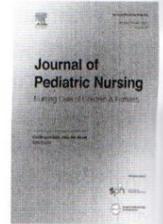




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Exploration of barriers and facilitators to the implementation of the DREPADO randomized controlled trial: A qualitative study

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ABSTRACT

Purpose: DREPADO is a randomized controlled trial (RCT) assessing the impact of a pediatric-adult transition program, on the health status of adolescents with sickle cell disease. Using a biopsychosocial approach with three main facets (educational, psychological and social interactions), it constitutes a complex transition program, which is quite difficult to implement. To facilitate the implementation of this complex program, the aim of this ancillary study is to explore barriers and facilitators at the early stages of this implementation.

Methods: A qualitative study with semi-structured interviews was conducted, according to COREQ quality criteria, in patients with sickle cell disease who had already experienced the transition to adult care before DREPADO, and healthcare professionals working on the DREPADO RCT.

Results: Semi-structured interviews were conducted with patients ($n = 12$) and healthcare professionals ($n = 12$) from November 2019 to May 2020. The main barriers identified by patients were time and implication required by this transition program. Healthcare professionals involved in the coordinating center mentioned changes in their working habits and also elements about the RCT regulatory procedures. Main facilitators reported by both patients and healthcare professionals were the positive perception of the transition program design, and especially the home setting for therapeutic education sessions.

Conclusion: This study led to the identification of main barriers and facilitators to the implementation of both the DREPADO intervention and RCT. These propositions could also be used to promote other complex public health interventions or/and other randomized controlled trials.

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Introduction

Sickle cell disease (SCD) is the most diagnosed genetic disease worldwide (Wastnedge et al., 2008). SCD care management starts at a very young age (Yawn, 2015) and includes regular medical follow-up, preventive measures and symptomatic treatment of clinical symptoms. Today, most children with SCD will experience a transfer to adult care. It is a period of changes in care management for these patients switching

from pediatric to adult care. This transfer takes place during adolescence, a time when major difficulties in treatment adherence are seen in patients with chronic conditions such as SCD, leading to increased morbidity and mortality (De Montalembert et al., 2014; Quinn et al., 2010). The transfer should be preceded by a preparatory transitional phase –called in this study “transition program”. To address the challenge of this transfer and its preparatory transitional phase and so improve SCD care management, the clinical trial “DREPADO - Impact of a pediatric-adult care transition program on the health status of adolescents with sickle cell disease” is being deployed. It is a French multicenter randomized controlled trial (RCT) (Hoegy, Bleyzac, et al., 2020). Its objective is to improve the health of adolescents with SCD, their quality of life and access to care (Fig. 1). It compares standard of care vs. a transition program based on a biopsychosocial approach and conducted

