

# Impact of a paediatric-adult care transition programme on the health status of patients with sickle cell disease: study protocol for a randomised controlled trial (the DREPADO trial)

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## Study protocol

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## Abstract

**Background:** Thanks to the advancements in medical care, a majority of sickle cell disease patients worldwide live beyond 18 years of age, and therefore patients initially followed in paediatric departments are then transferred to adult departments. This paediatric-adult care transition is a period with an increased risk of discontinuity of care and so morbidity and mortality. During this period, the patient will have to manage new interlocutors and places of care, and personal issues related to the period of adolescence. To take into consideration all these aspects, an interesting approach is to refer to the patient as a whole system as presented in biopsychosocial approach. The aim of this trial is to evaluate the impact of the proposed biopsychosocial paediatric-adult transition programme.

**Methods:** The DREPADO study is a multicentre randomised control trial comparing a control group ( Arm A ) versus an interventional group with paediatric-adult transition programme based on a biopsychosocial approach ( Arm B ). To be included, patients should suffer of SS, SC or S $\beta$ -form of sickle cell disease and aged between 16 and 17 years. The randomisation in a 1:1 ratio assigns the Arm A or B . The primary outcome is the number of hospital admissions and emergency in the index hospital for complications, in the 2-years after the first consultation in the adult department of care. Secondary outcomes consider the quality of life, but also included coping skills such as self-efficacy feeling and disease knowledge. To provide patient and parent knowledge and coping skills, the transition program is composed of 3 axis : educational, psychological and social, conducted in individual and group.

**Discussion:** By providing self-care knowledge and coping skills related to SCD and therapeutics, helping patient's empowerment related to pain management and emotions and facilitating the relationship to oneself, others and care in the Arm B of DREPADO study, we believe that the morbidity and mortality of patients with SCD may be reduced after the proposed paediatric-adult transition programme. Trial registration: ClinicalTrials.gov, ID: NCT03786549; registered on 17 th December 2018; <https://clinicaltrials.gov/>.

## Contributions To The Literature

- Regarding literature in chronic diseases, sickle cell disease is poorly represented and in particular on the management of care.
- Because it is a risky period of discontinuity of care and so morbidity and mortality, improving the paediatric-adult transition is essential. Based on scientific evidences, the proposed paediatric-adult transition programme used biopsychosocial approach to take into consideration patient and family as whole system.
- With the methodology of randomized controlled trial, this protocol contributes to the construction of evidence about the paediatric-adult transition of sickle cell disease patient.

## Background

Sickle cell disease (SCD) is a chronic, genetic disease, widespread both around the world and in France. After diagnosis, SCD requires a medical follow-up which is essential to prevent complications. The most frequent complications are vaso-occlusive crisis (VOC; which are painful), acute chest syndrome (ACS), and stroke. Thanks to the advancements in medical care, a majority of SCD patients worldwide live beyond 18 years of age [1], and therefore patients initially followed in paediatric departments are then transferred to adult departments.

For patients with chronic disease such as SCD, this paediatric-adult care transition is a period with an increased risk of discontinuity of care [2,3]. During this period, adherence to medication is sub-optimal [1,4] and the rate of missed clinical appointments is high [5]. Furthermore, the highest morbidity and mortality is observed between 17 and 18 years of age [6], and young adults frequently use acute care (emergencies and hospitalisations) after paediatric-adult transition [7].

During the paediatric-adult transition, the patient will have to manage new interlocutors and places of care, as well as a different organisation of this. An important aspect to improve the health status of patients is therefore to involve both paediatric and adult departments of care in the transition [3]. In addition, the patient will have to manage personal issues related to the period of adolescence [8]: a period of psychological upheavals and adaptations of family roles [9]. To assess the needs of SCD patients during this transition period, a qualitative study was conducted in Lyon (France). Parents, as well as adolescent and adult patients with SCD were individually interviewed about it. Results revealed individual and also family needs that concerned knowledge of the disease, coping skills, therapeutics, and psychosocial aspects [10].

To take into consideration all these aspects, an interesting approach is to refer to the patient as a whole system as presented in biopsychosocial or social-ecological model [11]. Based on this approach, the Social-Ecological Model of Adolescent and Young Adult Readiness to Transition (SMART) propose a conceptual framework that describes factors influencing paediatric-adult transition in SCD [12]. This includes bioclinical factors such as complications, psychological factors such as pain perception, and social factors such as scholar absenteeism [12]. Some of these factors may be modified and therefore these could become part of the patient's coping skills [11,12]. For instance, a coping skill for managing complications may be knowing when to go to the hospital based on its own pain threshold. For this a pluridisciplinary team is required [12].

Currently only pilot studies of transition programmes based on biopsychosocial approaches have been performed [13-16], with encouraging primary results [13].

The DREPADO open-label individual multicentre randomised controlled trial (RCT) proposes to assess a paediatric-adult transition program for SCD patients based on a biopsychosocial approach and SMART compared to standard care management. As compared to available studies that have investigated the paediatric-adult care transition [13], the originality of this study is the biopsychosocial approach coupled to its randomised controlled design. The purpose of the paper is to present the study DREPADO protocol.

