for communicating clearly with parents – challenges exacerbated by inconsistent messages from screening programs regarding the significance of sickle cell carrier status. Disclosure policy related to incidentally generated infant carrier results needs to account for these complex realities.
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INTRODUCTION

Newborn screening (NBS) programs assess infants who seem to be well to identify those few at an increased risk of having a disorder. Traditionally designed to reduce mortality and morbidity in affected children, screening programs may also generate incidental information, such as carrier status (ie, unaffected heterozygotes). NBS for sickle cell disorders (SCDs) provides a classic example. Screening for SCD is justified by evidence that early treatment with prophylactic penicillin leads to reduced mortality in affected children.[1] However, screening technologies that identify affected infants also identify virtually all SCD carriers. Routine disclosure of infant carrier results is typically defended as a right of parents rather than for clinical reasons, as SCD carrier status is thought to be clinically benign under normal physiological conditions. Yet little research has explored how lay and provider stakeholders actually interpret the SCD carrier state.

In a comprehensive review of the management of SCD, the US National Heart, Lung and Blood Institute argued that 'Individuals who have sickle cell trait (SCT) do not have vaso-occlusive symptoms under physiologic conditions and have a normal life expectancy. The inheritance of SCT should have no impact on career choices or lifestyle.'[2] However, the review acknowledges some risks: hyposthenuria, hematuria, urinary tract infection in women, earlier onset of end-stage renal disease in those with autosomal dominant polycystic kidney disease, splenic infarction and possible complications of strenuous exercise.[2] In addition, a wider range of more serious risks is identified in other peer-reviewed literature, including isosthenuria, glaucoma or recurrent hyphema, pregnancy-associated bacteriuria, renal medullary carcinoma and mild sickling.[3,4]

Newborn screening programs also identify some clinical risks in informing parents and providers about SCD carrier results. The leaflet produced as a resource for the general UK public emphasizes that the baby 'will always be a healthy carrier,' but acknowledges that carriers 'can experience problems in rare situations where their bodies might not get enough oxygen,' and recommends that parents alert health-care providers when operations requiring the administration of general anesthetics are considered.[5] Similarly, the educational resource for US physicians notes that 'Newborn (SCD carrier) infants are usually normal. Prognosis is good, with a normal life expectancy.' However, it also notes that individuals 'may have hematuria. Splenic infarction and an increased risk of sudden death associated with severe hypoxia, extreme physical exertion and dehydration have been reported.'[6]

Despite these acknowledged risks, arguments regarding the disclosure of carrier results incidentally generated by NBS for SCD concern

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the right of parents to all the health information that providers discover pertaining to their children, and the potential utility of carrier information for reproductive decision making.[7] A clinical rationale for disclosure is rarely advanced, or discussed cf.[8] Furthermore, despite the prevalence of NBS-generated carrier results (UK figures indicate approximately 6500 SCD carriers identified for 250 SCD cases[9]), the bulk of available evidence regarding the effects of identifying carriers through NBS focuses on the case of cystic fibrosis (CF).[10] This evidence suggests that a minority of parents and providers might misunderstand the meaning of carrier status, increasing parental stress and anxiety and the risk of the 'vulnerable child' syndrome.[7,11] Yet given divergent historical, cultural and clinical contexts, and the stage at which carrier status is confirmed during the screening process (ie, CF carriers are identified on confirmatory testing when using an IRT/DNA method, but SCD carriers are identified with the initial screening test), the relevance of research on CF for SCD is unclear. Therefore, we conducted a study in Ontario, Canada in 2006–2007. In this setting, SCD was a new addition to the NBS panel and policy makers were uncertain regarding the merits of routine disclosure of incidental SCD carrier results.