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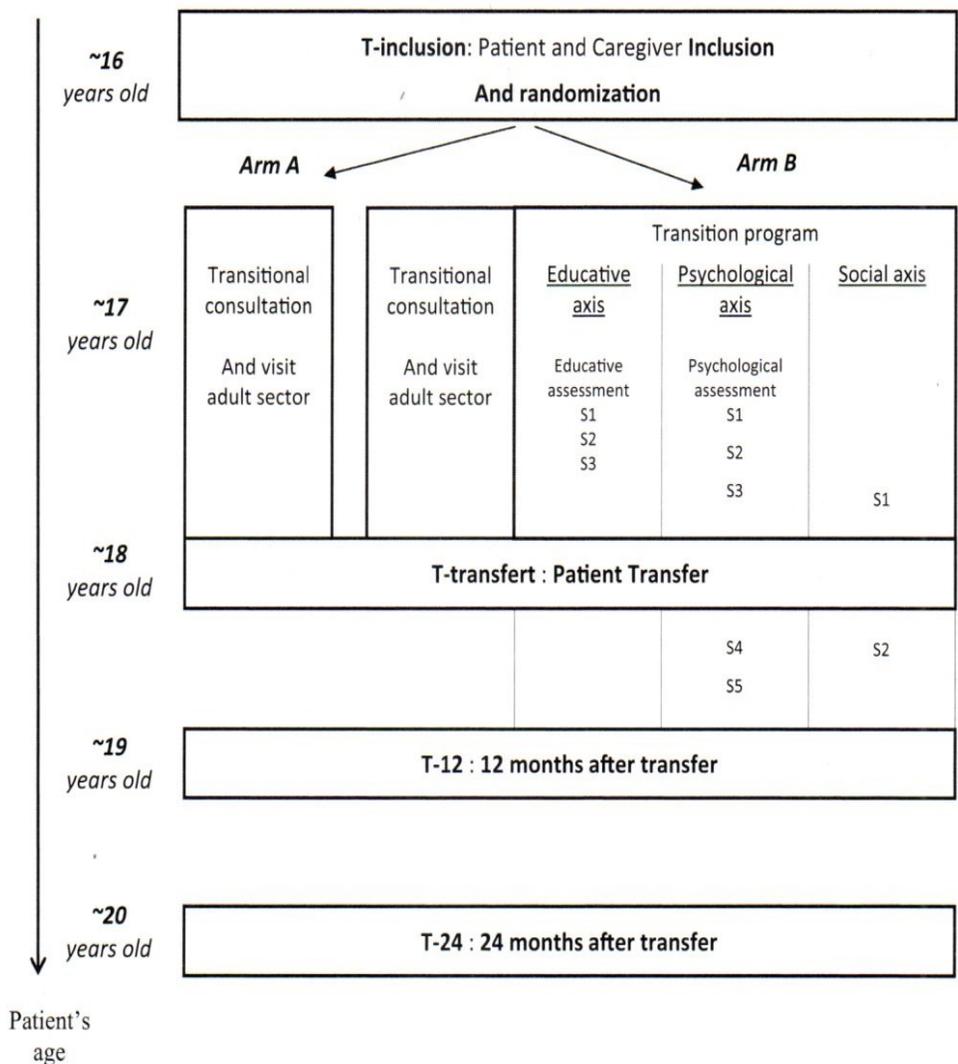


Fig. 1. DREPADO clinical trial design.

according to three main facets: educational sessions in a home setting (led by a healthcare professional proficient in therapeutic patient education), psychological support (conducted by a nurse or psychologist trained in therapeutic hypnosis) and social interactions (led by a patient/HCP duo experienced in therapeutic patient education).

The DREPADO transition program is complex; it involves different contributors –one for each facet- and is set in different locations (home and hospital). Integrating this program into a clinical research framework adds another layer of complexity, because in addition to implementing the program itself there is the added issue of conducting a randomized controlled trial. The proper implementation of this program will represent a major contribution to its future success (Pfadenhauer et al., 2017) it requires defining the different parameters, ones that are intrinsic to the program itself but also external ones (settings, context). To facilitate this DREPADO transition program implementation, it is necessary to identify elements that could impair or, on the other hand, improve its execution (Damschroder et al., 2009). This present study is an ancillary study as part of the evaluation of the RCT implementation process; its objective was to identify barriers and facilitators to the DREPADO transition program implementation within the coordinating center, including both person- and organization-related factors, to optimize its implementation and deployment.

Material and methods

Study design

This prospective qualitative study with semi-structured interviews was conducted among patients who already experienced the transfer

to adult care (not included in the DREPADO RCT), and among healthcare professionals (HCPs) working in the coordinating center. This study evaluates the implementation of the DREPADO transition program.

Participants

Inclusion and exclusion criteria were described in Table 1. Patients were recruited prospectively, during a hospital visit (inpatient or outpatient) and HCPs were contacted by email. For both groups, no prior sample size was defined. Participants from each group were included until data saturation, as evaluated by the analysts (PB & DH). Patients were enrolled using consecutive recruitment, from the internal medicine departments (inpatient and outpatient units). The HCPs selected were all professionals working on the DREPADO RCT within the coordinating center.

According to French laws, the DREPADO study protocol (including exploration of barriers and facilitators to its implementation) was approved by the French Ethics committee on November 6, 2019. All participants received oral and written information on the study, a signed consent form was collected before study inclusion.