## Methods/design

### *The aim, design, and setting of the study*

The DREPADO RCT seeks to assess the impact of a paediatric-adult transition programme. This trial is an interventional study. It is an open-label individual multicentre RCT comparing a control group (*Arm A*) versus an interventional group with paediatric-adult transition SCD programme based on the biopsychosocial approach (*Arm B*).

The DREPADO trial is a French national RCT including centres specialised in SCD patient care, involved in the SCD health network (*Maladie Chronique du Globule Rouge et des autres maladies de l'érythropoïèse Filière - MCGRE*) accredited by the French ministry of health and motivated to participate in this study. The coordinating centre is the Lyon University Hospital, and 5 other centres will participate (Créteil, APHP Kremlin-Bicêtre, Martinique, APHP Necker, Pontoise).

The follow-up period is a maximum of 4 years for each patient. Outcomes is assessed at baseline (T-inclusion), at transfer date – which corresponds to the first consultation in the adult department of care (T-transfer), 12 months after transfer (T-12), and 24 months after transfer (T-24).

### *Study subjects*

The study focuses on adolescent patients suffering from SCD and their caregivers. The dyad patient-caregiver is included. The inclusion period is expected to be 2 years.

### *Inclusion criteria*

Patients are included if they fulfil the following conditions: suffering of SS, SC or S $\beta$ -form of SCD; aged between 16 and 17 years; orally agreeing to participate. The caregiver is included if they fulfil the following conditions: parent or legal guardian of the patient; aged more than 18 years; having provided a signed written consent for him/herself and for the patient.

### *Non-Inclusion criteria*

Patients and caregivers with any of the following conditions is excluded: presence of any known and major cognitive or psychiatric disorder which could, according to the judgement of the investigator, hamper intervention or evaluation, and/or familial history of such disorder; patients considered healed after stem cell transplantation. No concomitant care, interventions, or enrolment to other trials are prohibited by participation in the DREPADO trial.

### *Withdrawal and discontinuation*

Participants can withdraw voluntarily at any time during the trial. Participants who are not present at intervention and/or evaluation are contacted by telephone; after four unsuccessful calls, participants are considered dropouts.

### ***Sample size and recruitment***

A total of 196 (98 in each group) is required to detect at least a 15% reduction of the hospitalisation rate for complications following the 2-years after the transfer in the intervention group compared to the control group. This reduction assumes a hospitalisation rate of 3.5 per patient per year [7] with 80% power and the use of a two-sided test at a significance level of 5% and a 10% inflation factor to anticipate study deviations (missing data, withdrawal, loss to follow-up).

Participants are recruited in the hospital when they come for a medical consultation or at the end of a hospitalisation for complications. Potential participants are screened. The investigator informs the patient and caregiver about the study, following which the patient gives oral consent and the patient's caregiver the written informed consent for patient participation. The information note and consent form is presented in Appendix 1. When the patient will become legally an adult (*i.e.* at 18 years of age in France), he will give his/her own written informed consent.

### ***Randomisation and blinding***

Participants are randomly assigned to one of the 2 groups at a 1:1 ratio using a minimisation algorithm. The minimisation factors are the centre, the type of SCD, and the occurrence of VOC during the year before the inclusion. Allocation is done using a central randomisation system (Ennov Clinical, version 7.5.710.4, San Francisco, California, USA). At each centre, a clinical research associate delegated by the investigator and who is trained in Good Clinical Practice logs into the central randomisation system and inputs patient information; a random number and group assignment are then immediately given by the system. Because DREPADO is an open-label trial, the clinical research associate directly informs the patient-caregiver dyad of the arm to which they are assigned (*Arm A or B*).

### ***Study scheme***

The SPIRIT flow diagram is presented in Figure 1 and the detailed study scheme in Figure 2.

### *Arm A – control group*

Patients and caregivers randomised to the control group receives the standard care management used in the study centre, including a joint consultation with a paediatrician and an internist / haematologist between the age of 16 and 18 years, and a visit to the adult department of care.

### *Arm B – intervention group*

In addition to standard management, patients and caregivers randomised to the intervention group benefits from the SCD paediatric-adult transition programme. Based on the biopsychosocial approach, this consists of three structured axis the objectives of which and practical details are summarised in Table 1.

The modifiable factors are worked as coping skills during the educative, the psychological, and the social axis. The objective of the educative axis is to provide knowledge and coping skills related to self-care management. It is conducted at home with the patient and his/her parent by a healthcare professional trained in the patient education. The objective of the psychological axis is to help patient empowerment related to pain management and emotions. It is conducted at hospital with only the patient by a healthcare professional trained in therapeutic hypnosis. The objective of the social axis is to facilitate the relationship to oneself, others, and care. It is conducted in a “neutral place” (not at home and not at the hospital) with a group of patients by a healthcare professional trained in patient education and an expert adult patient also trained in patient education.