METHODS

As part of a mixed methods study including a self-completion survey of health-care providers,[12] we conducted qualitative research involving (i) open-ended semi-structured interviews with 42 health-care providers; 8 community-based SCD advocates and 6 parents of 5 infants with sickle cell carrier status; and (ii) 12 focus groups with 66 new parents and SCD lay consumers (see Table 1). Provider respondents comprised key informants designated by professional associations or known to be interested in NBS, individuals referred through snowball sampling and survey respondents who were willing to participate in an interview. Community advocates comprised individuals active with local and provincial SCD organizations. We recruited parents of carrier infants through a hospital-based NBS for SCD program; at the time of the study, the provincial infant screening program did not disclose SCD carrier results. In addition, to gain insight into a wider set of lay attitudes among those more or less affected by SCD, and to take advantage of participant interactions that can enhance candor and illuminate the common language of a group,[13] we conducted nine focus groups with new parents (two with Afro-Caribbean-Canadian respondents) and three focus groups with lay people engaged with SCD agencies or services and with personal experiences with SCD (ie, affected in selves or in a close family member), who were recruited through community agencies, primary care organizations and targeted advertising within the Afro-Caribbean community. The research received ethics approval from the Hamilton Health Sciences Research Ethics Board and the relevant Hospital Board.

The interviews and focus groups involved respondents in the discussion of their experience with NBS or SCD, and considered three main questions: (i) how NBS-generated SCD carrier results should be managed (eg, disclosed, destroyed); (ii) whether the generation of SCD carrier results should alter the provision of NBS (eg, consent for NBS or carrier result disclosure); and (iii) if disclosed or not, how this should be carried out. During discussion of these three issues with both lay and provider respondents, unexpected interpretations of the meaning and clinical significance of SCD carrier status emerged. Thus, we probed interpretations of SCD carrier status in the discussion of the three core issues in subsequent interviews or focus groups.

All data were transcribed, entered into our database and coded in a collective and iterative manner by two to three members of the research team. We used qualitative data analysis software (NVivo, Version 7, QSR International Pty. Ltd., Doncaster, VIC, Australia) to assist with data organization. For this paper, we analyzed coded sections of each transcript in which the meaning or significance of SCD carrier status was discussed, rather than taken as given. Using writing as an analytic device,[14] we categorized coded sections to identify thematically coherent interpretations of SCD carrier status (eg, uncertainty, dissonance). Our analysis adopted a modified grounded theory approach. We integrated the iterative and constant comparative analytic method,[15] with

Table 1 Participants

			Additional information			
Method	*Type of participant*	*N*	*Focus group participants no. (range)*	*F*	*M*	*Cited as*
Focus groups						
	All	12	66 (3–8)	59	7	Parent FG
	New parents – multi-ethnic[a]	7	41 (3–8)	38	3	
	New parents – Afro-Caribbean[b]	2	10 (5)	7	3	
	SCD lay consumers[c]	3	15 (4–7)	14	1	SCD FG
Interviews	*Health care providers*					
	All	42	F	M		Provider
	Pediatricians	5	3	2		
	Midwives	6	6	0		
	Nurses (maternal/newborn)	7	7	0		
	Nurses (hematological)	2	7	0		
	Obstetricians	3	0	3		
	Hematologists	3	0	3		
	Genetics professionals	9	4	5		
	Family physicians	7	3	4		
	Community advocates: SCD	8	7	1		Advocate
	Parents of SCD-carrier infants					
	All[d]	6	Mothers	Fathers		SCD-infant
			5	1		

[a]New parents (infants 6–18 months) recruited through diverse community and primary care organizations in Hamilton, Toronto, and Peterborough, Ontario.
[b]New parents (infants 6–18 months) recruited in neighborhoods and through community associations and newspapers serving the Afro-Caribbean community in Toronto, Ontario.
[c]Parents of, and persons with, SCD recruited through patient advocacy and parent support groups serving the SCD community in Toronto and Ottawa, Ontario.
[d]New parents (infants 6 months to 2 years) recruited through a Toronto hospital with an in-house NBS for SCD screening program that reported carriers.

a reflexive approach to data interpretation that drew on preexisting theories (eg, labeling effects, stigma, biosocial disease experience) to guide us in understanding the data.[16]

RESULTS

Lay and provider respondents approached the question of what SCD carrier results might mean with different degrees of previous knowledge and awareness. Some providers and lay respondents had established conceptions of SCD carrier status. Others had limited previous awareness. Members of the study team informed those with less knowledge that SCD carriers are understood to be clinically unaffected under normal physiological conditions – abbreviated to 'clinically benign.' By contrast, members of the study team solicited input on the interpretation of, and experience of living with, SCD carrier status from the more informed respondents, in addition to providing information regarding its clinical significance.