Data collection

Prior to interviews, two study guides were developed (PB & DH) to perform these interviews with patients and HCPs (available in Tables 2 and 3). These study guides focus on the different components of the intervention (different types of sessions/actors) and the implementation context (time period, clinical research setting). The guide for HCPs also explored the research protocol framework,

Table 1
Inclusion and exclusion criteria.

	Patients	HPs
Inclusion criteria	<ul style="list-style-type: none"> - Adult patient with sickle-cell disease followed at the coordinating center - Age between 18 and 28 - Oral comprehension compatible with the semi-structured interview - Individual consent form signed before the interview 	<ul style="list-style-type: none"> - Healthcare professional working on the DREPADO clinical trial in the coordinating center - Oral comprehension compatible with the semi-structured interview - Individual consent form signed before the interview
Exclusion criteria	<ul style="list-style-type: none"> - Cognitive or psychiatric disorders interfering with the adequate conduct of the interview 	

implementation strategy and factors already used in the program or ones that could be used to improve it. These study guides were validated by a test interview. The semi-structured interviews were conducted by a researcher (PB - male pharmacy resident) previously trained in the qualitative research methodology.

All interviews were done in a one-on-one setting (interviewer/interviewee), audio-recorded and conducted at the hospital. For patients, the transition program was presented at the beginning of each interview. Data collected were anonymized and used solely in the framework of the qualitative study conducted according to the COREQ quality criteria (Tong et al., 2007). Data supporting these findings are available upon request.

Data analysis

Interviews were manually transcribed without rephrasing. The study material was analyzed separately by 2 researchers (PB & DH) using the 3-step inductive approach described by Thomas (Thomas, 2006): a) reading the raw script of the interviews; b) organizing data by categories according to the topics covered; c) reducing the material by selecting the most meaningful *verbatim* transcriptions, and organizing the different categories. After these individual steps, both

Table 2
Patient interview guide.

Key topics	Questions
Pediatric-adult care transition	- How did you experience your transition between pediatric and adult care settings?
Improvement opportunities	- Which aspects could improve this transition period between pediatric and adult care settings?
Presentation of the DREPADO clinical trial design to the patient	
Perception of the program	- What do you think of the DREPADO clinical trial? (How do you think this program could be useful or not?)
Utility of the program	- In your case, how could the transition program have been improved/ Could it have helped the transition between pediatric and adult care settings? - What did you like and dislike in the program?
Adherence to the program	- In your opinion, what seemed easy or difficult to follow in the DREPADO clinical trial? (Does it seem difficult to participate in all trial sessions?)
Improvement opportunities	- Do you see other aspects that could be improved in the actual pediatric-adult care transition?
Synthesis	- Do you have anything to add? - Rewording (summary of the interview)

Table 3
Healthcare Professional interview guide.

Key topics	Questions
Perception of the program	
Source of the program	- What do you think about the legitimacy of the [coordinating research center] to sponsor a clinical trial like DREPADO? (Comparison with an industrial sponsor, academic sponsor from another center, what do you think about the credibility of the coordinating team?)
Rupture with the usual care	- What is most different between the DREPADO clinical trial and the usual way of treating these patients?
Barriers and facilitators to the implementation	- According to you, what could facilitate or be an obstacle to the implementation and conduct of the clinical trial in your center?
Improvement opportunities	- How could we improve the DREPADO clinical trial? - Do you have anything to add?
Synthesis	- Rewording (summary of the interview)
Coordination/Communication between stakeholders in the center	
Communication among the Sickle-cell disease reference center	- What do you think about the communication between the different stakeholders in your [research center]? (How is it organized between the different actors (e.g. physicians, nurses, clinical research associates)?) - How do you think this communication could be improved? What is already working well?
Relationship with DREPADO stakeholders	- Which stakeholder of the DREPADO clinical trial are you already working with in routine care? - Which stakeholder have you never worked with? How do you see this new collaboration? - Do you have anything to add?
Synthesis	- Rewording (summary of the interview)
Rewording Regulatory	- To which regulator were you exposed during your work on the DREPADO clinical trial? - For each regulator: how could you qualify their role in the DREPADO clinical trial (facilitator or barrier) and why? - Do you have anything to add?
Synthesis	- Rewording (summary of the interview)

analysts compared their results and resolved their differences via consensus.