### ***Outcome measurements***

*The primary outcome* is number of hospital admissions and emergency in the index hospital for complications (*i.e.* VOC, ACS, and/or stroke) in the 2-years after T-transfer.

To evaluate the biopsychosocial approach, *the secondary outcomes* include bioclinical, psychological and social factors, measured at T-inclusion, T-transfer, T-12 and/or T-24, collected from patients and/or parents. With regard to the indirect bioclinical factors, the use of care is evaluated by the incidence of emergency visits and medical consultations at T-24. Medication adherence is also measured at T-inclusion, T-transfer date, T-12, and T-24 by adapted *Medication Intake Survey-Asthma* (MIS-A) [17] adapted for SCD and *Medication Adherence Report Scale* (MARS) [18]. Psychological factors, such as pain perception, and social factors, such as school absenteeism is measured by self-declaration. Quality of life is evaluated using the brief *World Health Organisation Quality of Life questionnaire* (WHOQOL-Brief), and skills are measured by questionnaires, such as the health literacy using the *European health literacy questionnaire* (HLS-EU-Q16) [19], self-efficacy feeling using the *Self efficacy specific instrument – sickle cell disease* (SCD-SES) [20]; these are measured at the T-inclusion, T-transfer, T-12, and T-24. All the data sources are presented in Table 2.

At the end of the study, the lived experience of a sample of patients, parents, and contributors regarding the intervention programme from is evaluated. The cost-effectiveness and the implementation of the transition programme are also secondary outcomes.

### ***Data collection & management***

The data collection plan is presented in Table 2.

The study data will be collected on a secure electronic case report form (eCRF) (Ennov Clinical, version 7.5.710.4, San Francisco, California, USA), that will be available at each centre through an Internet portal. In each centre, e-CRF users have their own personal login. A clinical research associate, delegated by the centre investigator and who is trained in Good Clinical Practice, enters data into the e-CRF.

No personal identifying information will be mentioned on the eCRF. Each subject included the study will be assigned a unique identification number that will consist of the identification number of the investigational centre, the initials of the patient, and the chronological inclusion number of the patient.

Multiple external validation checks will be applied: examination of the source documents and crosschecking with the data recorded in the eCRF as to its accuracy, the presence of missing data, and the consistency of data. The eCRF will only include the data necessary for the analysis to be reported in a scientific publication.

All study data will be stored securely in the university hospital of Lyon. All electronic data will be secured on a password-protected laptop. Paper-based study documents will be stored in a secure filing cabinet at each centre. All electronic documents containing names or personal identifying information, necessary for the follow-up of the study, will be stored separately from other study data and protected by a code number. Access to these files will be limited to research staff involved in the study.

The trial statisticians will have access to the data set for the final analysis of trial outcomes. They will receive checked and validated data from the e-CRF with no personal identifying information.

### ***Monitoring and participant safety***

The Trial Steering Committee (TSC) will be responsible for overseeing the progress of the trial and will meet at regular intervals. The TSC includes the principal investigator, the investigators of the centres, and the trial coordinators/project managers. The TSC has developed the study protocol and is responsible for data collection, management, publications, and the final data set. The committee is responsible for finding solutions to unforeseen questions/problems that may arise in the course of the study.

One monitoring will be conducted by year in each centre by the clinical research department of the Lyon University Hospital. To ensure conformity to Good Clinical Practice, the medical records, informed consent forms, and the e-CRF will be checked.

No interim analysis or harms are expected, and therefore no premature stop of the trial is anticipated and no auditing by an independent committee is needed. According to French law, the study does not require a formal data monitoring committee as it is a trial with known minimal risks.

### ***Statistical analysis plan***

Demographics and other characteristics are reported descriptively and according to treatment group. Means and standard deviation (SD), or medians and ranges when appropriate are calculated for continuous variables. Categorical variables will be presented using numbers and percentages.

The crude rate of hospitalisations due to complications will be calculated by dividing the total number of hospitalisations due to VOC, ACS, and stroke occurring after transfer by the total duration of follow-up of all patients in each group. The treatment effect will be assessed using a multivariable Poisson regression model with the study group as factor adjusting

for minimisation factors and relevant patient characteristics and the length of follow-up as the offset. Results will be expressed as rate ratio with 95% confidence interval. A negative binomial model will be fitted if data will be over-dispersed. The same analyses will be performed for the association between intervention and other secondary counts outcomes.

Analysis of covariance (ANCOVA) will be used to evaluate the intervention effect at T-24 on all the secondary outcomes evaluated by questionnaires. Scores will be computed and depicted at each assessment by following the scoring procedures for each questionnaire. Each ANCOVA will include the baseline measure (T-inclusion) and minimisation factors as covariates. Changes over time for each score will be also assessed using Generalized Estimation Equation analyses to test the effect of group, time, and the interaction group time after controlling for minimisation factors and relevant patient characteristics.

### ***Dissemination & data sharing statement***

Important protocol modifications will be communicated to the relevant parties by sending the updated protocol to investigators.