In this context, lay and provider participants generally suggested that SCD carrier status was clinically insignificant. However, other interpretations of infant carrier status vied with this 'benign' understanding, and strongly influenced the discussion of the need to disclose incidental carrier information. Among lay respondents, both uncertainty regarding clinical significance and dissonant claims of clinical significance circulated. Meanwhile, health-care providers referenced research knowledge to offer varied assessments of the possibility and significance of clinically symptomatic SCD carrier status.

Uncertainty

Influenced by their previous knowledge and experiences with SCD, some lay consumers expressed uncertainty with regard to the significance of SCD carrier status. Specifically, in focus groups with new parents who had limited knowledge of SCD, uncertainty regarding SCD carrier status sometimes arose as conjecture. Furthermore, among parents of infant carriers who had substantial previous knowledge, uncertainty sometimes arose as doubt.

We held seven focus groups with new parents who lacked previous knowledge or experience of SCD. These respondents were informed regarding carrier status and did not question this information. In one focus group, however, participants argued for disclosure because of conjecture regarding what future research might yield regarding the meaning of trait:

> I think I would want to know for all of the reasons already stated (eg, reproductive risk) but also that there's always new research being done and there's always new information being found out about cause and effect of things and what you can do or what you can't do. (Mother of infant, FG8)

Such conjecture also arose in one focus group with new parents from the Afro-Caribbean community, in which, despite the higher baseline knowledge of the disease, some participants identified themselves as uninformed. Also arguing that carrier results should be disclosed, this participant suggested that:

> For reproduction later on might be a good idea and for their own treatment probably if there's something they don't have a risk of something if they're driving or flying or certain jobs affect them or being around chemicals 'cause I don't know how it affects them genetically but if that was a risk it would be good to be informed. (Mother of infant, FG4)

Such conjecture was not apparent among respondents with established knowledge about SCD. Nonetheless, uncertainty did arise among these respondents in the form of doubt. All of the six parents of five infants identified as carriers through an in-hospital NBS for SCD program conveyed excellent previous knowledge of SCD and carrier status. They were aware that one of the parents was a carrier and that the infant might prove to be a carrier. Although concerns with regard to the significance of trait status were limited, some parents of carrier infants found it hard to be reassured regarding its benign nature.

Among one set of parents who were quite clear that trait status was inconsequential, expectations of a mild clinical effect created by a physician could not be fully dismissed. The mother was not a carrier and had investigated various sources to learn of possible health effects. She reported that a specialist physician had indicated that 'when they get a cold that they… the cold may hit them a little harder than the average person and it […] will last longer. So somebody who they would cut it in three days he would go for 7 days.' [SCD-infant2] The interviewer asked the father, a carrier, whether he found that 'to be true in your experience …?' But his experience could neither deny nor confirm the possibility:

> Because uhm… I, I have sinusitis and my sinusitis is always… it always compounds any cold, any cold that I have. So … (pause) … you know I, I can't, I can't say single out the trait as being the reason for, you know, my having the worst cold episodes. I don't know I, I think he's saying that the trait exacerbates, you know, colds. Whether or no that's true I don't know (SCD-infant2).

Another parent who learned through NBS that her infant daughter was a carrier was a nurse whose healthy husband was a carrier. Although well positioned to understand that the carrier state was not clinically significant, she was troubled by what it might mean.