Results

Participants

Patients

12 interviews were conducted between November 2019 and January 2020 (6 men, 6 women, mean age 22.6 years). Mean duration of interviews was 11 min (R: 5–33). A patient refused to be included in the study by opting out of the audio recording.

Healthcare professionals

12 interviews were conducted between November 2019 and May 2020 (11 women, 1 man). Among HCPs there were 6 physicians, 2 pharmacists, 2 registered nurses, 1 clinical research associate (CRA), and 1 clinical study coordinator, involved in the trial design but not involved in the implementation of the intervention. Eight of these HCPs were attached to the MCGRE (*Maladie Chronique du Globule Rouge et de l'Érythropoïèse - chronic disease of the red blood cells and erythropoiesis*) reference center. Mean interview duration was 17 min (R: 8–32).

Table 4
Sociodemographic characteristics of patients (PAx) and healthcare professionals (PRx) included in the study.

Patient	Age at interview (years old)	Sex	Age at transition (years old)
PA1	20	M	18
PA2	21	M	20
PA3	22	F	18
PA4	20	M	18
PA5	28	F	18
PA6	18	F	17.5
PA7	23	F	18
PA8	25	F	20
PA9	21	M	18
PA10	23	M	18
PA11	28	M	18
PA12	22	F	17
HCP	Occupation	Sex	Role in the DREPADO clinical trial
PR1	Physician (hematologist - adult)	F	Co-investigator
PR2	Physician (hematologist - children)	F	Principal investigator
PR3	Nurse	F	Patient visits coordination & organization
PR4	Study coordinator	F	Study coordinator
PR5	Physician (internal medicine - adult)	M	Co-investigator
PR6	Nurse / Clinical Research Associate	F	Trainer for educative and social sessions
PR7	Pharmacist	F	Co-project leader
PR8	Pharmacist	F	Project leader
PR9	Clinical Research Associate	F	Clinical Research Associate
PR10	Physician (Public Health)	F	Methodological support
PR11	Physician (internal medicine - adult)	F	Co-investigator
PR12	Physician (hematologist - children)	F	Co-investigator

Sociodemographic data of participants were detailed in Table 4.

Perceptions

Four common themes were derived from the interview data: (1) Management of the transfer to adult care before the DREPADO transition program, (2) DREPADO transition program, (3) Research protocol framework, and (4) Improvement pathways. The perceptions of patients and HCPs could differ. These themes are presented below with additional quotes for illustration. Authors of the selected *verbatim* transcriptions were identified as follow: PA(identification number) for patients and PR(identification number) for HCPs.

Management of the transfer to adult care before the DREPADO transition program.

If the transfer to adult care was experienced positively by 3 patients, 3 other patients reported a difficult period.

"I wanted to go back to pediatrics" [(PA8)]

The lack of anticipation was reported by 4 patients as the main difficulty, shared by patients who experienced this transfer both positively and negatively.

"I was not aware" [(PA4)]

The difficulty of this transfer was underlined by 4 HCPs. Three HCPs brought up the fact that DREPADO *"fills a void"* (PR2). Five adolescents had the feeling they were left to fend off for themselves in adult care:

"Lower level of care management" [(PA1)]

DREPADO transition program.

The transition program was reported as being positive by 8 patients and by all HCPs. 1 *"chance"* (PA8), while 2 patients did not find the program useful and 2 others had a neutral opinion. For 3 HCPs, it was deemed *"ambitious"* (PR1) and will help reinforce the organization of the transfer to adult care under different aspects: *"improve support"* (PR5) of adolescents (7 HCPs), develop therapeutic education interventions (2 HCPs), prepare patients to the transfer (4 patients) by:

"Giving them confidence" (PA7), *"preparing them for the change"* (PA7), *"sharing experiences"* [(PA11)]

The consultation dedicated to the transfer is an opportunity to *"present the new settings"* (PA12), which was very much appreciated by 3 patients:

"It helps" [(PA12)]

One of the main fears expressed by 1 patient and 5 HCPs about the transition program concerns the time and implication required from patients: *"requires availability, engagement"* (PR11). This apprehension is not shared by all HCPs, 3 of them underlined the *"flexibility"* (PR9) of the program, with *"freedom given"* (PR9) to adolescents.