There are no current plans for granting public access to the full protocol, participant-level data set or statistical code. However, if researchers wish to access the data set (e.g. for conduct of secondary analysis or meta-analysis) the project management committee will facilitate this.

The principal investigator will have access to the data and will take full responsibility for the analysis and publication of the results. Once the main analysis have been undertaken, data will be available upon reasonable request.

Results will be communicated through scientific publications, and one press release made in conjunction with a patient association (SOSglobi). Following this, an oral presentation will give to the SCD health network (*Filière MCGRE*) accredited by the French ministry of health.

## **Discussion**

Owing to the risk of discontinuity of care in chronic disease patients, it is essential to improve the paediatric-adult care transition. The DREPADO project is the first RCT designed to assess the impact of a paediatric-adult transition programme. The latter is based on the available literature [3] and on a recent previous qualitative study [10]. In accordance, it involves both paediatric and adult departments of care by starting the intervention in a paediatric department and continuing it in adult department of care. In addition, the qualitative study found that the needs of parents and patients were biopsychosocial, both individual and familial [10]. Added to that, the modifiable factors of the SMART [11,12] were included in the 3 axis of the programme, to become patients' coping skills. Furthermore, because the previous qualitative study [10] found the need for an integrated caregiver programme, the educative axis involves both the patient and their parent. This axis is conducted at home as this is patient's environment contrary to the hospital which is the environnement of care [21].

The primary outcome is bioclinical, which is more objective than complications measured in terms of pain. Secondary outcomes consider aspects related to the patient as a whole system, such as the quality of life, but also included coping skills such as self-efficacy feeling, health literacy, and disease knowledge. In addition, as the transition of care is stressful and generally experienced thoughtfully for both patients and their parents, lived experiences of the proposed care transition programme are also evaluated.

The major strength of the DREPADO trial is the proposed intervention with a biopsychosocial approach of the patient as a whole system, which aims to reflect as much as possible the real needs of patients and their family. In addition, the needs are assessed at the beginning of the psychological and educative axis, in order to individualise the intervention. Another

strength of the intervention is the participation of expert patients in the social axis; his/her experiential knowledge promote sharing between the adolescents in the group and provide real-life examples of coping skills and advices [22]. The major limitation of DREPADO trial is the difficulty to implement the transition programme because the intervention is complex [23]; it involves different departments of care, different places of intervention (home, hospital, “neutral place”), and different types of expertise (or the training of personnel in several different fields). This complexity requires good communication and coordination between interlocutors; to aid in this regard, the DREPADO study group provides to each centre tools for communication and training. Another potential limitation is patient adherence to the programme, and the strategies to improve this are also based on communication, using, for example, paper schedules and reminder text messages.

The DREPADO RCT has multiple perspectives. First of all, regarding patients and their parents, this trial should show a better health status, quality of life, and a better experience of this difficult period of care. For healthcare professionals, it is expected to provide a model of paediatric-adult care transition for SCD. Furthermore, the methodological quality renders possible the evaluation of the efficacy and efficiency of the proposed programme. If conclusive, it will be possible to adapt it and test it in other chronic diseases presenting the same care transition problem [2]. For public health, the DREPADO trial results will be multiple. By focusing on this population of sub-Saharan origin with low visibility and high social vulnerability [24], this study will reduce the social inequalities in healthcare system experienced by patients with SCD and their families. Also, by improving the health, quality of life, and care of patients with SCD, the indirect cost of complications will decrease.

The DREPADO study is the first RCT designed to assess the impact of a paediatric-adult transition programme based on a biopsychosocial approach. By providing self-care knowledge and coping skills related to SCD and therapeutics, helping patient's empowerment related to pain management and emotions, and facilitating the relationship to oneself, others, and care, we believe that the morbidity of patients with SCD may be reduced after the proposed transition programme.

## Abbreviations

ACS: Acute Chest Syndrome

PREPS: Projet de Recherche sur la performance du système de soins

RCT: Randomised Controlled Trial

SCD: Sickle cell disease

SMART: Social-Ecological Model of Adolescent and Young Adult Readiness to Transition

SPIRIT: Standard Protocol Items: Recommendation for Interventional Trials

VOC: Vaso-Occlusive Crisis

## Declarations

*Ethics approval and consent to participate*

This study will be conducted in accordance with the declaration of Helsinki. According to french law, the study protocol has been reviewed and the French ethics committee (*south west and overseas III Protection to Person Comitee*) approved the study for all center on September 26<sup>th</sup>, 2018. This RCT has been registered at [clinicaltrials.gov](https://clinicaltrials.gov) (number NCT03786549 on the 17<sup>th</sup> December 2018).

Any substantial change is subject to a written amendment submitted to the promoter, who must obtain a favorable opinion from this Protection to Person Committee before implementation. All amendments to the protocol must be made known to all investigators involved in the research.