> …You would expect her to not to have any, any changes in her life and she'll live a normal life. But… the trait it's still part of my daughter's life. It's still … part of who she is and it's not as simple as black and white. […] I still cried, and I still say like, 'Why her?' Like I look at her and I'm just like, 'I know you're okay, but are you really okay?' Like, I have those doubts in my mind (SCD-infant3).

Dissonant claims of clinical significance

Uncertainty with regard to the clinical significance of SCD carrier status existed alongside unambiguous claims that carrier status was clinically meaningful. Furthermore, such claims clearly departed from the scientific literature in placing carrier status on the disease spectrum, and were only articulated by those with self-declared expertise with SCD: from participants in the three SCD-affected focus groups and among SCD community advocates.

In the three focus groups involving people engaged with SCD agencies or services and with personal experiences with SCD, the balance between scientific and dissonant interpretations of carrier status varied. In one group, only one participant seemed to believe that carrier status was clinically meaningful, stating that 'You know but ah… I don't, but I think some of the problems that I have are related to the trait.' (Woman carrier, SCD FG3). In another focus group, opinion on the clinical significance of carrier was mixed, but several participants clearly assumed that trait was clinically

important. In one discussion regarding a participant's daughter, several respondents considered the clinical consequences of the daughter's carrier status:

> You know lately she's been saying her leg always hurts like anything she does, 'My leg hurts.' So I'm thinking, 'Is she just saying that or does it hurt because of the trait?' So I have to take her in for that but other than that she seems okay (Mother of carrier child, herself affected with SCD, SCD FG11).

Another participant asked about the pain, and the mother described it again and wondered aloud about its source, 'Because I know there's different degrees of trait.' (mother of carrier child, herself affected with SCD, SCD FG11).

In still another of these focus groups, the clear consensus was that SCD carrier status involved unusual clinical risks. Respondents made claims about their own ill health as carriers and discussed the symptoms experienced by their carrier children. One mother told the group that her carrier son had been misdiagnosed with the disease which,

> …lots of times it's the same as sickle cell disease, so he suffered a lot like he didn't go into full-blown crisis but he had like he had the jaundice he had pain in his legs and those sort of things you know we'd be at the hospital fairly regularly.' (Mother of 2 carrier children, SCD FG6)

Of our eight advocate respondents, four (including two trained as allied health professionals) insisted on a dissonant interpretation of clinical risk. For example, one advocate mother of a child with SCD struggled to make sense of her own experience as a carrier. She described herself as anemic and fatigued, and recommended that individuals know their own carrier status to better understand their experiences and 'live healthy.' She argued further that parents should know the child's carrier status to help them understand personal limitations that might otherwise be attributed to laziness:

> That's information that is important for a child to have, parents to have, because again, when this child is going to school and they're being pushed to exert themselves to a certain point and they can no longer do that it can actually affect the child's self esteem, their sense of ability to do things because, 'How is it that everybody else can do it and I can't?' […] 'How come I get so tired so easy? Am I lazy?' Well it's, it's not a matter of you're lazy, you know? You're slightly different than somebody and that's okay. Is it that this child needs to be on iron pills? Does this child need to be supplemented? So it's not just about knowing that while the treatment can be found for a sickler but it's about understanding what a trait is […] So the child doesn't think 'Well I can't… Why am I different?' (Advocate6)

Participants who had personal experiences with SCD commonly identified concerns regarding the inadequacies of care for SCD sufferers. Frustration toward providers who doubted the existence of symptoms in a person who had the disease was amplified for those who believed their loved one to be a symptomatic carrier. In one focus group exchange, a mother who was a carrier described the treatment her carrier son received in hospital, and others in the group empathetically wondered how a child with a 'strong' or 'dominant' (ie, symptomatic) carrier status would be treated if s/he sought medical attention.