The social axis of the transition program was seen positively (5 patients):

"Before I didn't even know there were other SCD patients like me" [(PA11)]

On the other hand, one patient felt *"embarrassed"* (PA6) to share in front of a group.

Home setting.

Patients (7) and HCPs (6) mostly perceived the home setting for educational sessions as a strong implementation facilitator. Three patients and 3 HCPs explained why.

"Happy that a professional comes to my home" [(PA11)]

"In their home environment ...they tend to share more" (PR5) It could help *'develop the city-hospital partnership'* (PR11) [(2 HCPs)]

Three patients also found it more practical; this was brought up by 3 HCPs as a facilitator to program adherence.

"They do not always come to the consultations...I think this will help" [(PR2)]

The home setting also has its limits. The intrusive nature was mentioned by 3 HCPs and the practical difficulties by 6 HCPs: additional time, getting back and forth from the hospital, changes in work habits and finally the patient's life environment, which needs to be compatible with the visit of HCPs.

"You pry into their intimate lives" (PR6), *"it takes more time"*, (PR10), *"if the patient lives far away"*, (PR11). *"they need to have the time and possibility"* [(PR6)]

Research protocol framework.
Research protocol aspects were only discussed with HCPs.

Difficulties

Integrating the transition program into a research protocol was perceived as a barrier for 6 HCPs, and other difficulties mentioned:

"Involves evaluations, data collection" (PR10); *"multiple persons involved"* (PR6) *"availability of the neuropsychologist"* [(PR9)]

Enrollment

Difficulties with enrollment were the *"consent form"* (PR12), language barrier for 2 HCPs *"ask for an interpreter"* (PR3) and the enrollment of the patient's parents for 2 HCPs: *"a child came with his older brother so we could not include him"* (PR12). To overcome these difficulties and facilitate enrollment, 2 HCPs insisted on the importance of taking the time to explain the situation in order to provide a better understanding of the intervention to the participant: *"the patient must be reassured"* (PR9). A *"close screening"* and *"systematic call to the patient before each inclusion"* (PR2) are done to ensure that: 1/eligible patients are considered, 2/they understand the RCT and 3/at least one of their parents attends the inclusion visit.

Four HCPs feared that patient included in the transition program would not come regularly and miss appointments, because of their health condition and age category.

"One of the barriers will be to honor their appointment" [(PR5)]

To improve this regularity, 3 HCPs insisted on the need to anticipate enrollment: *"inform ... come to an agreement"* (PR9). Change in the organization of the sessions was also proposed by one HCP to promote patients' regularity: *"less risk to lose them over time"* (PR6)

Human resources

The multidisciplinary team was seen as a good implementation strategy (1 HCP), but there were concerns about coordination difficulties.

"The difficulty is getting people to agree with one another" [(PR9)]

Three HCPs reported the importance of having one person available to coordinate the transition program on one hand, and the different HCPs involved in each center on the other hand: *"we need someone to coordinate everything"* (PR6). Barriers identified were lack of time (4 HCPs) and variable levels of involvement (1 HCP):

"We do not have more time" (PR11); *"there are people who are motivated on a whole other level"* [(PR8)]

Improvement pathways

Improvement pathways were suggested (3 HCPs) in order to set the settings adapted to the intervention: involving physicians in the therapeutic education sessions, involving medical secretaries and clarifying the repartition of tasks. Two HCPs insisted on a fair repartition of the different tasks.