According to French laws, all patient and caregiver will be verbally informed about the study and will receive information form. For the inclusion, the patient (*i.e.* before 18 years of age in France) will give oral consent and the patient's caregiver the written informed consent for patient participation. When the patient will become legally an adult (*i.e.* at 18 years of age in France), he will give his/her own written informed consent.

#### *Consent for publication*

Not applicable.

#### *Availability of data and materials*

The datasets used and/or analysed during the current study available from the corresponding author on reasonable request.

#### *Competing interests*

The authors declare that they have no competing interests.

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#### *Authors' contributions*

DH: writing the protocol, submitting the protocol to the national tender, enrolling the hospital centers & participating in its coordination. PO, ST: writing the methodology of the protocol, planning study. AD: performing the statistical analysis. ST: supervising the health economics study. AJD, NB, GC, AGV: cowriting and correcting the protocol, assessing the potential clinical impact of each error detected. CD, YB, AH: co-writing the protocol. All authors read and approved the final manuscript.

The DREPADO study group (*contactable to etude.drepado@chu-lyon.fr*) is composed of those authors and SPB: participating in its coordination; FN, KK and RG: correcting the protocol; DC: assessing the potential clinical impact of each error detected.

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The DREPADO study group collaborators:

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2. Pondarre, paediatrician at the Centre Hospitalier Inter Communal de Creteil
3. Galactéros, internist at the AP-HP Henri Mondor and medical coordinator of the *Maladie Chronique du Globule Rouge et des autres maladies de l'érythropoïèse (MCGRE) Filière*
4. Fois, internist at the AP-HP Henri Mondor
5. De Montalembert, paediatrician at the AP-HP Necker and president of the ROFSED

J.B. Arlet, internist at the AP-HP HGPE

1. Elana, paediatrician at the University Hospital of Martinique
2. Michaux, paediatrician at the University Hospital of Martinique
3. Guitton, paediatrician at the AP-HP Kremlin-Bicêtre
4. Chantalat, internist at the AP-HP Kremlin-Bicêtre
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DH: project manager, participating pharmacist, member of the P2S research unit, and member of the study group. AGV: paediatric co-investigator in Lyon center, and member of the study group. GC: adult co-investigator in Lyon center and member of the study group. AD: biostatistician and member of the study group. AH: adult co-investigator in Lyon center and member of the study group, chief of Lyon MCGRE center. YB: principal investigator, director of haematology pediatric department in Lyon and member of the study group. ST: scientific responsible and member of the study group. NB, PO: members of the study group. CD: director of the P2S research unit and member of the study group. AJD: 2e project manager, member of the P2S research unit and member of the study group.

#### **Standard of reporting**

The Standard Protocol Items: Recommendations for Interventional Trials (SPIRIT) checklist 2013 have been followed. It is provided in Appendix 2.

#### **Trial status**

The RCT DREPADO is a currently recruiting trial. The first enrolment was realised on 16 January 2019, and this article was submitted on 24 September 2019. To date, 8 participants have been recruited.

The recruitment will be completed at the approximate date of 1<sup>st</sup> April 2022.

ClinicalTrials.gov, ID: NCT03786549

This is the 1<sup>st</sup> version of the protocol, approved by a French ethics committee on September 26<sup>th</sup>, 2018.

When the last subject will undergo his final evaluation (T-24), the trial will be completed.