> Both my children have the trait. My oldest son appears to have the disease. When he hurts, he hurts everywhere. His eyes are jaundiced, his legs hurt, everything hurts… But when he comes into the hospital, when I've brought him into emergency and I've said my son has the trait they ask him, 'What is your pain level?' right? But unless I insist on certain things being done it doesn't happen, the minute you say they have the trait, right? (Mother of 2 carrier children, SCD FG6)

Health-care providers: equivocation

Some health-care providers shared lay uncertainty with regard to the meaning of SCD carrier status, conjecturing that new research might demonstrate its clinical significance. As one pediatrician noted, 'But who knows what, what if, if there's going to be new findings in ten years that say … that carrier status is associated with some disease we don't know about yet, right?' (Provider23) However, most providers who entertained the possibility that SCD carrier status was not strictly benign did so in relation to old research knowledge, although they differed in their assessment of the credibility and clinical relevance of this knowledge. One pediatrician, who often informed parents that their children were carriers, interpreted the typically cited circumstances under which trait symptoms could seem to be 'made up':

> *Pediatrician*: I go over it very clearly: 'This is trait, this is completely different. This is… your child is completely normal.' […] you know, often I'll make something up like, 'If you were a deep sea diver you might have […] if your child decides to climb Mt. Everest it might be a problem, but apart from that'… (Provider46)

However, other providers gave more credence to the existence of these types of risks, although they doubted their clinical significance:

> *Hematologist*: Sickle cell carriers … tend to be normal […] there's really no clinical implications. I guess there's some clinical implications in that some people have said, you know, if they go try and climb Mt. Everest or they go deep sea diving there's a slight increased mortality rate if you go to boot camp in the United States… but other than that it's really not… of any clinical… clinical importance … If you're a carrier it doesn't hurt you… (Provider35)

Finally, some providers were more convinced of both the existence and the clinical significance of these risks.

> *Pediatrician:* In identifying carriers you have the possibility to have intervention…
> *Interviewer:* Interventions for the carriers? I don't understand. Medical interventions?
> *Pediatrician:* I mean sickle cell carrier state is not, is not entirely asymptomatic for everyone… There have been reports raising concern regarding sudden death for sickle cell carriers which is not, directly linked to it although it's been associated with sickle cell carrier states. (Provider10)

DISCUSSION

As the scope of NBS expands, so too does the likelihood of incidental results. NBS for SCD is an exemplary case, as screening identifies both affected infants and virtually all SCD carriers. However, little research considers how SCD carrier information is understood, and that which does focuses solely on the experience of new parents. In this study, we report an analysis of the interpretations both of parents of infants identified as carriers (a relatively small sample, as Ontario does not currently disclose NBS-generated SCD carrier results), and of the wider community of health-care providers, new parents and SCD-involved parents and advocates – all of whom have a role in making sense of the carrier state. Although most of our respondents either assumed or insisted that SCD carrier status was clinically insignificant, our research unearthed a complex set of additional interpretations that escape ready categorization as either benign or clinically significant and that informed attitudes regarding the disclosure of incidentally generated SCD carrier results.

The meaning of SCD carrier status included uncertainty, expressed as doubt by some parents of carrier infants – as evidenced by the mother who could not let go of the possibility that her SCD carrier infant might face some risk. This case conforms to what is known regarding the undue concern some parents experience on receiving carrier or false-positive results from NBS programs,[11,17] leading to excess health service utilization[18] and the 'vulnerable child' phenomenon.[19] Uncertainty with regard to SCD carrier status was also aired as conjecture among those with little knowledge: as an expectation that carrier results might prove clinically helpful and that clinicians might now, or in the future, be able to manage individual patients better because of it. Some providers shared this optimistic conjecture, which provided perverse support for result disclosure.