"We must act and write these things" (PR8); *"important so that persons involved are not overwhelmed"* [(PR7)]

The patients and HCPs interviewed proposed improvement pathways to facilitate the implementation of the protocol: anticipating the issue of data sharing between pediatric and adult care (1 HCP), eliminating paper Case Report Forms (CRFs) to save time and reduce the risk of errors (2 HCPs), introducing *"sport education"* (PA10), and finally starting the program earlier in the adolescence period (1 patient):

"It [educational sessions] should be implemented before the age of 16" [(PA12)]

Discussion

This work introduces an original approach for exploring the implementation of complex public health interventions such as DREPADO transition program. The positive perception of the program constitutes a major facilitator for its implementation. The home setting is an aspect that could particularly encourage patient participation. Changes in professional habits, time and involvement needed from the patient along with integrating this program into a research protocol were the main barriers identified (Fig. 2). To address these challenges, different solutions were unveiled from the interviews: adjustments to the transition program (such as starting at an earlier age), anticipation and optimization of the enrollment, changing the repartition of tasks.

The transfer to adult care was reported as difficult by patients interviewed, which is similar to elements found in the existing literature on SCD (Hoegy, Guilloux, et al., 2020; Treadwell et al., 2011). Patients and HCPs concur on the difficulty of a sustained treatment adherence during adolescence, which was also described for SCD by other authors, since it is a time of psychological and behavioral changes, different care management habits (Crosby et al., 2009).

The main difficulty brought up by patients was the lack of anticipation: preparation to the transfer is essential to optimize the experience of these changes, and has an impact on treatment adherence in adult care. In fact, in many chronic health conditions, preparing for this transfer improves the health status of patients and their experience of this critical period (Viner, 1999). This validates the need for this DREPADO transition program, which is positively perceived among patients and HCPs interviewed. This is a major facilitator to the DREPADO transition program & also RCT implementation, because patients and HCPs who perceive a program's relevance become more involved and have a higher participation rate (Agustine & Pujiyanto, 2019).

The transition program offers patients a certain flexibility, particularly for the psychological axis: Middleton et al. (Middleton et al., 2013) explain that it can facilitate the appropriation and improve adherence. The program must adapt to the needs of each patient, which vary greatly from one patient to the next during the transition period: this is an important aspect to improve implementation (Calhoun et al., 2019).

Patients' adherence to sessions will be assessed during the DREPADO RCT evaluation: if it is lower than expected, adjustments to the program will be discussed to facilitate its implementation. One important facilitator underlined is the home setting for interventions, which was positively perceived by both patients and HCPs: validating its relevance. Actually, the home setting places patients at the heart of their life environment, making them more comfortable and open, as underlined in the literature on other chronic conditions (Middleton et al., 2013). A study in young patients with asthma also revealed that home interventions allowed parents to be more involved in their child care management (Dolinar et al., 2000). Furthermore, this setting can help reduce inequalities in access to healthcare, living far away from the

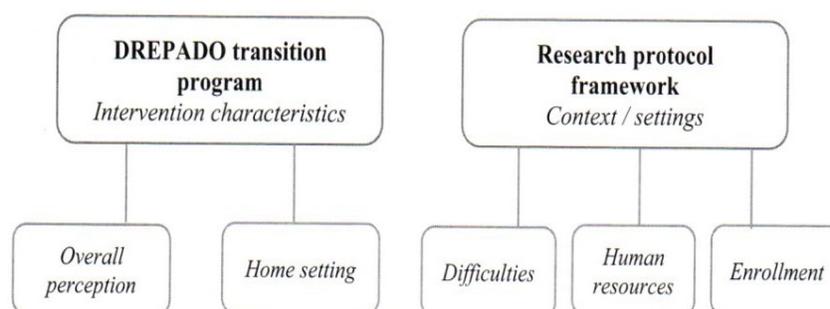


Fig. 2. Categories and subcategories results.

monitoring center being associated to lower treatment adherence (Andemariam et al., 2014). This home setting for interventions was often discussed during preliminary discussions with other centers participating in the DREPADO RCT, as it is an uncommon practice for hospital-based HCPs and because some centers manage patients living far away. It requires both efforts and adjustments from HCPs, but remains a key factor for the program implementation.

Another difficulty perceived by most interviewed HCPs is having the transition program integrated within a research protocol, because it implies evaluations and regulatory constraints (e.g. consent, agreements) (Siderowf, 2004). Implementing this transition program outside of a research protocol would probably allow more patients to benefit from the program and optimize resources (less time required to perform study procedures i.e. randomization, questionnaires), however this method allows us to assess its benefit (Ammerman et al., 2014; Gispén-de Wied et al., 2012).