## References

1. de Montalembert M, Guitton C; French Reference Centre for Sickle Cell Disease. Transition from paediatric to adult care for patients with sickle cell disease. *Br J Haematol.* 2014; 164: 630-635. doi: 10.1111/bjh.12700.
2. Berens JC, Jan S, Szalda D, Hanna CM. Young Adults With Chronic Illness: How Can We Improve Transitions to Adult Care? *Pediatrics.* 2017; 139. doi: 10.1542/peds.2017-0410.
3. Treadwell M, Telfair J, Gibson RW, Johnson S, Osunkwo I. Transition from pediatric to adult care in sickle cell disease: establishing evidence-based practice and directions for research. *Am J Hematol.* 2011; 86: 116–120. doi: 10.1002/ajh.21880.
4. Sabaté E, 2003. Adherence to long-term therapies: evidence for action. World Health Organization. <http://whqlibdoc.who.int/publications/2003/9241545992.pdf> Accessed June 20, 2018.
5. Crosby LE, Modi AC, Lemanek KL, Guilfoyle SM, Kalinyak KA, Mitchell MJ. Perceived barriers to clinic appointments for adolescents with sickle cell disease. *J Pediatr Hematol Oncol.* 2009; 31: 571-576. doi: 10.1097/MPH.0b013e3181acd889.
6. Quinn CT, Rogers ZR, McCavit TL, Buchanan GR. Improved survival of children and adolescents with sickle cell disease. *Blood.* 2010; 115: 3447–3452. doi: 10.1182/blood-2009-07-233700.
7. Brousseau DC, Owens PL, Mosso AL, Panepinto JA, Steiner CA. Acute care utilization and rehospitalizations for sickle cell disease. *JAMA;* 303: 1288-1294. doi: 10.1001/jama.2010.378.
8. Morsa M, Lombrail P, Boudailliez B, Godot C, Jeantils V, Gagnayre R. A qualitative study on the educational needs of young people with chronic conditions transitioning from pediatric to adult care. *Patient Prefer Adherence.* 2018 ; 12: 2649-2660 doi: 10.2147/PPA.S184991.
9. Kinney TR, Ware RE. The adolescent with sickle cell anemia. *Hematol Oncol Clin North Am.* 1996; 10: 1255-64.
10. Hoegy D, Guilloux R, Bleyzac N, Gauthier-Vasserot A, Cannas G, Bertrand Y, Hot A, Dussart C, Janoly-Dumenil A. Sickle cell disease perceptions of caregivers, adolescent and adult patients: barriers and facilitators to medical care adherence. *Journal of pain and symptom management*; submitted.
11. Crosby LE, Quinn CT, Kalinyak KA. A biopsychosocial model for the management of patients with sickle-cell disease transitioning to adult medical care. *Adv Ther.* 2015; 32: 293-305. doi: 10.1007/s12325-015-0197-1
12. Mulchan SS, Valenzuela JM, Crosby LE, Diaz Pow Sang C. Applicability of the SMART Model of Transition Readiness for Sickle-Cell Disease. *J Pediatr Psychol.* 2016; 41: 543-554. doi: 10.1093/jpepsy/jsv120.
13. Campbell F, Biggs K, Aldiss SK, et al. Transition of care for adolescents from paediatric services to adult health services. *Cochrane Database Syst Rev.* 2016; 4: CD009794. doi: 10.1002/14651858.CD009794.pub2.
14. Crosby LE, Joffe NE, Peugh J, Ware RE, Britto MT. Pilot of the Chronic Disease Self-Management Program for Adolescents and Young Adults With Sickle Cell Disease. *J Adolesc Health J Adolesc Health.* 2017 ; 60: 120-123. doi: 10.1016/j.jadohealth.2016.08.022.
15. Kaslow N, Collins HM, Rashid FL, Eckman JE. The Efficacy of a Pilot Family Psychoeducational Intervention for Pediatric Sickle Cell Disease (SCD). *Families, Systems & Health.* 2000; 18: 381-404.
16. Smith GM, Lewis VR, Whitworth E, Gold DT, Thornburg CD. Growing up with sickle cell disease: a pilot study of a transition program for adolescents with sickle cell disease. *J Pediatr Hematol Oncol.* 2011; 33: 379-382. doi: 10.1097/MPH.0b013e318211bb2e.
17. Dima Alexandra L ,Van Ganse Eric, Laforest Laurent, Texier Nathalie, de Bruin Marijn &the ASTRO-LAB Group. Measuring medication adherence in asthma: Development of a novel self-report tool. *Psychol Health.* 2017 Oct;32(10):1288-1307.
18. Misdrahi D, Verdoux H, Llorca PM, Baylé FJ. Therapeutic adherence and schizophrenia: the interest of the validation of the French translation of Medication Adherence Rating Scale (MARS). *Encephale.* 2004; 30: 409-410.

19. Rouquette A, Nadot T, Labitrie P, Van den Broucke S, Mancini J, Rigal L, Ringa V. Validity and measurement invariance across sex, age, and education level of the French short versions of the European Health Literacy Survey Questionnaire. *PLoS One*. 2018 Dec 6;13(12):e0208091. doi: 10.1371/journal.pone.0208091.
20. Edwards R, Telfair J, Cecil H, Lenoci J. Reliability and validity of a self-efficacy instrument specific to sickle cell disease. *Behav Res Ther*. 2000; 38: 951-963
21. Fugier P, « L'intervention socio-éducative au domicile. Un espace de rencontre des désirs d'intimité et d'extimité des sujets », *Vie sociale et traitements*. 2014 ;1 : 101-108.
22. Charoud M. « L'engagement des associations de patients atteints de maladies chroniques: Du « savoir patient » aux stratégies de communication ». *Politiques de communication*. 2017 ; 9, 37-62.
23. Morrison KM, Ball GDC, Ho J, Mackie P, Buchholz A, Chanoine J-P, et al. "The CANadian Pediatric Weight management Registry (CANPWR): Lessons learned from developing and initiating a national, multicentre study embedded in pediatric clinical practice". *BMC Pediatr*. 2018; 2018 ; 18 :237.doi: 10.1186/s12887-018-1208-6.
24. Lainé A, 2009. Construction d'un stigmat sanitaire : la drépanocytose entre situations locales et globales. hal-00436022. Accessed June 20, 2018.