In addition, consumers and advocates closely involved with the SCD community sometimes advanced forceful yet dissonant claims of clinical significance, suggesting that the carrier state produces a mild form of the disease. A plausible interpretation of these claims is that individuals who do, in fact, have one of the SCDs (eg, SC disease) have been misdiagnosed as carriers. Yet, Fullwiley,[20] who has identified the resilience of such claims in West Africa, cautions us to recognize the biosocial nature of the illness experience and the ways in which difficult life experiences can be somaticized. Indeed, those who insisted that carrier status is symptomatic had powerful reasons for this belief. Parents and advocates for people with SCD experienced distress trying to ensure care for loved ones. The fatigue and pain they experienced – that some attributed to carrier status – surely exist. These claims were asserted alongside powerfully expressed concerns that SCD is itself a poorly understood, even neglected, disease. Such concerns can be substantiated,[21] and the related claims are unlikely to be readily dismissed.

Providers interpreted the meaning and significance of SCD carrier status in relation to research knowledge. Many providers were unaware of this research and assumed that the carrier state is clinically benign. Others who were aware were equivocal about its relevance. Providers had to judge both the validity of this evidence – what effects to believe – and determine the clinical significance of this evidence – what effects really matter. Their varied responses reflected these dual judgments: what was to one provider an exaggerated potential and to another an irrelevant outcome, was for still another a meaningful risk effect – one that made it necessary for consumers to know, and for providers to discuss, an individual's SCD carrier status.

The quality of research knowledge and available guidance for consumers and providers is unlikely to resolve provider equivocation with regard to the clinical effects of SCD carrier status and may exacerbate lay uncertainty or misunderstanding. The UK leaflet for the general public stresses that 'The most important example' of the rare clinical problems that might arise for carriers 'is having a general anesthetic.'[5] By contrast, the US guidance argues that 'Surgery is not likely to be complicated by the fact that an individual has SCT. Individuals with SCT are not at increased risk for an adverse outcome from anesthesia, and they are not limited in their choice of anesthetic agents.'[2]

The history of population screening for SCD in the United States and the racialized experience of SCD bear on the interpretation of carrier status. Population screening for SCD in the 1970s involved widespread testing for carrier status without adequate program delivery, measures to protect confidentiality or education and awareness campaigns. As a result, carrier status was widely confused with the disease itself resulting in stigmatization and discrimination of many African Americans.[22] The response to this episode was to insist that carrier status was clinically benign. Indeed, any other characterization would allow unjust discriminatory measures to continue. Thus, a paradox of justice faces efforts to resolve lingering confusion with regard to the significance of 'trait.' To acknowledge the risks arising from carrier status – to grant them the imprimatur of clinical significance – may result in the damaging stigmatization of countless individuals. But to deny this significance may exacerbate the feelings of injustice and inattention that exist among members of a community that is disproportionately affected by this racialized disease.

To date, discussions regarding the management of SCD carrier results generated incidentally through NBS attend only partially to the complex meaning of 'trait.' Advocates of disclosure suggest that SCD carrier status is without clinical significance, but messages to parents say something different. In future, policy on the generation or disclosure of incidental carrier results needs to account for the effect of telling parents that their infant is a carrier and that 'Yes, there are some uncommon and severe, and some more common but relatively harmless, risks.' Policy also needs to account for the scientific uncertainty of such risks: the variable ways in which such risks will be understood as valid or valued as significant, and the inconsistency of scientific consensus and guidance for parents. Furthermore, policy should attend to the prevalence of dissonant interpretations of carrier status among informed community members: that carrier status implicates not only the uncommon or mild risks acknowledged by science but also the more protean risks of fatigue, pain and anemia that place carrier status firmly on the SCD disease spectrum. Finally, policy must consider the paradox of justice that frames messages regarding 'trait.'

These findings have important implications for clinicians and policy makers involved with NBS for SCD. Clinicians should consider the potential for variable interpretations of NBS carrier results in their discussions with families, and the effect of result disclosure on familial coping and downstream health-care utilization. In turn, policy makers in jurisdictions in which SCD carrier results are routinely disclosed, might reassess the feasibility of a goal of 'normalization.'[23] Furthermore, in jurisdictions in which deliberations regarding SCD carrier disclosure are ongoing, the challenge of comprehension, and of conveying a clear and consistent message, should encourage caution.

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