The multidisciplinary nature of the RCT can yield coordination and communication difficulties: it is a difficulty seen in many public health programs because it requires different HCPs working together regularly when they usually do not get to interact on a daily basis (Buljac-Samardzic et al., 2020).

To facilitate enrollment, HCPs interviewed suggested anticipating the program and insisted on positive aspects of the program such as home-based or group-based sessions. The proposal is to produce an informative brochure dedicated to investigators and CRAs to help explain the protocol to patients and caregivers as well as the enrollment process (Kaminsky et al., 2003).

Enrolling the adolescent's parent is also an aspect requiring anticipation. In fact, from the age of 16–17 parents can no longer be present during medical consultations. It would be interesting to warn them of this aspect before the consultation. Finally, the language barrier was brought up by HCPs in our study and is commonly described in the literature on SCD (Guitton & Perrin, 2013); it can be avoided by having an interpreter. To avoid these difficulties, it is recommended to conduct a close screening and call the patient before enrollment to assess potential language barriers or other practical difficulties.

Practice, policy and research implications

At the time of this implementation study, the DREPADO trial had only started in one center. Therefore, these results will facilitate the implementation in the coordinating center and other centers involved in the DREPADO transition program and also RCT (Damschroder et al., 2017). For instance, the home setting is a major facilitator expressed by patients and that needs to be implemented, in spite of disrupting the working habits of hospital-based HCPs, especially for patients living far from the hospital. Involving community based HCPs to conduct these therapeutic education sessions in a home setting could be another option.

This study could be reproduced in the framework of other complex Public Health interventions or RCTs. We identified implementation factors and strategies that could be used within different settings, and

for interventions with similar characteristics. The complexity of such interventions and clinical trials must be considered beforehand but also during the implementation in order to adapt to the reality of a given field or condition.

Strengths and limitations

To our knowledge this work is the first evaluating the implementation of a complex public health intervention such as the DREPADO transition program. According to the nature of barriers and facilitators explored and the early-stage of this RCT, the collection of quantitative data was not adapted to our objective; this is why we selected the qualitative approach. The qualitative evaluation, with semi-structured interview technique offers freedom to broaden the discussion to other topics spontaneously brought up by patients and HCPs interviewed.

As in all qualitative studies, interviews include a subjective aspect that can distort reality. However, the interviewer did not know any of the patients interviewed and was not part of their healthcare team. HCPs interviewed were all involved in the study design, set-up and/or conduct: this selection was made in order to get feedback on the DREPADO implementation from actors who are directly impacted, however this could affect their perception of the program since they are involved. Another limit was the fact that the analysis was done manually since the available software was only a manual analysis aid (Tong et al., 2007).

Interviews with patients were focused on aspects related to the transition program itself, and did not integrate the research protocol aspects, in order to avoid confusion between implementation of the transition program (i.e. educational, psychological and social sessions) and the clinical research aspects (i.e. protocol, procedures, questionnaires).

Conclusions

To conclude, this study allowed the exploration of barriers and facilitators to the implementation of the DREPADO transition program from the perceptions of patients and HCPs. Main facilitators identified were the home setting for educational sessions and the anticipation of the enrollment. Main barriers were the changes in habits of hospital HCP practices, time required from the patient, and the integration of the DREPADO transition program into a research protocol. These barriers and facilitators could bring solutions to promote the implementation of the DREPADO RCT as well as other Public Health interventions or RCTs.

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CRediT authorship contribution statement

Pierre Bourron: Conceptualization, Methodology, Formal analysis, Writing – original draft. **Giovanna Cannas:** Investigation, Writing – review & editing. **Audrey Janoly-Dumenil:** Methodology, Supervision, Writing – review & editing. **Claude Dussart:** Supervision, Writing – review & editing. **Alexandra Gauthier-Vasserot:** Investigation, Writing – review & editing. **Delphine Hoegy:** Conceptualization, Methodology, Formal analysis, Writing – original draft.

Declaration of Competing Interest

The authors of this manuscript declare no conflict of interests.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.pedn.2022.08.010>.

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