## Tables

**Table 1.** The three axes of pediatric-adult transition program

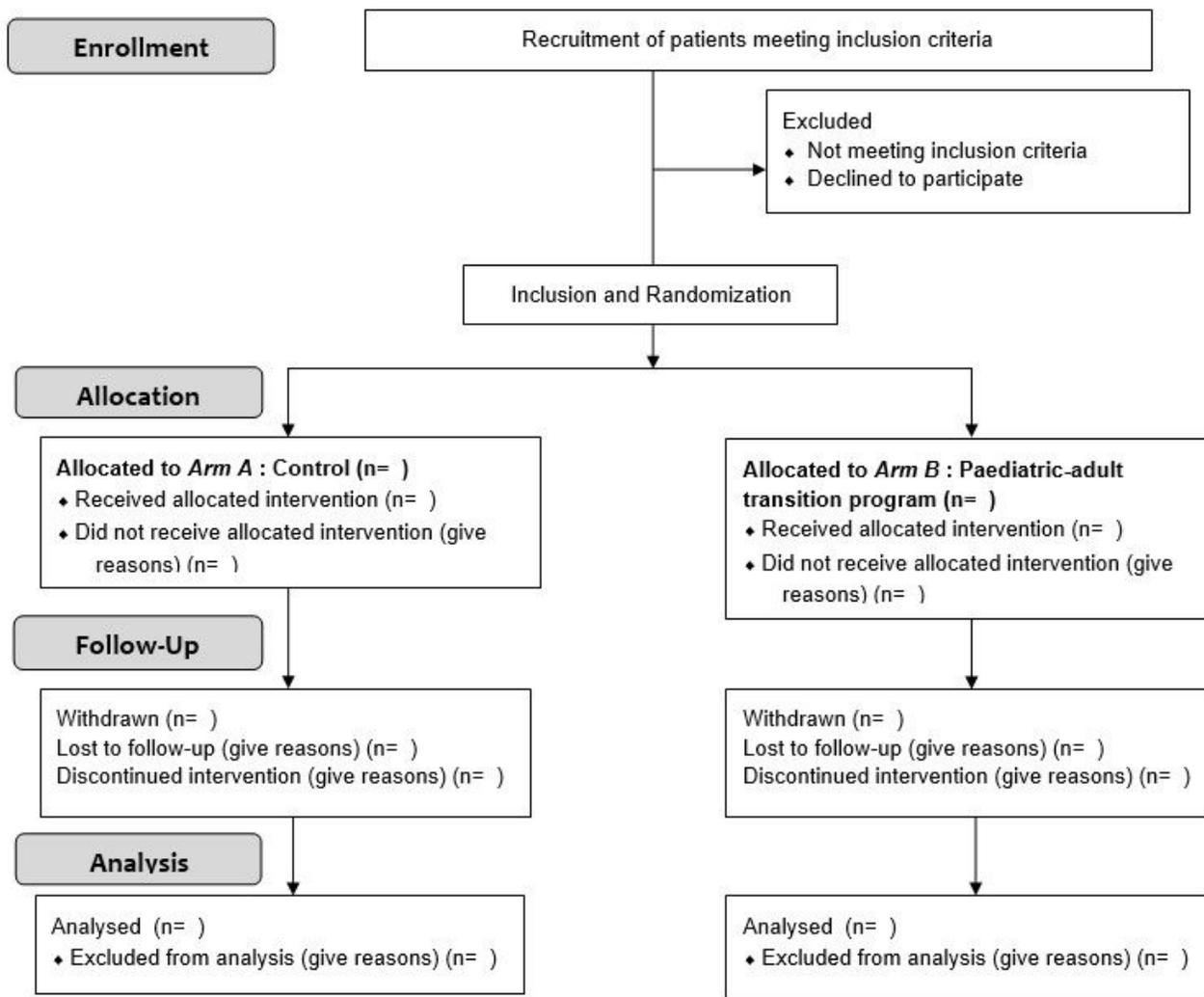
<b>Axes</b>	<b>Public</b>	<b>Objectives</b>	<b>Contents</b>	<b>Practical details</b>	<b>Providers</b>
<b>Educative</b>	Patient and caregiver dyad	Providing self-care knowledge and skills related to SCD and therapeutics	<i>Knowledge &amp; coping skills, with patient needs assessment</i>	Face-to-face At patients' home 3 sessions of 2h	One healthcare professional, trained in patient education and in SCD
<b>Psychological</b>	Patient in individual	Helping patient's empowerment related to pain management and emotions	<i>Knowledge &amp; coping skills, with patient needs assessment</i>	Face-to-face At hospital 6 sessions of 1.5h	One healthcare professional, trained in therapeutic hypnosis and in SCD
<b>Social</b>	Group of 4 to 8 patients	Facilitating the relationship with oneself, others and care	<i>Coping skills</i>	Face-to-face At "neutral place" as association patient place 2 sessions of 2h	One healthcare professional & one expert patient, both trained in patient education and in SCD

**Table 2** : Plan data collection

Outcomes		Time point				Population		Data sources
		T-inclusion	T-transfer	T-12	T-24	Patient	Parent	
Use of care	Hospitalisations for VOC, ACS, stroke		X		X	X		Medical records
	Emergency visits, medical consultations, imaging exams		X		X	X		Medical records
Medication adherence		X	X	X	X	X		2 questionnaires (MARS & adapted-MIS-A)
School absenteeism			X		X	X	X	Auto declaration
Quality of life		X	X		X	X		26 items questionnaire (WHOQOL-Brief)
Health literacy		X	X		X	X		16 items questionnaire (HLS-EU-Q16)
Disease & therapeutic knowledge		X	X		X	X	X	36 items questionnaire
Patient activation		X	X		X	X		13 items questionnaire
Self-efficacy feeling						X		9 items questionnaire (SCD-SES)
Transition preparation		X	X		X	X		20 items questionnaire (TRAQ)
Pain perceptions	At home			X	X	X		Auto declaration (book)
	Intensity during hospitalisations		X		X	X		Medical records

*Abbreviations* : ACS : acute chest syndrom; HLS-EU-Q16 : european health literacy questionnaire; MARS : Medication Adherence Report Scale; *adapted-MIS-A*: Medication Intake Survey-Asthma; SCD-SES : Self efficacy specific instrument - sickle cell disease; TRAQ : transition readiness assessment questionnaire; VOC: vaso-occlusive crisis; WHOQOL-Bref : World health Organisation Quality of Life bref-questionnaire.

## Figures



**Figure 1**

The SPIRIT flow diagram

Fig. 2 : Detailed study scheme of DREPADO trial

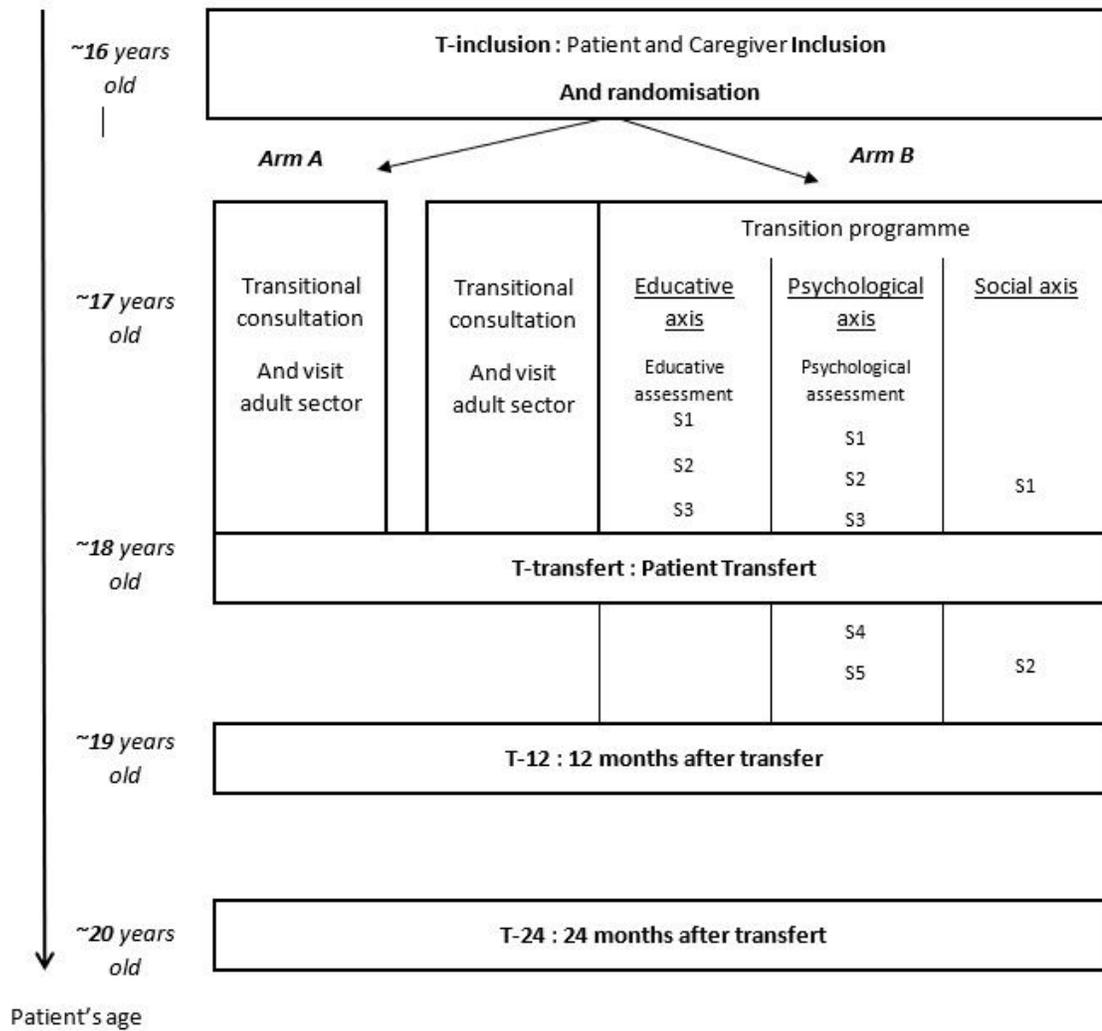


Figure 2

Detailed study scheme of DREPADO trial

## Supplementary Files

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